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FOREWORD

The School of Pharmacy and Pharmaceutical Sciences, Cardiff University, is the only school of pharmacy in Wales and is one of the top schools of pharmacy in the UK. The School's recent accolades include being rated first for pharmacy in Great Britain in the The Guardian league table and the Complete University Guide, and in the top 100 universities for pharmacy in the world. Our students graduate well-prepared and satisfied; our graduate's pass rate in the pharmacist registration examination is in the top five every year and we are consistently ranked highly in the National Student Survey.

The School supports individual pharmacists in their initial and ongoing education and development and has been selected by the Royal Pharmaceutical Society to be one of three accredited Foundation Schools. The School is also active in research that has been independently judged to be of international standing, more than half of which is world-leading or internationally excellent and with many interdisciplinary and external collaborators. Research at the School encompasses medicinal chemistry, drug delivery and microbiology, pharmacology and physiology, and pharmacy practice and clinical pharmacy, and it impacts on healthcare and pharmaceutical sciences throughout the UK and the world. Further information on the School's research activities and degree programmes, along with contact details for academic staff can be found at http://www.cardiff.ac.uk/phrmy.

At the Cardiff School of Pharmacy and Pharmaceutical Sciences, the combination of these strengths allows us to successfully deliver research-led learning and teaching. All of our MPharm students undertake a significant, independent Masters level research project in the final year of the four year degree, and present and defend their research. The high numbers of well-qualified UK, EU and international students that we attract to our postgraduate diplomas and degrees also contribute significantly to our research output.

This is the 15th year in which we have published the abstracts of our students' research. Within this publication the student is the first named author, and collaborators and supervisors follow. An alphabetical list of authors appears in the index.

Many thanks to our colleagues for their assistance in collating this book.

Rebecca Price-Davies & Justine Jenkins
July 2015

The antibacterial effect of honey against MRSA and its potential for antibiotic synergy

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Honey is a traditional medicine that is being increasingly recognised for application in modern wound management due to its significant antimicrobial properties.[1] Honey has been shown to act synergistically with antibiotics[2] and therefore have the potential to be employed to combat drug resistance. This study aims to investigate the antimicrobial activity of Manuka and Welsh honey alone and in combination with antibiotics against methicillin-resistant *Staphylococcus aureus* (MRSA).

An agar well diffusion assay was used to screen for initial antibacterial activity of three different Manuka honeys and 13 different types of Welsh honeys against MRSA NCTC 10442. The minimum inhibitory concentration (MIC) of each honey was determined using an agar incorporation method and synergistic combinations of antibiotics and honey extracts was determined using previously developed agar incorporation and E test strips. Antibiotics consisted of: oxacillin, imipenem, ciprofloxacin, and vancomycin.

The zones of inhibition shown by Manuka honey was found to be increased when compared to Welsh honeys. The MIC value for Manuka honeys ranged from 9 to 15 %w/v while those of Welsh honeys were 25 %w/v. It was observed that the honeys tested failed to enhance the antibacterial activity of oxacillin, ciprofloxacin, and vancomycin while combinations with imipenem caused decreased susceptibility.

In conclusion, all honeys studied demonstrated activity against MRSA. The activity of Manuka honey samples was superior to that of the Welsh honeys. The antimicrobial activity of Welsh honey is thought to be primarily due to hydrogen peroxide activity as bacterial inhibition was increased on dilution.[3] While no synergism was observed between any of our honey samples and antibiotics, we did observed evidence of antagonism which suggests the need of further research to ensure safe combinations of honey and antibiotics.

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Developing methods to label proteins as intracellular therapeutics

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Delivering proteins into cells could represent an effective method to treat conditions such as Lysosomal Storage Disease.[1] Protein transport into cells is however limited by impermeability of the plasma membrane to large hydrophilic molecules such as proteins.[2] To study protein delivery using a number of approaches, there is often a need to label it so that cell uptake can be analysed using techniques such as fluorescence microscopy. This study aimed to label biotinylated-Bovine Serum Albumin (bi-BSA) and Horseradish Peroxidase (HRP) as a model protein and enzyme respectively, with a fluorophore. This was to investigate the effect of labelling on HRP enzymatic activity; and to use avidin-biotin chemistry to deliver labelled BSA into cells.

BSA was labelled with Rhodamine-b-isothiocyanate (RITC), biotinylated BSA was labelled with RITC and biotinylated HRP was labelled with the fluorophore Alexafluor647. Labelling involved complexation of protein with fluorophore followed by characterisation of the protein sample using Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis, Typhoon Image scanning and ImageJ software. Following this, protein and fluorophore concentrations were calculated and the number of fluorophores per protein molecule was determined. HRP activity assays were developed to quantify enzyme activity and the internalisation of Bi-BSA-RITC into cells was performed using fluorescence microscopy.

Analysis of the protein samples revealed dye/protein labelling ratios of 1:3, 1:2, and 1:5 for experiments involving labelling BSA with RITC, bi-BSA with RITC and bi-HRP with Alexafluor647 respectively. HRP retained 89% of its enzymatic activity after labelling. Microscopy revealed clear evidence that internalisation of Bi-BSA-RITC was observed.

BSA, Bi-BSA and Bi-HRP were successfully labelled with RITC and Alexafluor647. A less than one dye/protein labelling ratio obtained may be due to the experimental conditions employed in this study, and the observed decrease in activity of labelled Bi-HRP was likely due to interaction between fluorophore and lysine at the active site of the enzyme.[3] It was concluded that employing mild reaction conditions for protein labelling will produce minimal effect on the activity of the protein. Thus further work is required to optimise these labelling procedures.

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The views, preferences and utilisation of MPharm3 students on feedback at Cardiff School of Pharmacy and Pharmaceutical Sciences

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Effective feedback provision is predominantly considered as an essential commodity in the education sector[1]. However, student dissatisfaction with feedback has been evidenced for many years[2] with no real progress in targeting this dissatisfaction. This study aims to investigate views of Cardiff MPharm3 students regarding whether they value feedback, as well as feedback preferences and usage and recommendations to improving current feedback practices.

Questionnaires were developed to obtain data on a wide range of issues. Approval was granted by the Cardiff School of Pharmacy and Pharmaceutical Sciences Ethics Committee. Question choices came from previous experiences and literature research. Piloting using a purposive sample of MPharm 4 students was undertaken. MPharm 3 students completed the anonymous questionnaire between lectures. Coding was utilised using SPSS (quantitative data) and thematic analysis (free-format answers) using an inductive approach.

The study achieved a 69% response rate. The respondents valued the feedback they received (81%) and utilised it in practice. The majority preferred feedback that was written (49%), task-related (44%), individual to themselves (85%) and contained both positive and negative criticism (85%). Responses for technology-based feedback were more varied. Confidence levels and grades, both good and poor played a major role in whether or not respondents used feedback. Formative feedback was more likely to be utilised over summative feedback. Respondents perceived useful feedback as detailed information identifying areas for improvements as well as what was done well and poorly.

The results identified that not all respondents prefer the same type of feedback as each other. A worrying trend was the lack of mention of self-regulatory feedback when in actuality it is critical to improving learning[3] and professional practice. More importantly, the results identified that not all students perceive effective feedback in the same way.[4] A potential action plan is proposed to improve current feedback practices.

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Patient satisfaction with information about their medicines at Cardiff and Vale University Health Board

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Patient satisfaction can be used as an outcome measure of quality of care.[1] Effective provision of information can improve satisfaction and reduce compliance issues.[2] NHS Wales standards state that organisations should provide appropriate medicines advice and information for patients which is timely and accessible.[3] This study was part of an All-Wales project aiming to investigate whether patients were satisfied with the information they

were given about their medicines whilst in hospital and on discharge and in doing this, identify ways in which Cardiff and Vale University Health Board (C&V UHB) can improve information provision.

Patients recently discharged from C&V UHB aged over 18 years old and on at least one medication were sent a bilingual questionnaire to assess their satisfaction with the information they were given about their medicines whilst in hospital and on discharge. Demographic data was recorded. Responses were analysed with SPSS and statistical tests were used to investigate whether sociodemographic characteristics affected satisfaction.

A questionnaire response rate of 27% was achieved. Satisfaction was high with 83% of patients satisfied with information provision during their stay and 92% on discharge. Patients experiencing problems with their medications were in the minority. The effects of sociodemographic characteristics on satisfaction were not statistically significant. Nurses provided information the most often and information about potential problems was received less than information about how to use medications. Respondents were given information verbally most frequently but preferred to receive it in both verbal and written format.

Satisfaction was high but there is a gap between what patients' want and what they are given with regard to the type of information they receive and the format they receive it in. Further work should be done to address these issues to maintain high satisfaction levels and optimise patients' experiences.

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The effect of benzalkonium chloride and sodium lauryl sulphate exposure on emerging antimicrobial resistance in *Escherichia coli* and *Klebsiella pneumonia*

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In recent years, there has been a steep increase in the usage of biocides, causing a concern to be raised about their overall efficacy and possible emerging microbial resistance.[1] This is especially worrying when low concentrations are used in products as it will create a selective pressure which leads to reduced susceptibility of bacteria towards biocides. Another valid point of concern is the possibility of cross-resistance to antibiotics following decreased susceptibility in biocides.[2] In this study, the effect of benzalkonium chloride (BZC) and sodium lauryl sulphate (SLS) exposure at low concentrations on the development of resistance and cross-resistance to clinically relevant antibiotics in *Escherichia coli (E. coli)* and *Klebsiella pneumoniae (K. pneumoniae)* was evaluated.

Minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC) and antibiotic susceptibility profile of *E. coli* and *K. pneumoniae* were determined for both BZC and SLS. After a 24-hour exposure to biocides at low concentrations, the tests were repeated and the data obtained was compared.

Both MIC and MBC values for both bacteria showed an increase after exposure to BZC and SLS, and there was no significant change in clinical susceptibility profile of antibiotics tested after exposure.

Increase in MIC and MBC values proves that reduced susceptibility to biocides was readily achieved after just a single exposure, indicating a trend towards resistance. Even though some data is statistically significant, two to five-fold increase in MIC and MBC cannot be considered clinically significant. No link to antibiotic cross-resistance was found. These observations point to the fact that there is no significant risk of resistance and antibiotic cross-resistance developing in *E. coli* and *K. pneumoniae* after a single exposure to a low concentration of biocides. However, further work and continued monitoring are crucial to improve our understanding regarding the impact of biocide use on the epidemiology of resistant microorganisms.[3]

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The use of cell lines to investigate extracellular trap formation

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Extracellular traps (ETs) consist of decondensed chromatin with associated granular proteins such as elastase and myeloperoxidase and have been shown to display antimicrobial properties.[1] They are deployed from innate immune cells in response to various stimuli and can trap pathogens, exposing them to histones and granular proteins in highly localised concentrations. The aim of this study was to determine whether different agonists, specifically Toll-like receptor (TLR) agonists, cause ET formation. The cell lines MC/9 and HL60 were used as *in vitro* models to achieve this.

A DNA assay using Sytox green, a cell impermeable fluorescence dye, identified any extracellular DNA produced from cells. The construction of a DNA standard curve was used to quantify any DNA produced.[2] Fluorescence microscopy, with Hoerchst DNA dye, was used to visualise the cells and any potential ETs. Phorbol 12-myristate 13-acetate (PMA) was used as a positive control to stimulate ET formation.

MC/9 cells didn't produce ETs under the conditions imposed on them, despite the optimisation of assay conditions. HL60 cells displayed the ability to produce ETs in response to PMA and Poly I:C, a TLR 3 receptor agonist.

Mast cells have previously been shown to produce ETs,[3] these studies have utilised bone marrow derived mast cells (BMMC) extracted from mice which were incubated with growth factors to mature them. The MC/9 cells are cloned from liver mast cells. The difference in origination to BMMC could be an explanation for their unresponsiveness. The HL60 cells didn't deploy ETs in response to most TLR sub-type agonists however with further investigation under varying conditions a response may be observed. The project reinforced the need to use specific assays such as an ELISA or microscopy as confirmation of ETosis. This is due to the fact that extracellular DNA could be a result of cell lysis.

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An *ex-vivo* investigation into the relative permeability and distribution of intravesical Mitomycin-C in the upper and lower urinary tract

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Mitomycin C (MMC) is the most commonly used intravesical chemotherapeutic in the treatment of superficial bladder cancer[1] and is also used clinically in the treatment of upper tract urothelial carcinoma (UTUC).[2] Despite significant work investigating drug concentrations achieved in the bladder, no studies to date have investigated the permeability of the upper urinary tract to MMC. Thus the main aim of this research was to provide comparative data on the concentrations of MMC achieved in the tissue layers of both the upper and lower urinary tract following topical application of a therapeutic dose of MMC to an *ex-vivo* porcine model.

Ex vivo porcine urinary tracts were instilled with MMC drug solution before tissue samples from areas of drug exposure were excised and sectioned using a cryostat. Drug was extracted from the sections and analysed by HPLC-UV. Resultant data was used to produce drug concentration-depth profiles.

Following 60 minutes intravesical exposure to 1 mg ml^{-1} MMC solution, drug concentrations in the ureter and renal pelvis were significantly higher than the bladder.

This study provides evidence of a difference in drug permeability between the upper and lower urinary tract possibly attributable to uroplakin heterogeneity. These findings, although only representative of one drug, could have potential impacts on the treatment and management of UTUC.

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The impact of temperature and humidity on the performance of hard gelatin capsules for use with a dry powder inhaler

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Hard gelatin capsules have been used as vessels for the drug delivery to patients via dry powder inhalers (DPIs) since the early 1970s.[1] Previous reports raise concerns about gelatin capsule brittleness at low humidity,[2,3] leading to throat irritation as a result of fragmentation.[4] This study aims to investigate, for the first time, the impact of low temperature (5°C) on the performance of gelatin capsules by puncture characterisation and subsequent drug delivery via a DPI.

For this study, gelatin capsules were conditioned at temperatures of 5°C or 20°C over saturated salt solutions, producing capsule moisture levels at either the lower or higher end of the specified 13-16% range. Conditioned capsules were filled with a budesonide and lactose powder formulation and subsequently punctured by a DPI before aerosolisation using a next generation impactor (NGI) and associated pump to expel the powder. Puncture characteristics were captured using light microscopy and optical coherence tomography (OCT), whilst capsule fragments were observed using scanning electron microscopy.

Unpaired t-tests found that changes in humidity and temperature had little effect on the gross amount of powder expelled from capsules. However, with 18.5% more irregularly shaped punctures and more than four times the frequency of fragmentation from capsules with low moisture contents (n=40), it seems that humidity significantly affects puncturing characteristics. Furthermore, capsules stored at 5°C produced fragments up to twice the two-dimensional area of fragments at 20°C.

Low temperature does not have a significant impact on the mass of expelled powder from gelatin capsules within a DPI. However, the impact of low temperature on the extent of fragmentation, may reduce patient acceptability and should be considered by pharmaceutical companies. OCT has proved to be a valuable tool for three-dimensional capsule puncture characterisation and its potential should be further explored for other applications of capsule analysis.

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Evaluation of inhaler technique in patients of the Cardiff and Vale University Health Board

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Inhaler devices are used in the treatment of many respiratory conditions. They are, in principle, excellent medical devices that allow delivery of the drug directly to the site of action. However, it is well known that generally patients' ability to use their inhalers effectively is poor.[1,2]

This study was conducted in two parts. The pharmacist arm of the study evaluated how pharmacists guide patients in the correct use of inhaled medicine by way of a semi-structured interview, the aim was to identify how, when and to whom patients provided advice. The results of the interview produced qualitative data that was thematically analysed [3] to develop codes and themes. The patient arm of the study aimed to evaluate patients' inhaler technique and identify what guidance, if any, they are provided with regard the use of their inhalers. This was done using a structured questionnaire and an AIMS device;[4] quantitative data produced was analysed in excel; Statistical analysis by Chi-square was used to identify whether there was any significant difference in the results we obtained.

The results of this study found that MDI technique is inferior to DPI technique in the patient population of Cardiff and Vale University Health Board. Overall 63% of MDI users failed the inhaler technique test compared to just 8% of DPI users. This difference was statistically significant (p-value <0.0001). The guidance patients are provided with is sporadic due to a number of barriers faced by healthcare professionals. Advice appears to have little effect on patients' ability to use inhalers efficiently indicating that the current methods of inhaler education are not working, this has long-term implications for patients' disease control.

Patients in the Cardiff and Vale University Health Board have poor inhaler technique. A review of how and by whom patients are educated on inhaler technique is recommended.

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Evaluation of inhaler technique in patients of the Cardiff and Vale University Health Board

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Patients must use their inhalers correctly to ensure they receive maximum benefit from their medication.[1] A large number of patients are not using their inhalers efficiently enough to reap full benefit.[2] 40-85% of health care professionals (HCP) lack the skills to counsel patients correctly on inhaler technique.[2]

An anonymous questionnaire was completed by inhaler patients. Each patient's inhaler technique was tested using an Aerosol Inhalation Monitor (AIMs). Patient data was analysed using the statistical package Prism. Chi-squared tests were used to compare metered dose inhalers (MDI) and dry powder inhalers (DPI) and also used to compare patient's technique against their age and gender. Semi-structured interviews were delivered to community pharmacists involving questions on patient's inhaler technique and usage. Anonymous interview data was coded using a standardised framework and then analysed using Microsoft Excel. All data collected was shared between nine researchers. Ethical approval was obtained from the SPPS Ethics Committee and the study was approved as service evaluations by the Cardiff and Vale University Health Board.

89 patients completed the questionnaire. The majority of the results recorded on the AIMs for both MDI and DPI were 'sub-optimal' or less. MDI use was worse than DPI use (chi-squared, p value = 0.0005). 45 community pharmacists were interviewed. 42% gave inhaler advice 'always' while 58% gave advice 'sometimes'. 60% of pharmacists believed they are the most appropriate HCP to give inhaler advice and 18% believe there's a collective responsibility of all HCP to provide advice.

Overall, patient technique is poor; leading to poor asthma control.[3] Patients may not be receiving adequate information or any information at all. Pharmacists are the last HCP the patient sees[4] and as such should ensure that adequate advice has been received. If all HCP are involved in the distribution of inhaler advice, patient's inhaler technique may improve.

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Pneumonia: development and evaluation of a learning aid

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Computer Assisted Learning (CAL) incorporates teaching packages based on particular topics aimed to facilitate learning through the use of computers. CAL packages have been tested in other medical fields where students have expressed enjoyment in their use and outcomes have shown they can be as effective as lectures.[1,2] This study aimed to develop and evaluate a CAL package for teaching information on pneumonia to 1st year undergraduate pharmacy (MPharm I) students with a potential use in Continuing Professional Development (CPD) for pharmacists.

The package aimed to aid learning by interaction through implementation of a quiz and utilising visual aids such as, pictures, diagrams and animations.[3,4] Dedicated CPD slides and the role of the pharmacist were included to ensure relevance to pharmacy practice.

All 110 MPharm I students were invited to participate in the study. A questionnaire containing 26 statements employing a 5-point Likert scale and 3 open questions was available online or in electronic format to gain feedback on the CAL package.

Twenty-five students completed the questionnaire. They agreed that the package was well-structured and provided useful information on pneumonia (92%, n=23). The CAL package was also deemed suitable for CPD update (84%, n=21). All students expressed the opinion that implementation of the quiz was useful and believed that CAL packages are an effective teaching tool. Preference for lectures over CAL packages was unclear as the majority stated no opinion (44%, n=11) but all students agreed that they would use the package to supplement their learning.

A generally positive attitude was perceived toward the CAL package, but this was limited by the low response rate. The results also indicated the package design would benefit from further improvements, since many students reported animation overuse. Additional studies should be conducted on practising pharmacists to clarify potential CPD value.

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Chemical analysis of creatine sports supplements – are they what they say on the tin?

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Creatine monohydrate is a sports supplement used to enhance performance in short, intense periods of exercise.[1] Sports supplement quality is often questioned, with studies showing that they may be contaminated with banned doping substances, heavy metals, and organic compounds.[2] This project investigated the levels of contaminants present in creatine monohydrate supplements, and examined the stability of creatine in aqueous solution.

11 samples of creatine monohydrate were collected, all of which were analysed by 1H-NMR for creatine and creatinine presence. HPLC was used to quantify levels of creatine, dicyandiamide, thiourea and creatinine, and all samples were sent to MEDAC Ltd for detection of mercury content. 6 samples were also analysed for cadmium content. The stability of creatine in D2O was assessed, as well the concentration change for solutions initially containing equal quantities of creatine and creatinine in D2O and H2O.

1H-NMR analysis confirmed creatine presence in all samples, and HPLC analysis showed the range to be 71.4-90.4%. Dicyandiamide was detectable in 7 samples, creatinine in 3 samples, and thiourea was below the

limits of detection for all. Arguably, the most important finding was that 10 out of 11 samples exceeded the EU limit for mercury contamination (0.1mg/kg).[3] Analysis of creatine solutions suggested that creatine is stable for at least 37 days in D_2O, and in the same conditions, the creatine-creatinine equilibrium favours the production of creatine. This is different to reported results where the equilibrium in H2O was found to reside at 50% creatine and 50% creatinine.[4]

The results of this project suggest that quality control within creatine monohydrate manufacture may not be adequate; especially in regards to mercury contamination. Further investigation into other sports supplements, particularly noting heavy metal content, may show if contaminants present pose a risk to the consumer.

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Formulation, preparation and testing of orally disintegrating tablets (ODTs)

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Oral delivery of medication is currently the gold standard method of drug delivery in the pharmaceutical industry. However some patients have difficulty in swallowing oral dosage forms, negatively impacting on patient compliance.[1,2] Orally disintegrating tablets, or ODTs, were developed to accommodate patients with whom swallowing conventional oral dosage forms is an issue. ODTs rapidly disintegrate in saliva without the need of water, and are then easily swallowed. Thus improving compliance in those patients who cannot swallow standard dosage forms.[3]

The aim of this project was to produce mechanically robust and physically acceptable ODTs with uniformity of content, which release the active within a suitable time frame. All tablets produced were manufactured using a GMP compliant Riva Minipress® single punch tablet press. A variety of British Pharmacopeia tests were conducted such as: tapped density of powders, resistance to crushing of tablet, friability, disintegration and dissolution. Along with other methods such as U.V. spectrophotometry and measuring tablet weight and thickness.

Tablet weights and thicknesses throughout the project were relatively close to the target values. Tablet resistance to crushing force decreased with the addition of active initially, yet later it increased. Increasing magnesium stearate content reduced the resistance to crushing of the tablet. All formulations produced passed the friability test when tested soon after production. All formulations tested disintegrated within 3 minutes, usually after 30 seconds, thus adhering to BP specifications.

New knowledge and insight into the production of a ODTs has been gained. The tablets produced were promising, as they disintegrated quickly, releasing the active into solution in a suitable time frame. The evidence suggests that suitable ODTs are achievable. Testing is needed to investigate taste masking capabilities of the sweeteners and flavours used. An artificial tongue could be used to identify this.[4]

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A comparison of the resistance of pressurised metered dose inhalers (pMDI's) with dry powder inhalers (DPI's) and the implications for the patient

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Pressurised metered dose inhalers (pMDI's) are the most common form of drug delivery for respiratory conditions such as asthma and COPD. pMDI's are currently believed to be low resistance.[1] The resistance of an inhaler is the force applied against the inspiratory effort of the patient to achieve airflow through the mouthpiece. A recent study concluded that variation observed in the flow rate which activated the whistle (indicates incorrect inhalation) on a valved holding chamber (VHC) was linked to the resistance of the pMDI attached.[2] This study aimed to investigate the specific resistance of pMDI's in comparison to that of dry powder inhalers (DPI's).

Flow rates were recorded that indicated optimal inspiratory flow rate on a current inhalational training device (AIM Vitalograph), and that activated the whistle on two types of VHC with a selection of pMDI's attached. Flow rates that produced given pressure drops across the inhalers were plotted against each other for a selection of DPI's and pMDI's, the reciprocal of the slope of each inhaler was calculated as the specific resistance of the inhaler.[3]

This study found the Vitalograph trains patients to optimally inspire with pMDI's at a flow of 16-90L/min and 15-60L/min with DPI's, this coincides with the literature.[4] The flow rates which activated the whistle on a VHC corresponds with the previous study.[2] The specific resistance of a selection of pMDI's and DPI's was calculated, four pMDI's demonstrated a higher resistance than the DPI's.

pMDI's have a higher specific resistance than is historically believed. Current inhalational techniques do not account for variation between inhalers with current training devices having one generic setting. The resistance of pMDI's should be considered when prescribing to those with advanced respiratory conditions as they may not be able to produce the inspiratory force required for optimal flow with high resistance inhalers.

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Effect of sodium lauryl sulphate and benzalkonium chloride exposure on emerging antimicrobial resistance in *MRSA* and *S. aureus*

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Microbicides are heavily used for their bactericidal properties in the food, health and cleaning industries and have been since the turn of the 20th century.[1] The recent upsurge in antibiotic resistance has caused some to question if widespread microbicide use is facilitating the development of microbicide resistance, and also antibiotic cross-resistance.[1, 3]

This study established the MIC (microdilution broth test in 96 microtitre well plates, incubated overnight at 37°C), MBC (number of CFUs counted after MIC plate is subcultured onto tryptone soya agar plates for overnight incubation at 37°C) and antibiotic susceptibility (disk diffusion method in Muller Hinton agar plates in line with EUCAST guidelines[2]) for methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *S. aureus* exposed to sodium lauryl sulphate (SLS) and benzalkonium chloride (BZC) for 24 hours. MIC, MBC and antibiotic profiling were measure before and after biocide exposure and results compared.

Unpaired t-test showed statistically significant differences between baseline MRSA and MRSA post exposure to 0.0025% and 0.0001% BZC and 0.0078% SLS for 24hrs MIC ($P<0.0001$, $P<0.0013$ & $P<0.024$ respectively). Also statistically significant were the MICs *S. aureus* exposed to 0.0025% ($P<0.0001$) and

0.0001% (P<0.022) BZC for 24hrs. However, there was no change in SLS susceptibility following biocide expsoure. BZC exposure caused no statistically significant change in MBCs between baseline and post 24hrs exposure of BZC in MRSA and *S. aureus*. Statistically significant differences were found in *S. aureus* antibiotic profiling following SLS and BZC exposure (p<0.0001) indicating cross-resistance to antibiotics has occurred.

This novel study tested real-life concentrations of microbicides; however SLS results fluctuated due to precipitation issues so exposure MICs and MBCs remain undefined.

Results obtained were overall very interesting, providing some data supporting previous studies on the effect of biocides on emerging bacterial resistance to antiomicrobials. [1, 3] However, this was a small six week study so further research is required.

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Rat mesenchymal stem cell elasticity after exposure to cold atmospheric plasma treated wear debris

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Ultra-high molecular weight polyethylene (UHMWPE) is the most common articulating surface being used during joint replacement surgery. However, the generation of wear debris from UHMWPE surface has been considered as a factor that reduces longevity of implanted prosthesis. Cold atmospheric plasma (CAP) treatment was previously introduced to improve UHMWPE, by increasing crosslinking between UHMWPE layers.[1] The origins and characterisations of wear debris that influence body cells and tissues were included in this study. This practical work was carried out for the first time to identify the cell elasticity changes after being exposed to either untreated or CAP treated wear debris.

UHMWPE samples were first treated with CAP for 7.5 minutes,[2] followed by non-stop wearing process with cobalt-chromium for one week (330 kc) and two weeks (660 kc) respectively. Bovine serum that acts as lubricant was injected constantly during the wearing process. UHMWPE wear debris would be isolated from bovine serum. The untreated and CAP treated wear debris were exposed to rat mesenchymal stem cells (MSC) and incubated at 37°C. Cell elasticity would then be investigated under atomic force microscope (AFM) after 24, 48 and 72 hours of exposure time.

An equation that fits the Hertz model was applied to calculate the cell elasticity. No significant difference has been observed in cell elasticity exposed to untreated wear debris. However, there were significant differences in the elasticity between cells that were exposed to CAP treated wear debris and the cells that were not exposed to any wear debris (P<0.05).

Rat MSC can be a good approximation as it has similar properties to human MSC.[3] Cell elasticity indicates the changes in vital cellular functions in response to the applied external force.[4] Overall, the data shown in this study is not sufficient to draw a robust conclusion.

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Review of Medication Administration Record (MAR) from care homes

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Elderly residents living in care homes are frail and are exposed to greater risks of medication errors.[1] The aim of present study is to document the incidence and nature of medication errors in care homes through the evaluation of paper-based medication administration records (MAR).

A retrospective study was conducted in 10 recruited care homes located in the ABMU Health Board. The results reported in this study were obtained from just one of these homes, from which MAR charts for 20 residents were collected. Analysis of medication errors was performed against a group consensus of medication error categories. These error categories are Administration errors, Risk errors, Regulatory errors, Stock errors and a category defined as 'cannot assess'. Within all categories, a set of sub-categories was further identified. The type and frequency of medication errors were recorded in Excel and data was subsequently transferred into SPSS for further analysis.

The residents from the studied care home had a mean age of 88 years old and were taking an average of 10 ± 4 medications. A total of 1227 medication errors were identified. Each resident was exposed to a mean of 61 ± 36 errors. Stock errors (50.3%) were the most common error type, followed by Administration errors (25.7%), Regulatory errors (19.8%) and Risk errors (4.2%). Within Administration errors, the most frequently occurring error was 'deviation from stated dose'. The BNF medication categories that were most subject to errors were ocular products, stimulant laxatives, analgesics, hypnotics and osmotic laxatives. PRN medications and controlled drugs contributed to 302 errors and 103 errors, respectively.

The analysis of paper-based MAR charts revealed that the incidence of medication errors in the studied nursing home is high. A safer medicines management system is required to improve the quality of medicines management in care homes.

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Evaluation of inhaler technique in patients of the Cardiff and Vale University Health Board

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Inhalers are a cornerstone in the prevention and treatment of Bronchial Asthma and COPD (1). Currently, 5.4 million asthma sufferers are being treated in the UK, with an estimated 3 million people also suffering from COPD (2). In 2011, around 1200 deaths in the UK were attributed to asthma, of which 90% were considered preventable (3). Inhaler technique is often found to be of inadequate standard amongst patients (4). The aim of this study is to evaluate the inhaler technique of patients in Cardiff & Vale University Health Board.

The study consisted of 2 areas of investigation. Firstly, a patient questionnaire providing background information for an inhaler assessment and secondly, short interviews with community pharmacists designed to determine the frequency and format of advice they provide to patients. Both sections were ethically approved and received permission to be run as part of an NHS service evaluation. Data from both sections was anonymised and required consent. Interview and qualitative data from questionnaires were analysed using content analysis. Statistical analysis was performed using Graphpad Prism.

89 patients took party in the study. Only 3% of MDI users and 29% of DPI users demonstrated correct inhaler technique. 68% of MDI users and 8% of DPI users failed the assessment. A P-value of <0.0001 was obtained in a Chi-square test indicating a significant difference in technique between DPI and MDI users. Nurses provided advice to 52% of patients, a further 22% by GPs and 6% by pharmacists. 44 out of 45 pharmacists interviewed stated that they gave patients verbal advice.

Issues such as pressure of time, confidence and patient interest were cited as barriers to giving advice. Improving generally poor standards of inhaler technique might require HCP training, patient education and the selection of the most appropriate inhaler for the user.

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A survey to assess public's knowledge on the absorption and removal of alcohol in the body

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Alcohol is one the leading causes of accidents, from domestic to traffic related.[1] Many interventions have been implemented to change drivers' dangerous behaviors. However, there was no study conducted on public's understanding on alcohol absorption and removal. Knowledge change is likely to lead to a change in behavior. The aim of this study was to evaluate the knowledge of the public on alcohol absorption and removal from the body.

An anonymous 13-item questionnaire with the objective to assess, a) factors that affect the absorption of alcohol and b) removal of alcohol and its influence on driving was designed. 150 participants were enrolled using convenience sampling in the Cardiff University compound. The questions were delivered to respondents verbally in a similar pattern. Respondents' knowledge was analyzed and correlated with their weight in the worksheet 'Drink-Me Simulation' prepared by Professor Nick Holford,[2] a clinical pharmacologist simulation model that was used to estimate blood alcohol concentrations and to evaluate on the number of standard alcoholic drinks which are likely to keep blood alcohol concentrations below the legal driving limit. A scoring system scheme was used, 1 allocated to an appropriate answer and 0 to inappropriate and unsure answer. Statistical analysis was done using SPSS (version 20.0) whereby Kruskal-Wallis test was used to compare the gender and age groups. Ethics approval was obtained.

The survey demonstrated moderate overall knowledge and knowledge on the factors affecting the alcohol absorption. The score for male group was significantly higher than the female on the overall knowledge (P=0.007) and knowledge on factors that affect the alcohol absorption (P=0.023) subscale. However, their knowledge on the removal of alcohol and its influence on driving appeared low.

Interventions have to be implemented to deliver knowledge on this topic to the public effectively to improve awareness and reduce the alcohol-related road casualties.

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The potential link between ageing, clathrin-independent endocytosis and Alzheimer's disease

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Alzheimer's disease (AD) is the most prevalent cause of dementia. The breakdown of amyloid precursor protein (APP) to form beta-amyloid (Aβ) is a major contributor to disease pathology with Aβ accumulation leading to neuronal cell death.[1,2] Clathrin-independent endocytosis has been implicated in the amyloidogenic processing of APP. Caveolins and flotillins are lipid raft proteins involved in this pathway and both have been shown to accumulate in AD brains.[3,4] Age is the biggest risk factor for developing AD, and little is known about its effect on these endocytic processes. The aims of this study were to determine and compare levels of expression of APP, adaptor proteins and clathrin-independent endocytic proteins in healthy human brains of varying ages.

Western blotting was used to determine expression of proteins in human, male prefrontal cortex tissue of three age groups: 20-30 years, 45-55 years and 70-85 years. Results were normalised against GAPDH levels and analysed using one-way ANOVA with Tukey's test to compare between the groups.

Results showed a significant increase in flotillin-2 with age, with $p<0.01$ between the young and older groups, and middle-aged and older groups. Caveolin-1 showed a definite trend for an increase with age ($p=0.0841$) although this was not significant. BACE-1 showed a significant decrease between the young and middle-aged groups ($p<0.05$). No significant changes were seen in the other proteins in relation to increasing age.

The variations in BACE-1 expression could reflect differences in individuals' APP processing, despite their age. Changes in caveolin-1 imply that its expression could be affected by age and may play a protective role in AD. It appears that the expression of flotillin-2 is affected by age, suggesting that it may play a part in AD pathology where ageing is a contributory factor. Whether the role of the flotillins is regulatory, permissive or protective against Aβ production is still an unanswered question.

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An investigation into what factors influence students' motivation and achievements, the perspective of final year Cardiff MPharm undergraduates

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Motivation is an umbrella term used to describe goal directed behaviour.[1] It is an important concept in the field of education as motivation is associated with positive learning environments. Self-Determination Theory (SDT) is widely used to explain how individual's motivation is linked to their work effort, distinguishing between autonomous and controlled motivation.[2] Achievement-Goal Theory (AGT) categorises an individual's goals based upon their motivation for achieving them.[3] This study aims to investigate factors which influence final year Cardiff MPharm undergraduates' motivation and achievement and relate its findings to Cardiff School of Pharmacy and Pharmaceutical Science (CSPPS).

From review of literature a topic guide was developed by the four researchers and supervisor with areas relevant to the aim of this project. These included: final year projects, teaching session attendance, assessments and coursework, and general MPharm discussion. Non-probability sampling (a combination of purposive and convenience) was used to recruit a wide demographic of students. Each researcher conducted four one on one, semi-structured interviews. With consent, students were audio recorded and each researcher transcribed their own interviews. Transcripts were shared between researchers and the data analysed independently using thematic analysis.[4] Ethics was approved prior to data collection.

From the 16 interviews conducted (four per researcher) four main themes were identified: "That's interesting", "People are influenced by those around them", "Motivation is multifactorial", "Apples and oranges - motivation differs inter-personally". Themes were identified primarily inductive using a deductive reasoning where appropriate.

Motivation is a complex concept that differs both intra-personally and inter-personally. The themes identified highlighted factors which influence students' motivation and goals and may be useful within CSPPS to help benefit these areas. This study was limited to a sample taken from within CSPPS and further work includes investigating how the findings of this study relate to other Schools of Pharmacy.

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A review of medicines administration records (MAR charts) from care homes: An analysis of errors that occur

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Studies have shown that a high number of errors occur during the medicines administration process.[1] The aim of this research was to determine the types and frequency of errors that occur by analysing MAR charts from care homes within the Abertawe Bro Morgannwg University health board.

MAR charts from a single 28 day period were received containing information on all service users, along with MAR charts from a second period containing information on 9 of the 14 service users at care home 9. Each MAR chart received was analysed for errors using 5 pre-determined categories. This information was entered into an Excel spreadsheet and later transferred to an SPSS database for statistical analysis.

The average service user was 79 years old with 13 prescribed medications, at least one controlled drug prescribed and 3 MAR charts. The most common errors were administration errors which accounted for 17.09% of all errors identified. The most common administration error was an omission. There were no significant differences between the errors seen in period 1 in comparison to period 2.

In conclusion polypharmacy is a key contributor to the number of errors that occur during medicines administration. The majority of errors identified appear to be as a result of the incorrect use of MAR charts. Fossey et al[2] state that training manuals are not evidence based, therefore could be a contributing factor to some of these errors. The consequence of each error has not been considered in this research; however consequences will undoubtedly depend on the circumstances of the service user. This aspect of medicines administration has not been assessed on this occasion; however it would be advantageous to professionals and service users to explore this facet in future research projects.

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Determining the differences in epidermal thickness at various skin sites in human volunteers using Optical Coherence Tomography

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The skin is the largest organ in the human body, made up of the epidermis and dermis. Its composition makes it a good target for both local drug and vaccine administration and systemic drug delivery. Whilst transdermal drug delivery systems have proven effective at delivering materials to the systemic circulation following topical skin application, overcoming the *stratum corneum* is a significant challenge.[1] Research has explored the use of microneedles for achieving local and systemic drug delivery via the skin[2,3] and an intimate knowledge of epidermal thickness will aid their design in order to reach appropriate targets within the skin. The aim of this study was to determine whether Optical Coherence Tomography (OCT), a non-invasive skin imaging technique, could be used for this purpose and to determine whether epidermal thickness varies between body sites and individuals.

OCT was used to determine epidermal thickness differences at different body sites and between different individuals. Ethical approval was granted and 30 participants were recruited. OCT data was analysed in Fiji and MatLab software programmes then processed to determine whether gender, age and BMI correlate with epidermal thickness.

The epidermis of the palm appeared significantly thicker than at all other body sites, but there was no significant difference between epidermal thickness of volar forearm, deltoid and face. Fiji gave slightly higher measurements of epidermal thickness than MatLab, though the differences were negligible except at the palm. Differences in gender, age and BMI did not correlate with epidermal thickness.

OCT images were clear with good resolution allowing simple and effective identification of skin layers and appendages. Findings from this study agree in part with the literature, however increasing sample size and comparison with histology would give more power to the results. The OCT instrument used in this study gave a high level of clarity and was suitable for assessing epidermal thickness.

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A comparison of the puncturing properties of two types of hypromellose capsules

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Hypromellose, for use in the manufacture of capsules, can be formed in different ways, creating a variation of hypromellose types/grades; resulting in a range of properties. These grades of Hypromellose can consequently be used within Dry Powder Inhalers (DPI's) [1]. Puncturing properties of the capsule are integral within DPI's.[1] This study aims to discover whether Quali-V®-I hypromellose capsules have an improved puncturing ability, via a DPI, than pharmaceutical Quali-V® grade hypromellose capsules with varying moisture contents.

Capsules were conditioned before testing in desiccators containing saturated salt solutions of Calcium Chloride (33% RH) and Magnesium Nitrate (56% RH); producing 2 sets of each capsule type at the lower and higher limits of their moisture content specification. The force required to puncture each type of hypromellose capsule at the cap was recorded using the Zwick-Roell material testing machine. The pin of a Plastiape® monodose 2-pin inhaler was tested in order to establish differences in the penetration process. Uniformity of the puncture was analysed via an Amscope Stereo Inspection Microscope looking at the area of both the puncture and the section not encompassed by the flap, the shape, and the zone.[2,3].

Quali-V®-I capsules had a majority of circular punctures (≥60%) within both conditions; with Quali-V® achieving a higher percentage of slightly Irregular within each condition (45-55%). Data regarding the area of puncture showed that Quali-V® was more affected by the lower RH condition than Quali-V®-I; significant differences were found between each capsule type at this condition ($p=0.021$).

Both capsules performed to a relatively equal standard within the higher moisture content condition; only showing variation in the shape. The largest variation of the capsules came from the introduction of a low moisture content; giving lower reproducibility.

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The design and synthesis of novel Bcl-3 inhibitors as novel antimetastatic agents

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Bcl-3, a protein encoded by the Bcl-3 gene, an atypical member of the IκB family, interacts specifically with NF-κB homodimers P50 and P52 causing transactivation of NF-κB leading to transcription and gene expression.[1] NF-κB is a known factor in metastasis,[2] which is the migration of cancerous tissue from a primary to secondary site. This causes metastases, the largest cause of death in cancer patients,[3] for which there is currently no effective treatment. A recent study removed the Bcl-3 gene from mice and concluded that deregulated Bcl-3 plays an extensive role in metastasis of cancers.[4] The reduction in metastatic tumour burden highlights inhibition of Bcl-3 as a target for the prevention of metastasis, identifying the need for design and synthesis of a novel inhibitor of Bcl-3.

Three ‘hit’ compounds (1-3) were selected for modification based on their activity in ELISA assay. These pharmacophores were rationally modified with the aim to improve activity, ultimately providing key information on the structure activity relationship (SAR) leading to new lead compounds. Suitable synthetic pathways were assessed, selected and implemented for all three compounds.

Derivatives of compound 1 were highly successful in their synthesis, being of high yield (more than half >70%) and all totally pure, ready for *in vitro* testing. Compound 2 derivatives developed challenges, as the final molecule had the potential for many isomers, as well as being difficult to purify, identifying future work. The intermediates in the synthesis of compound 3 were impure leading to difficulties synthesising pure final products.

A total of twenty two molecules were synthesised as novel inhibitors of Bcl-3. These drug like molecules have been successfully developed and synthesised, rationally based on the original pharmacophores which showed promising activity as inhibitors of Bcl-3. SAR information later collected will be used for future lead generation.

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Assessing the Impact of the WEDINOS Project

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In recent years there has been an increase in the supply, and use, of potentially harmful recreational drugs known as “legal highs” These products are mainly marketed online and are produced in an attempt to circumvent the law and to mimic the effects illicit drugs. There has been a sharp increase in adverse events associated with these products with deaths involving NPS in recent years more than doubling from 29 deaths in 2011 to 60 deaths in 2013 in England and Wales alone. The WEDINOS project was initiated to reduce public harm caused by these substances by analysing providing chemical analysis of samples. This study attempts to examine the clinical impact of the project and assess its value to the public.

“Leading Edge” websites analysed to provide topics of discussion within online forumsto examine behavioural trends before and after inception of the WEDINOS Project. This provided detail on the precise clinical impact of the service upon public health. Quanititive data was collected to assess any correlation between rising media attention on the project and number of users of the service. This data was then statistically analysed using the Pearson’s correlation coefficient.

Unique behaviours that had arisen as a direct result of the service identified. Content analysis threads containing WEDINOS citations produced three main themes of discussion, Community Support, Vendor Reaction and User Queries. There was shown to be no significant correlation between media attention and the number of users of the service

The WEDINOS project has been shown to have produced its own unique behaviours among online communities regarding NPS which have brought about more robust methods of harm reduction for the members which was not previously available. It has been well welcomed by the community and has shown a clinical impact upon the population in terms of public health.

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Exploring students' views on their Community Pharmacy Placement Scheme

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Clinical placements are valuable tools used in healthcare education to help students contextualise knowledge, develop clinical skills and gain an insight in professionalism.[1,2] As a major stakeholder, it is important to understand student views on placement schemes. The aim of this project was to explore perceptions of Cardiff MPharm year 3 students on the existing placement scheme. In particular, what parts they feel benefited them and what they feel needs to be improved. Results can be used so that the School can develop more efficient schemes.

The whole of the 3rd year student population was targeted for the study and a combined qualitative and quantitative approach was employed, in the form of a reflective questionnaire. After ethical approval was gained, quantitative data was analysed using the statistical package SPSS. Thematic analysis was undertaken for all the free text qualitative comments.

Satisfaction for the placement scheme over all was high with 84% of students scoring it a 4 or 5 (out of 5). A large number of students (over 90%) were also satisfied with certain aspects such as pre-placement information, supervision and structure. Five main themes were found using thematic analysis: Role models, Pharmacist role, Student involvement, pharmacy engagement and clinical development.

An important factor for student satisfaction seemed be the involvement of the student in pharmacy tasks. Improvements could be made in making the placement more personalised especially for international students. The benefits of the placement were seen to be development of student's clinical skills as well as a better understanding of professionalism.

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A snapshot in time: working with WEDINOS to look at the NPS used in Wales

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The market for Novel Psychoactive Substances (NPS) has increased rapidly since the early 2000s, with the ban of 'club-drug' Mephedrone in 2010 bringing this hidden market into the public eye.[1,2] The Welsh Emerging Drugs & Identification of Novel Substances project (WEDINOS) laboratory has been creating a database of NPS and since 2013, 2061 samples have been analysed.[3] This research aims to analyse the chemical structure of NPS being sent into WEDINOS and to compare the results with the latest NPS used in the rest of Europe

A series of analytical techniques are used, the first is Time of Flight Mass Spectrometry (TOFMS). TOFMS, however cannot identify isobaric substances, but they can be identified by further analysis of the mass spectrum or by Gas Chromatography (GC) or Proton Nuclear Magnetic Resonance. Analysis by GC can follow several methods; the most commonly used being psychoactive differentiation or the opiate differentiation.

Research by the Global Drug Survey has started to highlight drug use in different countries across the world.[4] My research analyses drugs received across Wales and some other parts of the UK. Samples were received from postcode regions SA, CF, LL, NP and SY, the majority being sent from CF. WEDINOS also provides the legal class of the substances received. Across Wales cocaine was the highest used drug sent in (18.5%), the GDS shows Belgium has a similar use (19.9%).

Identifying these substances poses a complex analytical challenge as there is very little analytical data published and an even greater challenge is faced when brand new substances are received with no knowledge of their structure. This study has highlighted the variability in the content of NPS and hopefully this research will show users the risk they are facing especially when used in combination with other illicit substances or alcohol.

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Drug discovery from Welsh daffodils

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In Western Europe *Narcissus pseudonarcissus*, more commonly known as daffodils, are grown commercially as a source of galantamine using a cultivar named 'Carlton'. Galanthamine is an acetylcholinesterase inhibitor licensed for the treatment of mild to moderate Alzheimer's disease. As well as galanthamine, other isocarbostyril alkaloids unique to Amaryllidaceae species can be found in daffodils. An example of such an alkaloid is narciclasine, which is currently being investigated as it possesses the potential for being developed into a drug for the treatment of brain gliomas.[1] The aim of this study was to extract novel molecules from a daffodil juice preparation produced from daffodil plant tops which were sourced from a *Narcissus pseudonarcissus* cv. 'Carlton' cultivar grown in Mid Wales.

The method consisted of using two polymer bound nucleophile scavengers; isothiocyanate and sulfonyl chloride, to react with nucleophiles which would then subsequently be cleaved from the resin under a specified set of cleavage conditions. The end product was then analysed using ESI-MS and novel compounds were searched for by ruling out potential contaminants[2] and previously recognised alkaloids[3] amongst other possible compounds.

The results show that both resins extracted a large number of molecules, many of which are yet to be identified. These could prove to be novel species however further investigations are required to confirm the identity of these molecules.

Overall, this study has shown that polymer bound nucleophile scavengers could be useful as a tool for discovering new drugs from natural sources.

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The design and synthsis of novel anti-cancer c-FLIP inhibitors

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It is thought that breast cancer stem cells (BCSCs) drive cancer reoccurrence and metastasis, the latter being the primary cause of mortality in breast cancer patients.[1] TRAIL has demonstrated tumour specific activity in clinical trials, whilst only exhibiting mild side effects in some cancer types. However, breast cancer cells are resistant to TRAIL. Resistance has been attributed to cellular FLICE-like inhibitory protein (c-FLIP) expression.[2] Knockdown of c-FLIP expression in the presence of TRAIL has demonstrated a tumour specific kill in BCSCs.[1] We have identified an inhibitor of c-FLIP through molecular modelling and virtual screening. Cellular based assays indicated potent activity where IC50 = 50 nm. The hit compound was used as a template to synthesise sulphonamides **1–17**. The aim of the present study was to synthesise a series of novel analogues of the lead sulphonamide.

Procedure 1 uses pyridine as the base and solvent.[3] Procedure 2 uses triethylamine as a base and dichloromethane as the solvent.[4]

Procedure 1 produced 17 highly pure compounds with generally moderate to high yields. Procedure 2, used to resynthesize one sulphonamide, only produced a third of the yield achieved with procedure 1 at lower purity. It was found that when the NH was in *meta* position, yield was highest, followed by *para* then *ortho*.

Procedures 1 and 2 are effective at synthesising analogues of the lead in question. However, despite procedure 1 taking 6h, good yields of highly pure products were achieved. In contrast, procedure 2 requires only 3h, but comes at the expense of yield and purity. We have successfully synthesised 17 novel analogues of the lead, meeting our objectives. We are now waiting for the biological testing and evaluation data of the analogues.

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Depression and polypharmacy in movement disorders

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Parkinson's disease (PD) and non-parkinsonian tremor (NPT) are the two most prevalent movement disorders. Dopamine deficiency is the primary cause of PD and results in motor symptoms which include bradykinesia, tremor, postural instability and rigidity.[1] It is thought that NPT is caused by disordered activity between movement pathways in the brain.[2] Non-motor symptoms (NMS), such as depression and cognitive deficits, are exhibited in both disorders.[3,4] The aim of this research is to investigate the relationship between polypharmacy and depression in movement disorder patients.

A retrospective study was conducted on Welsh Movement Disorder eNetwork. It contained information on movement disorder patients that attended clinics in The Princess of Wales and the University Hospital of Wales between 2000 and 2013. Prevalence of movement disorders and depression, along with basic demographics, antidepressant use and polypharmacy were examined.

This study included 1189 patients, 67% PD and 33% NPT. PD had a higher proportion of males and NPT had a higher proportion of females. Depression was more frequent in the PD population (52%) than NPT (28%). Of the depressed population, 77% of PD and 91% of NPT patients were prescribed antidepressants. SSRIs were prescribed more frequently than TCAs in both disorders. Patients taking antidepressants were prescribed a significantly higher number of drugs from different classes than depressed patients not taking antidepressants and non-depressed patients. This pattern was seen in both PD and NPT patients. The motor symptoms of depressed PD patients were more severe than non-depressed PD patients; this was deduced by speculating that anti-parkinsonian drug regimen correlated with disease severity.

There is a clear relationship between disease severity and depression within PD. However, polypharmacy is seen to be more closely linked to whether a patient with depression is treated with antidepressants or not.

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The potential link between ageing, clathrin-mediated endocytosis and Alzheimer's disease

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Alzheimer's disease (AD) is thought to be caused by an over-production of beta-amyloid from APP following clathrin-mediated endocytosis (CME),[1,2] and age is the greatest risk factor.[3] The aim was to determine the effect of ageing on the expression of proteins involved in CME and APP processing in human cortices from 3 age categories to investigate the role of ageing in AD aetiology.

Protein expression was determined by Western blotting in human prefrontal cortex tissue from men aged 20-30 years, 45-55 years and 70-85 years, normalised to GAPDH and compared via a one-way ANOVA and Tukey's statistical tests.

Clathrin expression increased five-fold from the young to older category ($p<0.001$), and 1.94 times from the middle to older category ($p<0.05$). Increases in PICALM, AP180, and dynamin-1 were seen with age but were not significant. Levels of BACE-1 decreased significantly from the young to middle category ($p<0.05$). AP2, BIN1 and presenilin-1 levels appeared to decrease with age but this was not significant. APP levels were not significantly altered by age.

The rise in clathrin levels, along with AP180, dynamin-1, and PICALM, seen with ageing suggests that the ageing process incorporates a substantial rise in CME, and that ageing may contribute to AD aetiology via an increase in beta-amyloid production. Some protein levels did not increase with age, however, further research is required to investigate this as large individual variation was observed.

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Development of a novel chemoselective method for natural product discovery and isolation from marine sponges

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A fruitful area for natural product research has been marine sponges with currently three FDA approved drugs of marine sponge origin.[1,2] Despite the efforts made to improve methods used in natural product research, the isolation and purification processes are still considered a burden.[3,4] To overcome this a novel method has been devised, which has proven to work in principle but remains a new area of research.[3,4] The aim of this study was to explore this novel chemoselective solid phase extraction method for the discovery and isolation of nucleophilic natural products from marine sponges.

Three marine sponge species were used: *Agelas oroides*, *Petrosia ficiformis* and *Aplysina aerophoba*. These sponge species were extracted in methanol to provide crude extracts and reacted with electrophilic resins: polystyrene functionalised with isothiocyanate and sulphonyl chloride functional groups. To analyse and purify the samples recovered from both resins analytical and preparative thin layer chromatography were used. LC-ES-MS and MarinLit was used for compound identification.

Results showed that this method successfully isolated compounds as each experiment recovered material. Percentage recoveries demonstrated that the efficiency of the resins to extract compounds varies between species and resins. Mass spectrum analysis of a sample recovered from *A. oroides* identified a brominated compound with m/z 533.0. A MarinLit database search showed that this was a known compound, taurodispacamide from *A. oroides*. Mass spectra results for other samples showed that this method had extracted five potential novel compounds from *A. oroides* and *P. ficiformis* with m/z 268.9, 926.7, 963.8, 993.8, 1216.0.

Low percentage recoveries restricted full structural analysis by NMR, yet this process still identified potential novel compounds which are valuable. This method has extracted both known and potential novel compounds from different species of sponge; it is hoped that this study has demonstrated the potential use of this method in future research work.

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Evaluation of suppressed genes CYP2B6 and STARD13 derived from novel endocrine resistant breast cancer models

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Breast cancer can be categorised as oestrogen receptor positive (ER+) or negative. ER+ disease is further divided into luminal A (ER+/HER2 negative) and luminal B (ER+/HER2 positive).[1] Endocrine resistance is a serious issue in breast cancer and is either present *de novo*[2] (no initial response to treatment) or acquired after an initial response to treatment.[3] The Breast Cancer Molecular Pharmacology group has developed 11 long-term (3 year) acquired resistant models from responsive luminal A and B cells to investigate the biology of acquired resistance. CYP2B6 and STARD13 gene expression were suppressed in two luminal B-derived resistant models by Affymetrix microarray analysis. The aim of the project was to further identify any involvement of the genes in endocrine resistance in breast cancer.

PCR was used to validate the mRNA profiles of CYP2B6 and STARD13 and explore their expression in all 11 long-term resistant models. Densitometry determined their expression with actin normalisation. Gene ontology and association with clinical tamoxifen outcome were explored using publically-available bioinformatics resources.

CYP2B6 and STARD13 were found to be significantly suppressed in the luminal B but not luminal A-derived resistant models. Bioinformatics studies revealed association between a higher intrinsic expression of STARD13 or CYP2B6 and longer time until relapse in a tamoxifen treated luminal B patient expression dataset. Ontology investigation found CYP2B6 was implicated in the metabolism of tamoxifen and chemotherapeutics to active metabolites while STARD13 was anti-proliferative but also had controversial ontological results.

Using cell model, clinical profiling and ontological studies, decreased expression of these two potentially tumour suppressive genes was commonly demonstrated in luminal B-derived endocrine resistance. In conclusion, the evidence accumulated supports roles for loss of CYP2B6 and STARD13 in the mechanism of acquired endocrine resistance but further work is necessary to confirm this.

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Comparing the specificity of *Bacillus* specific bacteriophages

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Bacteriophages are being increasingly considered as the threat of multi-drug resistant bacteria grows.[1] From the studies available regarding specificity, it is apparent that bacteriophage binding sites vary between bacteriophages and hosts. Bacterial resistance to bacteriophages does occur and 'phage-cocktails' are developed to prevent and combat this.[2] Studies have occurred for near a century to establish standardised methods for their propagation and testing.[3] These methods still offer varying results; in response, researchers appear to optimise them frequently.[4] Objectives: Identify and isolate strains of *B.cereus* and *B.thuringiensis*

spontaneously resistant to bacteriophage; screen resistant strains against other bacteriophage; and identify candidates for combination into a wide-spectrum 'phage-cocktail' active against strains of Bacillus.

This study adopted several established methods for the identification and isolation of bacterial strains and the propagation and screening of bacteriophages. Methods were developed and optimised for the generation and screening of resistant bacteria. The Phage-Host Spread method was used as a room temperature equivalent to the Double Agar Overlay method. The Susceptible Host Elimination method was used to screen resistant bacterial strains of *B.cereus* and *B.thuringiensis* against other bacteriophages.

Three resistant colonies of *Bacilli* were isolated. The experiments proved that *Bacillus* specific bacteriophages do express different mechanisms of action to infect and lyse bacteria. Bacteriophage RW has a different mechanism of action against *Bacillus cereus* from that/those of bacteriophages AB1, LCH and γ.

The Susceptible Host Elimination method, though most laborious, was the most effective and reliable method for the generation of bacteriophage plaques. From the results presented, bacteriophage RW warrants further investigation within a bacteriophage cocktail with at least one of bacteriophages AB1, LCH and γ; to produce a formulation with more than one mechanism of action against *Bacilli*. *Bacilli* use multiple mechanisms to mount resistance against bacteriophages to which they are usually susceptible.

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Development of a homology model of *Bacillus anthracis* MetRS1 as a tool for drug design

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Bacillus anthracis methionyl tRNA synthetase (MetRS) structure has not been obtained yet, the bacteria causes anthrax and can be lethal if treated late, so effective antibacterials need developing; researchers' aims are to prevent bacterial growth; one way is to target MetRS1 which is an enzyme essential for protein synthesis.[1] The aim was to build a homology model of *Bacillus anthracis* MetRS1 by analysing and comparing the protein sequences of other MetRS1 enzymes and to build the model using a suitable structure template.

ExPASy was used to analyse protein sequences, and comparison of the sequences used Clustal Omega; this identified similarities by matching residues between the templates and the query sequence. The Phylogeny server produced a phylogenetic tree to observe closely related species. The Protein Data Bank, (PDB) identified suitable structure templates. Building the homology model required Molecular Operating Environment, (MOE) 2012 software.[3] Several validation methods; Ramachandran plot, ERRAT, Verify 3D, ProSA and docking were used.

The active site was confirmed for *Bacillus anthracis* MetRS1 when comparing sequences, as key residues such as HIGH and KMSKS were identical; these are located in the conserved regions of the Rossmann fold (2). *Bacillus anthracis* MetRS1 model had a potential zinc binding region using *E. coli* as a template. Model validations looked at the side chain environments and the backbone of the protein structure using five different methods, overall the model was of a good quality. The natural substrate, methionine was docked and it was able to interact within the active site; key residues being Gln57, Gln60, Lys61, Asp133 and Asp 159.

The model contained the conserved regions found in the MetRS1 general class. Poor quality residues were located outside the active site so the template used was appropriate. Docking ligands confirmed an active site; this can be used as a tool for drug design.

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An evaluation of inhaler technique in patients in the Cardiff and Vale area

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The use of inhaler devices has become the favoured route of drug delivery in the therapy of respiratory conditions such as Asthma and COPD.[1] This is due to the localised effect of inhalers. The NHS spends £1 billion annually on asthma treatment, the majority of which is spent on the most symptomatic patients.[2] It is well documented that inhaler technique in patients[3] and in Healthcare Professionals[4] is of poor standard. The aim of this study is to evaluate the inhaler technique of patients in the Cardiff and Vale area.

This study had two arms; a semi structured interview with pharmacists to cover how they guide patients with inhaler technique, and a short questionnaire for patients followed by an inhaler technique test. A total of 45 pharmacists were randomly selected to represent the health board. The data was presented as a coding sheet and analysed using thematic analysis. Quantitative data was analysed using Graphpad Prism. All data was anonymised. Ethical approval was granted and the study was accepted as an NHS service evaluation.

89 patients were recruited for the study. Only 3% received a good score using the MDI (n=67) and 29% using the DPI (n=48). Of the HCP's studied, more than half of patients were seen by the nurse and only 6% saw the pharmacist. Just over 12% of patients had never been shown. Only 36% use In-check/Aims devices when giving advice. When asked how often advice is given, the results were Always (42%), Most of the time (27%), Sometimes (58%) and Rarely (4%).

Patient inhaler technique was generally poor. Also, healthcare professionals should receive more training and use of teaching tools should be increased such as the In-check/AIMs devices. Patients should be reminded frequently of correct inhaler use to reinforce the importance of correct treatment.

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The use of mast cell and neutrophil cell lines to study extracellular traps

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Neutrophil extracellular traps were first documented in 2004 by Arturo Zychlinsky and co-workers.[1] They were described as web like DNA structures decorated with granule proteins that trap and kill microbes. Research has more recently discovered that extracellular traps (ETs) are not limited to neutrophils; other cells of the immune system such as mast cells are capable of producing ETs.[2] The precise stimuli of ETs are still unknown. In this paper Toll-like receptors, a family of innate immune receptors capable of responding to pathogen associated microbial patterns, were tested to determine their role in ET stimulation.[3]

Mouse liver mast cell line MC/9 (ATCC CRL-8306) and Human HL-60 cell line were cultured and incubated with Phorbol Mystyrate Acetate (PMA) and human Toll-like receptor agonists to stimulate ETs. PMA artificially stimulates cells by activating protein kinase C.[4] DNA release was quantified using Sytox green, a DNA dye which cannot permeate cell membranes. Cells were fixed and stained for fluorescence microscopy using Hoechst, a fluorescent dye.

Liver mast cells proved to be problematic and were unresponsive to artificial stimulation with PMA and physiological agonists. High levels of DNA release was measured from untreated and treated cells. The absence of ETs was confirmed by fluorescence microscopy; however the cells did respond to activation in the form of cell adhesion. HL-60 cells responded to PMA, confirmed by microscopy, however due to time constraints it was only possible to complete a small range of assays with Toll-like receptor agonists.

Overall it is possible to conclude liver mast cells are unable to produce ETs, but did respond to PMA demonstrated by increased cell adhesion. The HL-60 cells produced ETs, but due to time constraints it is not

possible to conclude about the involvement of Toll-like receptors in ET stimulation, hence further work is required.

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Can Src kinase inhibition improve chemotherapy response in breast cancer?

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Triple negative breast cancer (TNBC) represents an aggressive form of breast cancer with no defined drug targets.[1] As such, treatment typically consists of chemotherapy, although the long-term prognosis remains poor.[2] Studies have revealed a role for the pro-metastatic Src family of kinases as mediators of chemosensitivity in various cancer types, where increased Src activity is associated with reduced drug response.[3] The aim of this project was to investigate whether inhibition of Src can improve response to epirubicin in a cell model of TNBC.

MDA-MB-231 cells (TNBC) and MCF-7 cells (a model of ER+ breast cancer as a comparison) were exposed to the Src inhibitor, saracatinib or epirubicin as single agents and changes in cellular growth measured using the MTT assay. The effects of treatment with saracatinib and epirubicin combined on cell viability were determined by MTT assay and Immunocytochemical staining for the proliferation antigen, Ki67. Src activity was monitored by Western blotting, as was any change in apoptosis, using antibodies that recognised PARP cleavage.

The study showed that addition of saracatinib did not further reduce growth inhibition in the MDA231 cell line, despite reduction in Src activation and a reduction in the proportion of Ki67 positive cells. Conversely MCF-7 combination treatments demonstrated a moderate dose-dependent increase in chemosensitivity versus either agent alone, although this was not accompanied by a decrease in Ki67 positive cells.

Despite decreasing Src activity, saracatinib had little effect on growth inhibition. This is likely due to the more prominent role that Src plays in pro-invasive pathways that promote tumour metastasis, as opposed to cell growth.[4] Further evaluation of the effects of the combination treatment on proliferation, and investigation into any potential anti-metastatic role is required to determine if this combination treatment has a future in the clinical setting.

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What influences motivation for student academic achievement? The perspective of final year Cardiff MPharm undergraduates

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Motivation has been defined as '*the willingness to attend and learn material in a development program*'.[1] Self-Determination Theory suggests that intrinsic and autonomous extrinsic motivation facilitate the promotion of learning and achievement and can be enhanced or impaired by others, such as academics.[2] Teaching practices, assessments and many other factors within Cardiff University's school of pharmacy and pharmaceutical sciences (CSPPS) can also affect motivation.[3] The aim of the project was to identify what influences motivation for students' achievement throughout the MPharm degree from the perspective of final year undergraduates at Cardiff MPharm.

A topic guide was developed through literature review and discussions within the research team and was approved by CSPPS research ethics committee. Each project student conducted four 1-to-1 semi-structured interviews that were arranged according to the participants (final year MPharm students). These were recorded after obtaining consent. The interviews were transcribed, shared within the research group and individually analysed qualitatively using inductive and deductive thematic analysis[3] to determine what factors affect participant's motivation.

Sixteen MPharm IV students were recruited. Three main important themes were identified; motivation towards final year project, assessments and attendance at teaching sessions. It is clear that lecturers play a crucial role in the identified themes, and was identified by the participants that they were generally highly motivated by concise, clear, passionate and supportive lecturer traits. Most participants were found to be extrinsically motivated towards high weighted assessments. However, they were also intrinsically motivated towards assessments that they enjoyed or found interesting.

The findings from this investigation may be useful to CSPPS for identifying factors that motivate undergraduate students, however, it is clear that the MPharm IV interviewee's are all individually motivated by different factors and by varying degrees, thus, it would be impractical to use a universal approach to enhance academic motivation.

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How does patient counselling affect the application forces people use to apply microneedle patches?

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First conceptualised in the 1970s[1], microneedles (MN) provide an alternative to intradermal injections and do so by circumventing the barrier properties of the stratum corneum. MN allow painless delivery across the skin[2] with minimal infection risk.[3] Use of MN by patients is not currently fully understood, with only one previous study describing application of MN by patients following instruction.[4] A baseline study, previously conducted by the research group, determined the intuitive forces used by people to apply 'dummy' MN patches. Our study aims to develop a patient counselling session to minimise variability and increase reproducibility of MN application forces by participants.

A counselling session comprising practical demonstration and verbal counselling was developed. The session utilised a 'sponge' training tool allowing participants to practice application force. Participants were recruited by purposive convenience sampling. Following counselling, participants applied 'dummy' MN patches to themselves and the researcher. A feedback questionnaire completed after the study provided opinions about MN and patient counselling.

Results from the 52 participants displayed a reduction in mean application forces and standard deviation values for counselled participants compared to baseline (18.28±12.39 N to 9.97±5.67 N). A reduction in the range of forces used (58.76 N to 29.87 N) and maximum application force (59.68 N to 32.10 N) was also observed. Responses to the questionnaire showed a positive participant attitude towards MN application and the use of practical demonstration as a means of counselling.

The study demonstrated that patients can be trained towards a more consistent application force enhancing potential MN usability in the future. The counselling session was effective and well accepted by participants, demonstrating potential use in the clinical setting for increased patient acceptance of MN with minimal additional cost. In conclusion, this study has provided evidence that patient training has considerable impact on increasing reproducibility and reducing variability of MN application force.

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Patients' perceptions of the inclusion of 'prescription drug costs' on dispensing labels

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In the UK, medicines wastage costs the NHS an estimated £300 million each year.[1] It has been proposed that the inclusion of prescription drug costs on dispensing labels would increase patient awareness of the cost of medicines, leading to reduced wastage. The aim of this project was to gain an insight into patients' perceptions of the cost of medicines and gauge the potential effect of the scheme on patients if it was implemented.

Ethical approval was granted by the SPPS Research Ethics Committee.Thematic analysis of data collected prior to the project from 50 community pharmacy patients was conducted. Participants ranked medicines in terms of cost, followed by a short discussion including whether the cost of medicines affects how they take or order their medicine. Themes that emerged from analysis were used to inform the design of a patient leaflet which would accompany medicines given out about the scheme. The leaflet was piloted in a convenience sample of 5.

Fourty nine (98%) participants ranked medicines in terms of cost incorrectly suggesting patients' perceptions of the cost of medicines are generally poor. Eighteen (36%) participants said knowing the cost of medicines would cause them to consider more carefully whether to order them. The leaflet pilot suggested a short description of the cost should be included on the label so that the cost would have a clearer meaning.

The inclusion of prescription drug costs on dispensing labels has the potential to increase patients' awareness of drug costs and therefore to decrease wastage to some extent. It is recommended that the scheme is piloted on a small scale to establish whether wastage would be reduced in practice.

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Review of Medication Administrations (MAR) charts from care homes

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Care home residents are subject to numerous medication errors. The aim of the group study was to determine the type of errors that occur through the study of Medication Administration Records (MAR), and the frequency of each error type.

10 volunteering care homes in the Abertawe Bro-Morgannwg University Health Board (ABMUHB) area provided MAR charts for each patient in October. Meetings were held over three weeks to determine the types of errors to be categorised along five main divisions; Regulatory error, Administration error, Risk error, Stock error and 'Cannot be judged'. Two validations were carried out to ensure the standardisation of the group. One care home was then randomly allocated to each member of the group for data collection.

The 17 residents of the care home studied were on average 85.65 years old and taking on average 8.65 medications (± 3.79). Residents had an overall mean of 65.47 errors (± 47.51), with the mean number of Regulatory, Administration, Risk and Stock errors were 7.58, 40.87, 3.45 and 18.29 respectively. By sub-categorising each error type, omissions were identified to be the highest source of error, weighted at 48.3% of the total errors.

Inaccurate records of medication administration can affect patient safety to different extents. The inaccuracy of MAR charts may reflect on the difficulties faced by staff when administrating medication to patients, and it is clear that schedules can be difficult to adhere to when nurses are faced with numerous medications. Other failures such as inadequate stock control can lead to medicine wastage and financially impact on the care home, and action is needed to ensure consistency between staff members.

Evaluation of inhaler techniques in patients of the Cardiff and Vale Health Board

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Correct inhaler technique is essential for effective drug delivery and response to treatment yet it is well recognised in literature that many patients are unable to use their devices correctly.[1] Patient education is a large factor in achieving correct technique and regular interventions to reinforce information are needed[2] from healthcare professionals[1,3] (HCPs). The aim of this study was to evaluate the impact increased length of time without healthcare professional intervention has on inhaler technique by assessing a sample of patients and interviewing community Pharmacists within the Cardiff and Vale UHB

Both patient and Pharmacist groups were recruited opportunistically. Patients were asked a series of background questions prior to being assessed using a Vitalograph Aerosol Inhalation Monitor to produce a score of good, sub-optimal or fail based on several parameters related to correct technique. Pharmacists completed a semi-structured interview. The interviews were transcribed verbatim and evaluated using thematic analysis.

There was no clear association between patient inhaler technique and length of time since last educated by a HCP. Of the 15 patients who had been shown how to use their inhaler in the last month, none could achieve a 'good' score and 9 actually 'failed', indicating a problem in the education provided by healthcare professionals which were further explored.

Patients are not retaining information to the level HCPs believe they are. Annual reviews alone increase preventable patient risks and demands on the healthcare system. Pharmacists are ideally placed for opportunistic interventions to reinforce correct inhaler technique within primary care and relieve this burden from other areas but this needs to be recognised by patients and other HCPs alike. Where patients are found unable to use a device, alternatives should be considered and the motivation for prescribing inhaler types with higher failure rates reviewed.

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How does 'device feedback' affect the forces people use to apply a dummy microneedle patch?

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Microneedles are a promising new drug-delivery device. While having been in existence for over 15 years, there has been little investigation into how people might use them. A previous study ("Baseline Study", unpublished) found that people intuitively used forces of 2-60N to apply a dummy microneedle patch. With such variation in application forces, there is likely to be variation in the penetration efficiency of microneedles and therefore variable drug delivery.[1,2] This study aims to determine how 'device feedback' affects the application forces people use.

Following brief explanation of microneedle technology and study instructions, participants (n=50) applied force, using a Sauter®FH100 digital pressure gauge, to dummy microneedle patches located on the forearm and deltoid of themselves and the Researcher. The gauge was programmed to 'beep' and show a red light at 15N – this acted as 'device feedback'. Maximum force used (from 3 measurements) on each site was recorded. A questionnaire was designed to gather participants' views of various study aspects

'Device feedback' significantly reduced the variance of forces seen in the Baseline study ($p<0.001$). Participants used less force when applying a dummy patch to the Researcher (17N±2.43), than when applying it to themselves (19.28N±4.46). Participants generally felt confident in applying the dummy patch, attributable to the 'device feedback', namely the 'beep', assuring them of the correct application force. Suggested changes to the indicators included a louder 'beep' and repositioning the red light.

With incorporation of 'feedback' technology, application forces used by patients would be more reproducible. This means that researchers, healthcare professionals and patients can be more assured of microneedles' ability to effectively and consistently deliver medication. Further work needs to be done, to determine how 'device feedback' could be incorporated into microneedle or applicator design and whether it would be cost-effective or detract from microneedles' merits.

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How can error recording and investigation improve the processes for the issue of blood in Wales?

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The Welsh Blood Service is involved with collecting, testing, processing & distributing blood components to 16 hospitals in Wales.[1] The project focussed on the issuing process, which is comparable to dispensing. The aim was to explore and investigate 'unissued' errors within the issuing process and determine causes and contributing factors. 'Unissued' errors are errors detected within the department prior to them leaving the building resulting in the products being unissued. The objectives were to develop an in-depth understanding of the process; draw parallels between issuing and dispensing; identify the nature of errors and explore the root causes.

A retrospective analysis of errors from the previous 12 months was conducted to determine the nature of errors, which were used to develop an interview schedule. Ten semi-structured interviews were conducted with staff to explore the causes and reasons of errors. Purposive and convenience sampling was used to include a variety of participants. Interviews were transcribed and analysed into themes and displayed using fishbone diagrams.

Key topic areas derived from the retrospective analysis included errors involving incorrect number (14%), groups (13%), components (9%), hospital (13%), expiry related errors (10%), specific requirements (8%) and high frequency of errors on Monday and Friday mornings (21%). Causes fell into six categories: Work Environment, Communication, Team, Task, Equipment and Individual. The staff's perceptions of causes included interruptions, high workload, being short staffed, legibility of forms and similar names.

The issuing process is continuously developing and much has been learnt from analysing 'unissued' errors. Four recommendations were made to target key factors and reduce errors; development of a web-based system, re-arrangement of staff during busy days, separately storing similar sounding commercial products and regular error team meetings. These recommendations were based on developments seen within pharmacy to reduce dispensing errors,[2,3] since similarities were seen between the two processes.

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What could affect one's motivation? Exploring the views of 4th year MPharm students at Cardiff

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According to Self-Determination Theory,[1] motivation drives someone to do something. Two basic type of motivation are intrinsic and extrinsic motivation. Intrinsically motivated people do something due to interest while people who are extrinsically motivated do something due to external pressures.[2] No studies have been

published in relation to motivation specifically in final year MPharm students at Cardiff. It was decided to explore the views of 4th year students on factors that could motivate them in relation to the degree and to identify the possible ways in which the school may further increase student motivation.

Four researchers and a supervisor developed a topic guide together through review of the literature and group discussions. Researchers first piloted interviews with each other. Following ethical approval and piloting, each researcher conducted 4 semi-structured interviews.[3] A combination of purposive and convenience sampling was used to recruit 16 participants with various characteristics. The interviews were audio-recorded with consent and transcribed ad verbatim. Transcriptions were shared amongst researchers but analysed independently using inductive and deductive approach of Thematic Analysis (TA).[4]

The major themes identified were: 1) Impact of lecturer characteristics, 2) Sees the relevance to future professional life 3) To what extent an individual performs and participates, 4) Influence of others 5) Motivation is not a constant.

There were several motivating factors that affected students in the study and two major motivating factors were lecturer characteristics and students being able to see the relevance of teaching sessions and topics to their future career. Lecturers may wish to address issues that could negatively influence students and ensure course topics relate to their future career. This could lead to an increase in attendance of teaching sessions and/or development of interest in topics. Students were motivated differently throughout the programme therefore further longitudinal investigation is needed.

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Which polymer is best? A meta-analytical study to identify pattern in molecular imprinted polymer performance

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The field of molecular imprinting has grown substantially over the last few decades. Molecular Imprinting is a method of forming complementary sites for a specific template molecule through the use of various fundamental components.[1] This produces a resulting polymer product around the template. When the template is a drug molecule the resulting polymer resembles the drug receptor.[2] This study aims to see which type of design method produces the best Molecular imprinted polymers (MIP), specifically the design method producing MIP which bind tightly and have a good capacity of binding. The study measures the MIP binding affinity and binding capacity using the dissociation constant (Kd) and Bmax values respectively.[3]

An in depth meta-analysis was undertaken. Relevant research articles on MIP containing bound vs free binding isotherms were found, design methods were noted. Data was standardised by converting the free and bound data to uM and nmol/mg concentrations respectively. Graph pad plotted the new standardised binding isotherms and generated Kd and Bmax values. MIP produced by the different design methods could now be compared.

Kd values evaluated the strength of binding within MIP. MIP designed by computational methods showed to have the lowest Kd and thus greatest affinity (N=5 Mean Kd=5.54), followed by combinatorial (N=2 Mean Kd=208.3), NMR (N=6 Mean Kd=365.2) and lastly intuitive methods (N=12 Mean Kd=397.50). The capacity of binding was measured using Bmax values. Combinatorial methods producing MIPs had the best Bmax values (N=2 Mean Bmax= 201.91) followed by Computational (N=5 Mean Bmax=181.38), intuitive (N=12 Mean Bmax=144.43) and lastly NMR (N=6 Mean Bmax=90.04).

Computational and Combinatorial design methods showed promise as the best for producing MIP, after analysing the binding indicators. The design of MIP through Intuitive or NMR methods showed limited potential in producing MIP with good binding efficacy.

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Synthesis of anti-dengue virus nucleoside analogues

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Dengue fever affects 50–100 million people each year, with over 2.5 billion people being at risk of infection. Even though dengue infection appears relatively mild and self-limiting, up to 5% of infected individuals may develop more severe forms of dengue namely Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) which can be fatal.[1] There are no licensed medication to treat dengue infection. NS5 polymerase has received great attention as a potential therapeutic target since polymerase activity is essential for viral replication. The aim of this project was to synthesise a novel nucleoside analogue **1** that will inhibit NS5 polymerase.[2] Compound 1 would then be sent for biological evaluation as a ProTide in the future.

The synthesis of compound 1 involved a 5-step process which was taken from published literature experimental procedure.[3]

In step 1, compounds 6a, 6b, 7, and 8 were synthesised by nucleophilic aromatic substitution reaction. The low yield obtained of compound 6a led to alterations in literature experimental procedure which proved to be beneficial as greater yield of compound 6b was achieved. Step 2 involved the reduction and cyclisation of compounds 6b and 7 to form compounds 9 and 10. It was apparent that this step may have been temperature sensitive. In step 3, very low yields of compounds 11 and 12 were obtained. This may have been attributed to product degradation because formamide was added in excess. Steps 4 and 5 were unable to be carried out due to the low amounts of compounds 11 and 12.

To conclude, eight intermediate compounds were synthesised from steps 1 to 3. The low yields obtained suggests that further optimisation is necessary when these steps are carried out again in the future.

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Patient satisfaction with information about their medicines at Betsi Cadwaladr University Health Board

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The NHS always aims to improve patient experiences and satisfaction.[1] Patient satisfaction and the effectiveness of medicines management are important indicators of the quality of hospital services delivered to patients.[2,3] Standards for Health Services in Wales support the NHS to ensure patients receive appropriate medicines information.[4] The aim of this study was to identify patient experiences and their satisfaction with information provided about their medicines during their stay and on discharge from hospitals within Betsi Cadwaladr University Health Board.

After ethical approval was obtained, recently discharged medical (Wrexham Maelor) and surgical (Ysbyty Gwynedd) patients were identified from discharge prescriptions and patient demographics were recorded. To be eligible for participation, patients had to be over 18 years old and on at least one medication. A questionnaire in English and Welsh, a covering letter and a free-post envelope were distributed to all eligible patients over a two-week period. Responses from the returned questionnaires were inputted and analysed by using SPSS. Chi-square statistical test was conducted to determine the significance of answers.

A total of 394 questionnaires were distributed, which yielded a 38% response rate. The mean age was 68.06 years (SD 14.345) and 56% of the patients were female. The mean number of medicines taken by patients was 6.62 (SD 4.506). Most patients were either satisfied or very satisfied with the information provided about

medicines whilst in hospital (85%) and on discharge (92%). The majority (82%) of patients were given the opportunity to discuss their medicines. There was a significant association between level of satisfaction and opportunity given to discuss medicines ($p < 0.001$). Some areas for improvement were identified.

Although satisfaction was high, this study demonstrates further opportunity for improvement in the quality of medicines information provided to patients.

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Characterising protein complexing with drug delivery vectors called cell penetrating peptides

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CPPs have gained increasing interest over the last two decades in their involvement in drug delivery and their attachment to various cargo for cellular delivery of therapeutics. Visualisation of the complex formation between CPPs and their nucleotide cargo using gel shift assays are shown in many manuscripts before complexes are introduced into cells. These assays are routinely used for siRNA and other nucleotides, comparing band migration as the molar ratio of CPP to cargo is increased.[1] So far, only a few manuscripts cover the visualisation of comple**x** formation between proteins and CPPs[2] and predominantly only focus on the effects CPPs have on the intracellular delivery of the proteins in question.[3]

During the course of this study, three methodologies were tested to help visualise complexation between CPPs and the model protein, bovine serum albumin (BSA). These methodologies consisted of agarose gel electrophoresis, sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS PAGE) and native PAGE. This was via observing the migration of CPP/Protein bands through a gel with increasing molar ratios of CPP to protein and quantifying band intensity.

Results showed streaking of all protein bands in the agarose gel, but as CPP/Protein ratio increased, band intensity gradually decreased. SDS PAGE showed no alteration in band intensity as molar ratios increased due to denaturing of the protein and affecting the complex. Native PAGE displayed a marked decrease in protein band intensity along with a reduction in band migration as CPP/Protein ratios increased.

Overall, native PAGE proved to be the most optimum methodology of the three, as it successfully showed a reduction in both band intensity and band migration. Therefore giving rise to the possibility that it could become a new standard procedure for visualisation of CPP/Protein complexes in the future. This represents a promising template to further explore and monitor the capacity of CPPs to complex proteins and then deliver them into cells

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Design and synthesis of bacterial MetRS inhibitors

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Methionyl-tRNA synthetase (MetRS) is one of twenty aminoacyl-tRNA synthetases that play the key role of aminoacylation of tRNA in protein translation.[1] Inhibition of this enzyme leads to cessation of protein synthesis and thus inhibition of bacterial growth and replication.[2] The aim of this project was to design and synthesise a range of novel inhibitors to inhibit MetRS in resistant bacteria, attenuating their growth and division.

Design of the compounds was achieved through inspection of Al-Moubarak and Simons' homology model of C.difficile MetRS.[3] This allowed the adaptation of a lead compound from a previous MPharm project.[4] Three main adaptations were made to the apparent pharmacophores; the biaryl, aryl and linker moieties were modified. Example compounds were docked in the MetRS active site using MOE software to analyse interactions.

Docking was performed on MOE with conformation of best fit visually inspected followed by inspection of binding interactions. Two broad compound groups were synthesised, thioureas and sulfamides. The thioureas were synthesised with a simple 4-step synthetic method while sulfamides were synthesised with a 5–step method.

Two novel thioureas and three novel sulfamides were synthesised with respectable yields achieved in each synthetic step. Products were characterised as analytically pure by TLC, NMR (^{1}H and ^{13}NMR), melting point and mass spectrometry where appropriate. Synthesis using a hypoxanthine base was not successful due to 1,4-disubstitution accountable to tautomerisation.

To conclude, the synthetic pathways were successful in forming novel compounds in preparation for antimicrobial screening and could be used in future for the rapid synthesis of many more possible inhibitors. The role of the linker, biaryl moiety and aryl substituents were investigated to explore the SAR of MetRS inhibitors.

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Can Src inhibition improve chemotherapy response in colorectal cancer?

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With approximately 40,000 new cases and 16,000 deaths annually in the UK,[1] colorectal cancer (CRC) remains a fatal condition. Treatment of CRC currently involves chemotherapy; however acquired resistance poses a major threat to successful treatment.[2] Recently, studies looking at the pro-metastatic Src family of kinases have discovered that CRC resistance is associated with elevated levels of Src activity.[3] Consequently the role of Src inhibitors has become an extremely interesting area of research. The aim of this project was to investigate if Src inhibition would improve sensitivity to epirubicin in CRC cell models.

Saracatinib, a Src inhibitor, and epirubicin were individually applied as treatments to two CRC cell lines, HRT18 and HT29. Growth inhibition of cells was determined by MTT assay. Combination therapy was explored and changes in cellular growth were again measured by the MTT assay, whilst cell proliferation was determined by Immunocytochemistry which involves staining for Ki67, a proliferation antigen. Western blotting was used to reveal Src activity levels of both cell line, and antibodies recognising cleavage of PARP were used to detect apoptosis.

Whilst this study showed that saracatinib monotherapy was ineffective in HRT18 and HT29 cells despite suppression of Src activity, epirubicin treatment greatly reduced HRT18 cell viability, whilst only affecting HT29 viability at its highest concentration. HRT18 cells responded well to combination therapy as an extensive reduction in cell growth and in the number of proliferating cells was observed. Despite this, Src activity remained unaffected in HRT18 cells. Conversely no clear correlation was obtained for HT29 cells following combination therapy, although interestingly there was a reduction in Src activity.

This data suggests that Src inhibition alongside chemotherapy may be of benefit but only in specific cases. Further research is needed to identify cellular determinants of combination chemosensitivity.

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Evaluation of the induced genes MAML2 and GNE derived from novel endocrine resistant breast cancer models

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Breast cancer is a disease closely linked to oestrogen, with 70% of breast cancers being oestrogen receptor positive (ER+),[1] making adjuvant endocrine therapy very useful.[2] However, 40% of patients develop acquired endocrine resistance, resulting in poor prognosis.[3] An acquired endocrine resistant cell panel to model long-term resistance to tamoxifen, Faslodex or oestrogen deprivation in Luminal A and B subtypes of ER+ disease has recently been developed. Preliminary Affymetrix microarray analysis showed MAML2 and GNE gene expression was induced in all three types of resistance derived from Luminal A MCF7 cells. This study aims to verify the profile of MAML2 and GNE in the MCF7-derived cells and examine if they are similarly induced throughout the Luminal A and B-derived resistant model panel, considers if their expression is linked to ER status or to clinical endocrine outcome, and investigates their ontology.

PCR was used to monitor MAML2 and GNE expression in Luminal A (MCF7 and T47D) and Luminal B (BT474 and MDA361) derived resistant models. Relation to clinical endocrine outcome was examined using KM plotter and PROGgene tools and ontological information gathered from Pubmed and Genecard.

Both MAML2 and GNE showed increased expression in MCF7-derived and further Luminal A-derived resistant models but not in Luminal B-derived resistant lines. No strong relationship was found between gene induction and model ER status. Clinical endocrine outcome data showed a poorer prognosis for tamoxifen-treated Luminal A patients with high basal MAML2 or GNE. The genes had growth signalling (NOTCH pathway) and metastasis-related enzyme ontology respectively.

Increases in both genes appear to be predominantly related to Luminal A-derived resistance in vitro and in patients. As ontological research suggested both genes have adverse effects in cancer and targeting could perhaps be feasible, it can be concluded that studying the genes further is warranted in endocrine resistance.

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Discharge Medicines Review (DMR) service: a case study at the Royal Gwent Hospital

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The DMR service aims to facilitate the transition of patient care between care settings. The Community Pharmacist undergoes a medicine's reconciliation process, comparing a patient's discharge medication regimen with the first prescription written in primary care. Any discrepancies identified are reported to the GP for amendment.[1] An evaluation of the DMR service was commissioned in 2013; one of the findings was that whilst hospital pharmacists refer patients for a DMR, they are unaware if any of their DMR referrals are completed, and if so, the interventions made.[2] The aim of this study was to evaluate the DMR service referral system at the Royal Gwent Hospital by; determining how many referrals result in DMR's, identifying the types of interventions made and establishing the drugs most commonly involved in DMR discrepancies.

From the DMR forms obtained for the initial evaluation,[2] those completed on patients discharged from the Royal Gwent Hospital were collated. The forms were reviewed and the relevant data collected from them. The data was analysed using Microsoft Excel® 14.1.4. Ethics approval was obtained from CSPPS

Four community pharmacies had completed DMR's on patients discharged from the Royal Gwent Hospital. Of the 79 DMR forms reviewed, 94% were found to be direct hospital service referrals. There were 154 discrepancies reported on 56 DMRs resulting in a mean of 2.8 discrepancies per DMR (range 1-12). Almost half (48%) of the discrepancies were attributed to the unintended omission or inclusion of drugs on the first prescription post discharge. Cardiovascular drugs represented 42.5% of all discrepancies reported.

The hospitals DMR referral system is beneficial and should be continued. It ensures primary care healthcare professionals receive complete and accurate discharge information in a timely manner, enabling an efficient transfer of patient care and allowing community pharmacists to make interventions where necessary.

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The potential link between ageing, clathrin-mediated endocytosis and Alzheimer's disease

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Alzheimer's disease (AD) is a progressive neurodegenerative disease. Accumulation of neurotoxic amyloid-β (Aβ) generated by the amyloidogenic cleavage of amyloid precursor protein (APP) is a hallmark pathological feature of AD.[1] APP is taken up into vesicles via clathrin-mediated endocytosis (CME) and is cleaved within endosomes.[2,3] The study aimed to determine whether changes in CME occur in mice with AD-like pathology and with age.

Expression of the key CME proteins clathrin, PICALM, dynamin I and BIN1 in transgenic (Tg) and age-matched wild type (WT) mice cortices aged 3-, 9- and 18-months was studied. Tg mice over-expressed the London mutation of human APP and so over-expressed Aβ. Proteins were examined by Western blotting and enhanced-chemiluminescent detection and the resultant immunoblot protein bands were quantified by densitometry and statistically analysed.

Compared to WT mice, increased expression in all key proteins, except BIN1, was observed in 3- and 9-month Tg mice; however, clathrin and dynamin showed a decrease at 18-months. BIN1 expression decreased at 3- and 18-months. Dynamin expression decreased with age in WT mice whilst similar levels of clathrin and PICALM were expressed at 3- and 9-months and decreased at 18-months. In Tg mice, clathrin levels decreased significantly with age. PICALM and dynamin expression increased at 9-months compared to 3- and 18-months. Some results were not statistically significant.

The CME protein expression changes indicate an upregulation of CME in Tg mice at certain ages with a downregulation of CME with increasing age in WT mice. A decrease in clathrin expression in Tg, compared to WT, mice occurred at an earlier age suggesting AD-like pathology could have influenced endocytic protein expression and therefore CME. Further investigation is required to determine CME activity in Tg mice with increasing age. Endocytic changes noted could affect the production of Aβ and hence contribute to AD pathology.

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Exploring the downstream signalling effects of zinc transporter ZIP7 and the implications for cancer

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The essential trace element zinc has recently been discovered to be an intracellular second messenger.[1] Zinc concentration must be tightly controlled by zinc transporters that regulate its homeostasis.[2] Zinc transporter ZIP7 is located on the endoplasmic reticulum and releases zinc into the cytoplasm in response to an extracellular stimulus.[2] This stimulates signalling pathways that cause cell proliferation and migration, a process exploited by some cancers.[3] Blocking ZIP7 is therefore a potential target for novel cancer therapy.[3] Phosphorylation of amino acid residues S275 and S276 is essential for ZIP7 function[2], this study investigated potential downstream effectors of ZIP7-mediated zinc release.

Western blotting was carried out using MCF-7 cell lines transfected with wild-type ZIP7 or S275A/S276A mutant, where A blocks phosphorylation. Cells were lysed after 0, 2, 5, 10, 15 and 20 minutes of ZIP7 stimulation. Cell lysates were probed for activation of downstream signalling molecules and pZIP7S275/S276. Samples were normalised to V5 and densitometry data was analysed using Prism software. Statistical analysis was carried out using ANOVA tests, with Dunnett post-hoc tests on any significant results. Significance was assumed with $P < 0.05$.

The results suggest that other amino acid residues besides S275 and S276 may be phosphorylated during ZIP7 activation, as AKT is activated in the S275A/S276A mutant. However the full significance is unclear due to conflicting results. This study demonstrated the activation of some novel downstream signalling pathways that were activated by ZIP7-mediated zinc release.

More investigations are needed on alternative residues to assess the importance of phosphorylation, however the suggestion of involvement in ZIP7 function in this study opens the door to more potential targets for ZIP7 inhibition. The discovery of novel pathway involvement suggest that ZIP7 is a good potential target for novel cancer therapy.

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MarinLit database mining in drug discovery

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MarinLit, a commercially available electronic database that is dedicated to marine natural product research has been established by Royal Society of Chemistry (RSC) lately[1]. Due to the rise of marine drug discovery in recent years[2], an extensive database is needed for rapid dereplication. The aims of this study were to use this MarinLit database to analyze existing data and in the meantime outline the role of this database in marine drug discovery.

To evailuate the potential of this database, a group of extracts molecular weights from different sponge species that are active against Methicilin-resistant Staphylococcus aureus (MRSA) bacteria was evaluated using MarinLit. Firstly, the compound hits were searched in both MarinLit and SciFinder Scholar (SFS) using the molecular weights given and then compared to access the usefulness of MarinLit. By utilizing the 'taxonomic search' and ChemSpider link available in MarinLit, the hits found were then evaluated using refinement approach in terms of taxonomy, mass spectrum and drug-like properties to search for the best candidates of interest.

Significant lower number of hits found in MarinLit than in SFS by molecular weights were shown and the conciseness of MarinLit in marine natural product was proven. 75 molecular weights were proposed to be novel compounds and 32 molecular weights were suggested as possible novel compounds using MarinLit. In total, 299 drug-like candidates were identified from more than 2000 suggested compounds for the samples after refinement method.

The results shown that Marinlit is a useful and effective database as it has unique searchable features and powerful dereplication tools that helps to analyse the enormous sets of data and identify the potential novel compound. Also, it is more concise and less-time consuming compared to the comprehensive database like Scifinder. In short, it is helpful to the marine natural product researchers in marine drug discovery.

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Assessment of the physiochemical stability of neonatal lipid and vitamin parenteral nutrition (PN) mixtures when stored in different types of delivery containers

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PN must be sterile and stable throughout manufacture and storage to ensure administration of a safe product and to minimise harm to patients. PN has been effectively stored in glass and plastic containers like infusion bags[1], however administration devices such as syringes are increasingly being used to store and then deliver PN despite a lack of research into their safety and suitability for this task. This study aims to assess lipid emulsion (comparing the preparations; Intralipid® 20% and SMOFlipid® 20%) stability when stored in infusion bags, glass bottles and syringes. The research focusses on using globule size analysis and pH measurements to assess the stability of said lipids when stored in the specified containers over 72 hours.[2]

Mixtures of 10ml multivitamin preparation, Vitlipid® N Adult and 40ml of the lipid emulsion were prepared in a class 100 laminar air flow cabinet and then stored in the specified containers at 35°C. Aliquots, aseptically extracted were then tested at 24 hour intervals to detect changes in stability such as an increasing globule number, size and changes in pH using laser diffraction, light microscopy and pH measurements.[3]

Both lipid emulsion mixtures remained stable with little variation observed between the different storage containers. A small increase in globule size distribution was detected in all cases, with the largest globule measured being 1.906µm in size as measured by laser diffraction, which is below the 5µm minimum threshold typically used to assign stability.[4] The largest observed via microscopy was 30µm and a slight decrease in pH was seen in all cases.

Little variation in the stability of lipid emulsion mixtures stored in the specified containers was observed, however due to the lack of overall evidence on syringe storage devices such as their extractable properties, more research is needed before this should be advised. Unfortunately, an investigation into vitamin stability was not possible in the timescales of the project however it would be beneficial to do so, to gain a wider understanding of PN admixture stability overall n these type of containers.

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Characterising the impact of temperature and humidity on the puncture performance of hypromellose capsules to be used in a dry powder inhaler

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Dry power inhalers containing two-piece hard capsules are used to treat pulmonary diseases. Gelatin has been the preferred capsule material.[1] When gelatin capsules are exposed to low humidity conditions the capsules tend to become brittle and can fragment upon puncture.[2] Hypromellose (HPMC) is a material derived from plants and was the first pharmaceutical grade approved alternative to gelatin.[3] The aim of the study was to study investigate the impact of temperature and humidity on the puncture performance of HPMC capsules to be used in a two-pin dry powder inhaler and to develop an innovative method, using optical coherence tomography (OCT), to characterize capsule puncture.

The capsules were stored at 5°C and 20°C over saturated salt solutions to create relative humidities of either 42% (lower end of normal range) or 52% (higher end of normal range). Each capsule was filled with 12.8mg of a budesonide and lactose powder formulation. Conditioned capsules were filled and subsequently punctured with a DPI, connected to a next generation impactor, in ambient laboratory conditions. Following actuation of the device, the mass of aerosolised powder was calculated and the characteristics of punctured capsules were evaluated by light microscopy and OCT.

Overall, HPMC capsules that were conditioned at higher humidity and lower temperature produced slightly larger puncture areas. All HPMC capsules displayed the ability to be punctured in a reproducible manner, which facilitated efficient capsule emptying and there was no evidence of capsule fracture.[4]

The study indicates that temperature may have an impact on the geometry and size of punctures created in HPMC capsules however further work is required to establish this. OCT has been used successfully for the first time to provide three-dimensional characterisation of capsule punctures and therefore may be a useful method to further define capsule puncture performance.

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Characterising the deposition performance of formulation released from conditioned hard shell capsules punctured in a dry powder inhaler

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Dry powder inhalers (DPI) are used to deliver a variety of formulations to the lungs. Capsules for these inhalers can either be made out of gelatin or HPMC[1] and if they're being used across the world, they can become subject to a variety of environmental conditions, such as varying temperatures and humidity. The study aim is to determine how capsule composition and conditioning affect lung distribution of the formulation released from an actuated hard shell capsule via a DPI.

A budesonide/lactose blend was selected as an appropriate formulation for use in the study. Blend uniformity was assured through analysis of a variety of blending methods, where it was found that sieving was the most effective.[2] The formulation was dispensed into HPMC or gelatine capsules, each having been conditioned at differing temperatures and humidity, and actuated in a DPI through a next generation impactor. This allowed the aerodynamic particle size (Fine Particle Fraction (FPF), Mass Median Aerodynamic Diameter (MMAD) and Geometric Standard Deviation (GSD) to be measured for each sample.[3]

A statistical T-test was applied to the dataset which determined two significant differences, one between the FPF ($p=0.009$) and the other between the MMAD ($p=0.03$) of gelatin and HPMC capsules when conditioned at 'Room Temperature and High Humidity'. No statistical differences were found between the capsules at any of the other conditions tested.

A wide range of variability was seen between samples within each environmental condition which may be due to potential unsatisfactory formulation properties, such as the API being unable fully dissociate from the carrier.[4] The results suggest that under 'Room Temperature and High Humidity' conditions, HPMC capsules are more likely to release a higher percentage of API within the respiratory range when compared to gelatin. At all other tested conditions, HPMC and gelatin capsules are likely to perform equally.

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Examination of the adherence ability of spores from epidemic *C. difficile* strains in response to bile salt sodium deoxycholate

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Clostridium difficile is an anaerobic, spore forming bacterium and the leading cause of antibiotic-associated diarrhoea in the UK.[1] Use of broad-spectrum antibiotics causes disturbances in gut flora.[2] *C. difficile* cannot survive outside the anaerobic environment and sustains survival by production of spores.[1,3] Once spores are ingested, they pass through the intestinal tract and come into contact with bile salts, some of which act as spore germinants.[3] In this project, the aim was to explore the action of the bile salt sodium deoxycholate (SDC) on epidemic *C. difficile* spores and find out whether it affects the outer surface properties of the spores, as well as their adherence to stainless steel.

Spores of *C. difficile* DS1813 and DS1748 strains were exposed to 0.1%, 1% and 10% SDC solutions for 10 minutes. Spore solutions were enumerated before and after SDC exposure. Relative hydrophobicity (RH) of the spores was obtained using a MATH test. Stainless steel plate transfer assays were performed on the spores to establish whether SDC affected spore adherence to stainless steel. Scanning electron microscopy (SEM) images were produced to visually analyse differences in spore appearance, before and after SDC exposure.

SDC reduced the viable counts for both strains at all concentrations, except for DS1748 at 1% SDC, where the viable count increased, compared to the neat spores. SDC had varying effects on spore RH, with DS1748 spores at 1% SDC displaying the biggest increase in RH. SDC changed the extent of spore transfer from stainless steel to agar plates. The SEM images appear to show morphological changes in spore surfaces.

The results indicate that SDC is affecting spore surface properties in various ways for the different strains. More research is needed to establish SDC's true action against *C. difficile* spores of additional strains.

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Material and antimicrobial properties of orthopaedic bone cements

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Bone cement is a material used in orthopaedic surgeries to hold implants in bone for hip replacement and knee replacement surgeries.[1] However, infections after these surgeries causes a significant risk, leading to development of antibiotic loaded bone cements.[2,3] This study aimed to look at whether different formulations of bone cements affect the antimicrobial efficiency of gentamicin. This study also looked at the difference in antimicrobial efficiency of gentamicin loaded bone cements (GLBC) in different types of formulations. This study also looked at the difference in time required for the different types of bone cements to mature before and after addition of gentamicin.

Antimicrobial efficiency of different types of GLBC such as the Polymethylmethacrylate (PMMA), Hydroxyapatite (HA) and Brushite were evaluated against common species of microorganisms in orthopaedic surgeries. Moreover, a time sweep rheology test was carried out on all the three types of bone cements with and without gentamicin in order to look at the difference in time required for the bone cements to mature.

Results showed that all three types of GLBC were effective against S. aureus, MRSA and A. baumaannii but not S. epidermidis. Gentamicin loaded HA and brushite bone cements also showed prolonged lag phase of S. epidermidis as compared to gentamicin loaded PMMA. Time required for bone cement to set also increased after addition of gentamicin.

The RP62A strain of *S. epidermidis* was resistant towards 2% GLBC. HA and brushite bone cements are more porous compared to PMMA bone cements, causing it to release more gentamicin, therefore more antimicrobial effect observed. There were also slight changes in the time required to set bone cements after addition of

gentamicin, as increased number of different composition of ingredients will tend to increase the polymerisation time. In conclusion, GLBC are effective against common species of microorganisms in orthopaedic surgeries.

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Can Src inhibition improve chemotherapy response in colorectal cancer?

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Colorectal cancer (CRC) represents a common form of cancer in both males and females globally with a high mortality rate.[1] Treatment of CRC typically consists of chemotherapy although the long term prognosis can remain poor in cases where treatment resistance is apparent. Recently, studies have revealed a role for the pro-metastatic Src family of kinases as mediators of chemosensitivity in cancer, where increased Src activity is associated with reduced drug response.[2] The aim of this project was to investigate whether inhibition of Src can improve response to epirubicin in cell models of CRC.

Two CRC cell lines, HRT18 and HT29, were exposed to the Src inhibitor, saracatinib, or the chemotheraprutic agent, epirubicin, as monotherapies and changes in cellular growth measured using the MTT assay. The anti-proliferative effects of these agents in combination was again determined by MTT assay and further explored through Immunocytochemical staining for the proliferation antigen, Ki67. Both Src activity and expression of the apoptotic marker, PARP, were monitored by Western blotting

This study demonstrated both cell lines are sensitive to saracatinib but respond differentially when treated with epirubicin. Combining saracatinib and epirubicin improved the growth-inhibitory response with a larger response seen in HRT18 cells. Combination therapy also significantly suppressed the Src and Ki67 expression, but did not enhance apoptosis.

Saracatinib had no significant growth-inhibitory effects despite being able to suppress Src activity suggesting Src signalling is not involved in the intrinsic growth capacity of these cell lines. However, further reduction of pSrc in response to combination treatments may implicate indirect Src regulation by epirubicin. Src inhibition might have sensitized CRC cells to chemotherapy as they respond better to combination treatments compared to monotherapies. Overall, Src inhibitor-containing combinatorial therapies may have important clinical implication in CRC. Further study of combination treatments over a broader dose range is needed.

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The development and evaluation of a computer-assisted learning (CAL) package on anxiety and its management

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Recent advancement in technology has given Computer Assisted Learning (CAL) the potential to revolutionize traditional educational methods.[1,2] The aim of this project was to evaluate the potential of a CAL package on anxiety and its management for teaching purposes with MPharm III undergraduates.

A CAL package was constructed using Microsoft PowerPoint consisting of up-to-date and evidenced-based information on anxiety and its management. Images were included to increase student understanding and reduce usage of text. Animations allowed interactive learning and quizzes and case studies allowed students to test their understanding. The role of the pharmacist was included to bridge the gap between theory and practice.[3] A 4-point Likert scale questionnaire was distributed using Google Docs to collect feedback on package presentation, content and overall impression of CAL.

A total of 31 out of 109 students responded (response rate = 28.4%). A majority of the responses were positive. Respondents thought that the structure of the package (87.1%, n=27) and animations used were appropriate (77.4%, n=24). Overall, 96.8% (n=30) of respondents agreed that the diagrams helped their understanding of information. The content was considered relevant (90.3%, n=28) and suitable for MPharm III (87.1%, n=27). Quizzes and case studies were well-received which is consistent with other studies[4]. All students found the package useful and 83.9 % (n=26) would use it for revision.

The majority believed the package was useful and would benefit their practice as pharmacists. However, some improvements were suggested: inclusion of videos, increased information on some topics and more quizzes and case studies. In conclusion, the package is a useful and efficient way of presenting information and should be used in higher education as a teaching aid. Future studies may include determining the value of CAL for CPD purposes and student learning preferences (CAL packages as a supplement or replacement to lectures).

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Molecular modelling studies on the Chikungunya virus polymerase

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Chikungunya (CHIK) is a viral disease which is caused by Chikungunya virus (CHIKV). Currently, there is no vaccine or drug to fight against CHIKV in the market.[1] So, there is an immediate need to develop one and to do so researchers need to know and understand which part of the virus that they are targeting. The aim of this study was to investigate and to build the model of RNA-dependent RNA polymerase (RdRP) of CHIKV (nsP4) by using homology modelling.

Norwalk Virus polymerase was the template used in this study. After optimization was being done on the model, it was being docked with T-705 and T-1105. Both T-705 and T-1105 are nucleoside inhibitor shown to be effective in inhibiting nsP4. The objective of the docking was to improve the model by understand the interaction between the ligand and the model. Then, the model was validated by using Errat and Procheck. When errors were found in the structure, amendment was done by using rotamer explorer or adjusting manually.

Basically, the validation result was improved from the first model to final model through optimization. The final model was considered to be accurate because it managed to include most of the structurally conserved regions of RdRP. One of the examples is the GDD amino acid sequence which is crucial for the coordination of divalent cation in the model.[2]

Overall, the outcome of the study was achieved. However, there is still space for improvement in the study and more optimization is definitely ideal. Also, this study can be followed by discovering the compound which is able to inhibit nsP4.

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Evaluation of FZD5 and MAML2, induced genes derived from novel endocrine resistant breast cancer models

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Breast cancer is the most common female cancer and over 70% express oestrogen receptor (ER+ve disease).[1] Commonly used treatment is endocrine therapy; however, 40% of ER+ve patients acquire resistance[2] causing

tumour metastasis and poorer prognosis. BCMPG have developed a new cell panel that models acquired endocrine resistance in luminal A and luminal B ER+ve disease sub-types. Preliminary Affymetrix profiling suggested that MAML2 and FZD5 genes are induced in two of the acquired resistant models. The project aims to further explore whether these genes are relevant to acquired endocrine resistance.

Resistant models had been derived from luminal A (MCF7 and T47D) and luminal B (BT474 and MDA361) cells cultured with endocrine treatments for 3 years. Expression profiling of MAML2 and FZD5 was performed using RT-PCR. Relationship of gene expression to tamoxifen-treated patient survival outcome was analysed using computer-based bioinformatics tools. Gene ontology was obtained to understand more about their function.

In MCF7-derived cells, MAML2 and FZD5 were significantly induced in anti-oestrogen-resistant models. In T47D cells, significant MAML2 and FZD5 induction was seen in anti-oestrogen and also oestrogen deprivation resistant models. No induction of MAML2 and FZD5 was seen in luminal B-derived resistant models. There was no obvious relationship between ER loss and induction of the genes. From bioinformatics analysis, higher expression of both genes associated with shorter relapse-free-survival in tamoxifen-treated luminal A patients. Gene ontology indicated both genes played a role in signalling pathways (Notch or Wnt)[3,4] that contribute to development and progression of cancers.

MAML2 and FZD5 are commonly induced in luminal A-derived endocrine resistant models, relate to clinical endocrine outcome, and have adverse ontology, suggesting both may be resistance-related genes. Although more studies are needed, in conclusion the findings suggest there might be targeting/biomarker value for both genes in resistance which can develop in endocrine-treated disease.

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Protein labelling with a fluorophore for visualisation in cells as models for intracellular therapeutics to treat lysosomal storage diseases

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Large macromolecular drugs demonstrate great potential as novel therapeutics for a number of disorders including lysosomal storage diseases(LSD).[1] LSD describe a group of rare inherited disorders characterized by malfunction or lack in synthesis of lysosomal protein which resulting in accumulation of undegraded metabolite in the lysosome, causes cellular dysfunction and clinical abnormalities.[2] Delivery of functional protein to replace the absent or faulty protein represents one method of treatment.[3] However delivery into cells can be difficult due to the barrier posed by the plasma membrane. Delivery vectors are needed to assist in delivery of these macromolecules into cells. Labelling of these macromolecules assist in visualisation in cells using fluorescence microscopy to initially determine the success of delivery in in vitro methods.

Three model proteins were fluorescently labelled: bovine serum albumin (BSA), biotinylated BSA (B-BSA), and horseradish peroxidase enzyme conjugated to streptavidin (SA-HRP). The fluorophore rhodamine b isocyanate (RITC) was used to label BSA and B-BSA, Alexa Fluor488 was used to label SA-HRP. Labelled protein were analysed with SDS PAGE and spectrophotometric assay were conducted to determine the labeling efficiency. Visualisation of uptake of labelled protein into HeLa cells was determined using wide-field fluorescent microscopy. The enzyme activity of SA-HRP was determined using colorimetric assay to compare the activity before and after labelling.

All three model proteins were sucessfully labelled with respective fluorophores and labelling efficiencies calculated. Labelled protein were taken up by HeLa cells seen as bright endocytic vesicles under the microscope. Labelling did not affect enzyme activity as determined using horse radish peroxidase assays.

Further work should investigate whether a similar approach could be used to label a clinically relevant protein/enzyme such as beta-galactosidase enzyme. Replacement of beta-galactosidase enzyme deficiency

in G_{M1}-gangliosidosis disease will be advantageous for development of macromolecular drugs as treatment for this and other diseases.[4]

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Evaluation of the suppressed genes IGFBP4 and CYP2B6 derived from novel endocrine resistant breast cancer models

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70% of breast cancers are ER+ and treated with anti-hormones.[1] ER+ disease can be divided into luminal A (ER+, HER2-) and luminal B (ER+, HER2+) subtypes.[2] Around 30% of the ER+ patients that respond to anti-hormone treatment will relapse because the tumour has acquired resistance.[1] The BCMP group has developed a 3 year *in-vitro* model panel to mimic long term acquired anti-hormone resistance from luminal B (MDA361, BT474) and luminal A (MCF7, T47D) breast cancer cells. The group has applied preliminary Affymetrix microarraying to two MDA361-derived resistant models, showing decreased IGFBP4 and CYP2B6 expression. This project aims to explore further whether suppression of IGFBP4 and CYP2B6 could be important in helping resistance emerge when breast cancers are anti-hormone-treated.

PCR was performed to look at the suppression profile of both genes in 11 luminal A and luminal B derived resistant models versus control cells. Bioinformatics tools were used to study IGFBP4 and CYP2B6 ontology and KM plotter to explore clinical relevance.

IGFBP4 and CYP2B6 mRNA suppression was verified in MDA361-derived resistant cells. Decreased IGFBP4 expression was common to both luminal B and luminal A-derived resistant cells. Decreased CYP2B6 expression was only seen in luminal B-derived resistant models. The suppression of both genes had no relationship to ER status across the panel. There were relationships between low intrinsic level of both genes and shorter time to tamoxifen relapse in ER+ clinical breast cancers. Further support from ontology studies suggested the genes have potential tumour-suppressive signaling or metabolic function.

This project's findings support the concept that suppression of IGFBP4 and CYP2B6 may help development of resistance to anti-hormones, either in both ER+ subtypes (IGFBP4) or within the luminal B subtype (CYP2B6). In conclusion, with further study restoring IGFBP4 [3] and CYP2B6 [4] might possibly prove beneficial to control anti-hormone resistant growth.

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Effect of biocide exposure on emerging antimicrobial resistance in bacteria

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There is a lack of extensive data on biocide resistance. The pattern of biocide application might not correlate with the emergence of antibiotic resistance. However, theoretically there is a possibility that pre-exposure to biocides might magnify the selective pressure exerted by antibiotic use, which is currently assumed to be the major culprit of antibiotic resistance in clinical practice. SCENIHR opinion in January 2009 confirmed that some

resistance mechanisms are similar in both biocides and antibiotics.[1] An experiment exposing *S.aureus* and *MRSA* to sub-MIC triclosan and chlorhexidine has been conducted out to investigate the development of biocide resistance and cross-resistance towards antibiotics.

Minimum Inhibitory Concentration **(**MIC) and Minimum Bactericidal Concentration (MBC) assays are done based on high throughput microdilution broth for both baseline and sub-MIC biocide-exposed bacteria. Antibiotic susceptibility testing (AST) profile is done based on EUCAST method for both baseline and sub-MIC biocide exposed bacteria. Both techniques are thought to investigate if there is any significant difference between these two test parameters to support the hypothesis.

Findings demonstrated that the both *S.aureus* and *MRSA* have become less susceptible to both triclosan and chlorhexidine post-exposure. Besides that, sub-MIC biocide-exposed MRSA has portrayed increased resistance to a few antibiotics. Interestingly, *S.aureus* and *MRSA* have shown increased susceptibility towards tobramycin after chlorhexidine sub-MIC exposure.

This suggests that the decreased susceptibility to both biocides after exposure could be due to bacteria adaption and was accompanied by cross-resistance towards certain antibiotics as seen in *MRSA.* However, the decreased susceptibility may be stable or unstable. Interestingly, increased susceptibility seen in *S.aureus* and *MRSA* towards tobramycin after chlorhexidine exposure could be due the mechanism of chlorhexidine targeting the membrane which prevents antibiotic entry. Further laboratory work is required to determine phenotypic adaption, stress responses and exposed bacterial feedback mechanism to antibacterial agents.

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An investigation of particle bounce in cascade impactors and the implications for large scale powder fractionation

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Cascade impactors fractionate aerosol particles according to their aerodynamic size based on inertial impaction.[1] A common problem faced by cascade impactors is particle bounce where larger particles hit the collection surface, are re-entrained in the airstream and deposited on stages of smaller cut-off diameter.[2] The aim of this research is to investigate particle bounce in the Next Generation Impactor (NGI) and the implications for large scale powder fractionation.

The study was conducted at a flow rate of 60L/min using NGI on three compounds (Lactohale, silicon dioxide and talc) for 6 and 18 capsules run respectively. Capsules were filled to approximately 170mg with each compound and were used in the Spinhaler device. Powders collected on NGI cups were weighed on accumulative basis and analysed. Mass median aerodynamic diameter (MMAD) was determined with progressively higher powder loadings. Re-aerosolisation of powders collected from the Stage 2 of the NGI and observation of fractions collected from Stage 2, using light microscope were the methods of analysis used in this study.

The MMAD results varied for both 6 and 18 capsules experiments. However, no significant difference was found between MMAD and number of capsules aerolosied into the NGI. Powders collected from Stage 2 were found fractionated across the 7 stages and micro-orifice collector (MOC). Agglomeration and properties of powder could be the causes of powder fractionated across all stages in the re-aerosolisation experiment.

Particle bounce may not be significant in this study although it may be present as it is negligible due to the insignificant difference in MMAD. Therefore, particle bounce may have minimal implications for large scale powder fractionation.

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Exploring the downstream signaling effects of zinc transporter ZIP7 and the implication for cancer

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Zinc is involved in many biological processes and has been recognized as an intracellular second messenger.[1] Zinc is highly guarded by two families of zinc transporter, ZIP and ZnT transporters.[2] My study focuses on ZIP7 (SLC39A7) transporter that has been associated with the development of anti-hormone resistance in breast cancer due to an increased expression.[3] ZIP7 is responsible for zinc release from the intracellular stores as a result of phosphorylation on S275 and S276 by CK2.[2] Zinc releases inhibited PTP, which activates tyrosine kinase receptors and leads to cell proliferation and migration.[3] Zinc can activate the AKT pathway known to enhance cell growth and migration.[4] The aim is to investigate whether there are alternative phosphorylation sites in ZIP7 and the respective downstream signalling pathways.

Potential phosphorylation sites of ZIP7 were identified using the Kinexus database, which highlighted alternative phosphorylation sites in ZIP7. Consequently, non-transfected MCF7 cells and MCF7 transfected with wild type ZIP7 (WT) or mutant ZIP7 were treated with zinc and lysates were probed by Western analysis for activation of downstream signalling pathwyas and pS275/276-ZIP7 to assess any effect on ZIP7-mediated zinc release.

Testing of the different ZIP7 mutants suggested that there was evidence of hierarchical phosphorylation which needs further investigation. Furthermore, it was shown that ZIP7-mediated zinc release could activate a number of noveldownstream signalling pathways suggesting a mechanism of increasing growth and migration. These findings now need further investigation.

This work confirmed the activation of novel downstream signalling pathways by ZIP7-mediated zinc release and suggests that ZIP7 might be good target for breast cancer therapy.

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Evaluation of inhaler technique in patients of the Cardiff and Vale University Health Board

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Inhalation technique is important in the management of both asthma and COPD, poor technique can lead to insufficient dose levels; this in turn can result in poor control of the condition.[1,2] Asthma is a very common condition in the UK with one in nine people diagnosed at some stage in their life along with over 1500 deaths every year.[3] The aim of this study was to survey how effective inhaler technique is in the patient population of the Cardiff and Vale University Health Board and to get a better understanding of the importance of pharmacists in giving guidance to patients using inhalation devices.

Patients were recruited from clinics in hospitals and pharmacies to undergo a short questionnaire regarding their condition and inhaler(s). Patients were then asked to undergo an inhaler technique test using an AIMs device. Pharmacists were recruited by ringing up pharmacies to see who would be willing to undergo a short semi-structured interview regarding how they deal with patients who require inhaled medication. Participants in this study had previously been given an information sheet explaining what was expected of them, whilst also providing a point of contact. Participation was voluntary and all data collected was anonymised.

The study showed that inhaler technique amongst patients was of a very poor standard. It was found that MDI technique was significantly worse than DPI technique with only 3% of patients achieving a good result using MDI's with 63% failing. DPI's had 28% achieve a good result with only 8% failing. In addition to this it was also

found that patients who claimed to have never received advice on how to use their inhalers outperformed those who had received advice in the last month.

The fact that patients who had received advice on how to use their inhalers in the last month performed the worst implies that healthcare professionals are giving out poor quality advice regarding inhalers. In addition to this there also seems to be a lack of support for these patients with only 32% claiming to have received advice in the last 6 months. Overall inhaler technique was bad but it was clear to see that MDI's were significantly worse than DPI's, It is bizarre that this is the case as asthma and COPD are common problems whilst MDI's are still the most commonly prescribed inhaler to deal with these issues.[4] Some pharmacists feel there is a lack of support for themselves, to counter this support devices should be made more available to pharmacies.

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Computer aided drug design of CYP121 inhibitor for the treatment of M*ycobacterium tuberculosis*

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Tuberculosis (TB) is a bacterial disease caused by *Bacillus mycobacterium tuberculosis* and predominantly affects the lungs. The site of infection can vary from the lungs to other parts of the body such as the nervous system and the bones. *Mycobacterium tuberculosis* (*Mtb*) is the second largest cause of death worldwide from an infectious disease with Human Immunodeficiency Virus (HIV) being the leading cause of death due to a single infectious disease.[1] The gene encoding the cytochrome P450 CYP121 is essential for the viability of *Mtb.*[2,3] The aim of this study was to design novel inhibitor compounds that bind to CYP121 using Molecular Operating Environment (MOE).[2]

MOE was used to carry out chemoinformatic processes such as, building molecules, docking, development of compound database, and pharmacophore modelling. Two alternative methods were used to design novel inhibitor compounds; this included the generation of pharmacophore models by identifying the most common interactions present between the potential inhibitors and the active site of CYP121.[3] Method two consisted of visual inspection of superimposed potential inhibitors within the active site to identify exposed pockets. Novel compounds were designed by combining structures from superimposed ligands to achieve optimal fit within the active site.

Six novel compounds were designed from the pharmacophore models, all six compounds interacted with CYP121. Forty two novel compounds were designed from the visual inspection of superimposed ligands, thirty eight of these compounds interacted with CYP121. Overall four compounds were unsuccessful in interacting with the active site of CYP121.

Compounds were analysed to identify whether they would make good drug candidates, they were checked on the basis of Lipinski's rule of five[4] and the presence of chirality. This narrowed the number of compounds that could potentially be used for the treatment of TB once the theoretical data obtained is validated.

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What influences the motivation of final year pharmacy students towards the MPharm degree at Cardiff University?

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Motivation has been identified as the "driving force or forces responsible for initiation, persistence, direction and vigour of goal-directed behaviour".[1] An individual's motivation can be classified as to whether it is of intrinsic or extrinsic propensity: the premise of the established Self-Determination Theory.[2] Students displaying intrinsic motivation perform activities because of inherent interest whereas, extrinsically motivated students perform activities to achieve a desirable outcome.[3] Motivation is an under-researched area within pharmacy education and this study aims to explore the factors which influence final year pharmacy students motivation towards the MPharm degree at Cardiff University.

As a research team (four project students and supervisor), a topic guide was developed based upon discussions and a literature review. After ethical approval, practice and pilot interviews enabled constructive interview experience. Non-probability (convenience and purposive) sampling was used in recruitment to obtain a student sample with different characteristics. Audio-recorded, semi-structured, one-to-one interviews were undertaken, transcribed verbatim and anonymised. Transcripts were shared then independently thematically analysed using inductive and deductive approaches.[4]

Sixteen interviews were conducted and nine themes were identified: 'Peer Influence', 'Group Work', 'Lecturer Teaching Style', 'Percentage Contribution of Assessments to the Degree', 'Engagement with Project', 'Activities adjunct to the MPharm Degree', 'Reasons for Choosing to Study Pharmacy', 'Value of the Interview to the Student' and 'Suggestions for Future MPharm Degree Developments'. Many factors were described affecting students intrinsic and extrinsic motivation. Many portrayed an enjoyment to learn alongside a desire to achieve academically.

This work has demonstrated motivation is multifaceted and individualistic. Findings have provided an illustration of motivational influences and how these can stimulate or hamper learning. Extrinsic factors were perceived to have a potentially powerful influence on intrinsic motivation. Furthermore, students suggested enlightening ways the school could facilitate their motivation. This study provides the basis for further exploration.

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Rheological properties of normal and osteoarthritis (OA) simulated bovine cartilages

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Rheology is a type of mechanical properties of the cartilage. Osteoarthritis is a common disease for damaged cartilage. The aim of this study is to understand the rheological properties of normal cartilage and rheological changes in osteoarthritis and what cause the changes. Literature reviews has done in this study. Literature reviews are about to know what growth factors involve in healthy and osteoarthritic cartilage and mechanical properties of the cartilage. It is hypothesise that there is changes in rheological properties in osteoarthritic bovine cartilage because of the depletion of glycosaminoglycan (GAGs). An experiment has conducted on healthy and osteoarthritic cartilage to find out the differences in terms of rheology.

The cartilage sample was taken from the ankle of bovine. Healthy cartilage was treated with trypsin for 24h to produce osteoarthritic cartilage. Trypsin will destroy the protein in the cartilage and cause GAGs loss. The rheometer conduct the experiment for 20 minutes for healthy and osteoarthritic bovine cartilage sample with a normal force of 25N, temperature of 37°C, the strain was 0.1% and the frequency range was 10Hz to 0.01Hz.

The results showed a significant different (P<0.005) between healthy cartilage and osteoarthritic cartilage in rheological properties. The results that used in this study are complex modulus, storage modulus, loss modulus and phase angle. Complex modulus, storage modulus and loss modulus has a higher value in healthy cartilage sample than the osteoarthritic cartilage. On the other hand, osteoarthritic cartilage has higher value in phase angle than healthy cartilage.

The osteoarthritic cartilage has less overall viscoelastic behaviour. In osteoarthritic cartilage it showed more fluid like and less elasticity. GAGs loss is the reason that cause changes in rheological properties. As a conclusion, there is significant different in terms of rheological properties between healthy cartilage and osteoarthritic cartilage.

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The development of an assay to determine antibacterial activity of novel methionyl tRNA synthetase inhibitors

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The increasing rate of *Clostridium difficile* infection (CDI) outbreaks has contributed to the emergence of antimicrobial resistance in *C. difficile*.[1] Accordingly, methionyl tRNA synthetase inhibitors (MetRSI) were designed based on homology to the MetRS of *C. difficile* as novel antibacterial agent to treat CDI.[2] The aim of this project was to develop an assay using 96-well microtiter plate, to determine the potential antibacterial activity of six novel MetRSI against two strains of *C. difficile* (DS1813 and DS1748) and methicillin-resistant *Staphylococcus aureus* (MRSA).

Dimethyl sulfoxide (DMSO), which is a bacteriostatic agent was used as solvent for MetRSI at a non-toxic concentration.[3] A sensitivity assay of DMSO against the bacteria was done to determine the non-toxic concentration of DMSO. Subsequently, each MetRSI (0.5-64 µg/ml in final well) was dissolved in DMSO and was screened against bacterial culture; *C. difficile* DS1813 (2.68×10^5 CFU/ml), *C. difficile* DS1748 (2.33×10^3 CFU/ml) and MRSA (1.68×10^5 CFU/ml) in the microtiter plate. The antibiotics; vancomycin and gentamicin were included as the positive controls for *C. difficile* and MRSA respectively.

5% DMSO was used as solvent for novel MetRSI in the screening assay against *C. difficile* and MRSA. From the assay done, MetRSI have statistically showed a significant favourable activity against the *C. difficile* strains (ANOVA test; $p<0.0001$, $n=6$) and MRSA (Kruskal-Wallis test; $p<0.0005$, $n=6$) as compared to the growth control containing bacteria and broth only.

However, this must be investigated further; precisely by modifying the present growth control with addition of DMSO, and a standardised bacterial concentration also should be utilised. In conclusion, the developed method provides reliable results, as the minimum inhibitory concentration (MIC) of the antibiotics was within the standard MIC range; 0.5-1.0 µg/ml (vancomycin) and 8 µg/ml (gentamicin).[4] Additionally, the proposed assay is simple, high-throughput, highly reproducible, rapid and efficient.

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Computational analysis of tricyclic xanthine HSV-1 inhibitors through docking and pharmacophore evaluation

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Herpes Simplex Virus Type 1 (HSV1) predominantly presents as orofacial lesions (cold sores,)[1] but may also infect the genital tract or invade the central nervous system (CNS) causing the serious encephalitis infection.[2] Currently approved anti-herpetic treatments target HSV1 thymidine kinase (TK) which is a key enzyme in viral DNA synthesis, HSV1-TK accepts a broader range of substrates than human TK and can therefore be inhibited selectively.[3] As current treatments have issues of poor bioavailability and limited CNS penetration, mortality and morbidity rates against viral encephalitis remain high.[4] The study aims to identify potential pharmacophore features of known HSV1-TK inhibitors to design a pharmacophore model and that maintains optimal properties for CNS penetration.

Computational techniques were used to analyse the active site, ligand properties and interactions against the target active site. Docking simulations were performed against three series of tricyclic xanthine derivatives, with known inhibitory action against HSV1-TK. Docking conformations were examined and compared alongside ligand properties and anti-viral activity to identify functional groups of interest.

The overall results of the study show that an imidazole ring, carbonyl group (attached to the tricyclic structure,) di-hydroxyl group of the acyclic chain and a phenol derivative as the R1 side chain are likely key ligand areas for active site interaction. Results show that some compounds may contain a pro-drug entity which affects anti-viral activity via lipophilicity and cleavability (releasing the active moiety.)

To conclude, a total of four pharmacophore features have been identified which may be incorporated into a pharmacophore model to aid novel HSV1-TK inhibitor design. Data has identified the presence of a pro-drug entity in some tricyclic derivatives, which may be a useful point of interest for optimising lipophilicity for CNS penetration. However, experimental data is required to validate the study's findings.

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Review of Medication Administration Review (MAR) charts from care homes

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Medication error can be defined as "preventable inappropriate use of medications".[1] Medication error has been a major issue for elderly people living in care homes for various reasons including polypharmacy, comorbidities and medicines management systems.[2] Medicines administration record (MAR) charts play an important role in patient care, by keeping record of patients medication. MAR charts contain residents' details, medication details, allergies information and special instructions, if any, for medication to be taken.[3] The aim of this study was to review medicines administration charts from care homes to identify the types of errors, quantify the prevalence of errors and establish correlations contributing to medication errors.

Care homes were sampled from Abertawe Bro Morgannwg University (ABMU) Health Board to obtain diverse sample with respect to size and type of care provided. Anonymised paper-based MAR charts were collected, labelled and allocated randomly to ten researchers. Four main categories of errors were classified (with a number of subcategories to represent each one) plus a category for errors that could not be assessed. These were: 1) administration errors 2) regulatory errors 3) stock errors 4) risk errors and 5) cannot assess. Errors were recorded in an Excel spreadsheet. Means of error counts and association with number of users and number of medication were calculated using SPSS© version 20.

Eight nursing and two residential homes agreed to participate in this study. In one nursing home, 63 services users were on a mean of 7.86 medications per person and had 2.62 charts per user. Service users in this care

home were exposed to a mean of 48.16 errors per person in 28-day administration. Administration errors were the most common errors. Significant correlations were found between number of medications and number of charts per user with number of errors made.

Various factors may contribute to medication errors either technically or individually. Introduction of a monitored dosage system (MDS) to improve the medicines administration has yet to be established in the home studied, however this may help minimise the time taken during medication round.[2] Steps should be taken to address the errors identified and interventions to reduce the risk of medication errors should be developed.

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Exploring supervisors views on the Hospital Pharmacy Placement Scheme

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According to the General Pharmaceutical Council (GPhC), "the MPharm degree must include practical experience of working with patients, carers, and other healthcare professionals".[1] This is due to the role of the pharmacist shifting from the dispensary setting to the clinical setting, involving more patient-contact.[2] The GPhC does not provide guidance on the practical experience so the requirement is open to interpretation. To incorporate pharmacy practice to the curriculum, pharmacy schools organise placements for students such as in community pharmacies and hospitals. This project aims to explore the views of supervisors on the hospital pharmacy placement for the ongoing review and development of the School's scheme.

A qualitative approach was adopted to explore supervisors' perceptions. A semi-structured interview schedule composed of open and closed questions was designed. Non-probability purposive sampling was used to recruit supervisors. Interviews were conducted face-to-face or by telephone and recorded then transcribed *ad verbatim.* Thematic analysis was used to identify major themes. Ethics approval was obtained.

Fourteen interviews were conducted; six face-to-face and eight by telephone. Ten major themes were identified and divided into subthemes. The major themes were: departmental benefit for pre-registration recruitment, preparing supervisors for placements, preparing students for placements, students' preparedness for placements, expectations from students, length of placement, impact of placement on students, impact of placement on supervisors, challenges for supervisors, and collaboration between the School and hospitals.

The range and number of interviewees yielded valuable feedback for the School. Suggestions for future improvements have been made. Further research into students' perceptions of the placement would allow a better understanding of the results. The objectives were met as the perceptions of supervisors were captured. This project was the first to look at supervisors' perceptions of the hospital placement scheme, and the results may inform the design of future projects and placements.

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Exploring the downstream signalling effects of zinc transporter, ZIP7 and the implication for cancer

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Zinc balance is essential for the human body as deficiency of zinc can cause disastrous effects[1], while excess zinc can cause cellular toxicity[2]. Various zinc transporters control zinc level in our body and ZIP7 is a member of a family of zinc influx transporters located on the endoplasmic reticulum[3]. Recently, it has been proven that

phosphorylation on Ser^{275} and Ser^{276} of ZIP7 leads to an increase in the intracellular concentration of zinc, activating tyrosine kinases and phosphorylating AKT, leading to cell proliferation[4]. In this project, the downstream signalling pathways activated by ZIP7-mediated zinc release and the importance of residues Ser^{293} and Thr^{294} on ZIP7 transporter activation was investigated.

MCF-7 cells that were non transfected and transfected with, wild type ZIP7, S293A mutant or T294A mutant were treated with zinc over 20 minutes and probed for pAKT, pZIP7, GSK3β, and CREB by Western Blot. The effects of the different recombinant ZIP7 on phosphorylation of respective antibodies were analysed.

From this project, it is proven that ZIP7 mediates AKT signalling pathways by increased phosphorylation of Ser^{275} and Ser^{276} on ZIP7, which increases intracellular zinc concentration by generating ZIP7-mediated zinc release. This zinc release also activates CREB. Mutant S293A ZIP7 was found to show decreased phosphorylation of AKT and ZIP7 but increased phosphorylation of CREB while mutant T294A ZIP7 showed decreased phosphorylation of CREB. The role of wild type ZIP7 and both mutants in the ZIP7-mediated inhibition of GSK3β is not conclusive.

From this work, it can be concluded that ZIP7 mediates activation of AKT, CREB and inhibition of GSK3β, consistent with a role in cell proliferation and providing ZIP7 as a potential target for anticancer treatment. Residues Ser^{293} and Thr^{294} in ZIP7 show promising roles in ZIP7 mediated downstream signalling pathways and need to be investigated further.

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A levels as a predictor of academic success on the MPharm

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Despite A-levels are used as the predominant selection criteria by which most students are accepted into universities, few studies have evaluated their validity[1] and none have been conducted on pharmacy students. It is important that the Cardiff School of Pharmacy and Pharmaceutical Sciences identify the particular determining factors which predict the success on the MPharm course and apply them to the undergraduate selection procedures and student support mechanisms. The aim of this study was to investigate the relationship between A-level grades and academic success on the Cardiff MPharm degree. In addition to understand the interrelationship between A-level grades and degree outcomes, statistical analysis was conducted on the 3 most popular A-level subjects and first year modules of MPharm.

This study was designed as a retrospective analysis of students graduating with the MPharm degree between 2010 and 2014, 415 students had A-level results upon entry and graduated from the degree without repeating any year or withdrawing from the course were included. Anonymised admission data of students' A-levels results were mapped to their corresponding MPharm transcripts. Tables and graphs were drawn in Excel spreadsheets and SPSS programme was used to determine the correlations between variables.

The results have shown that there are correlations between A-level results, first year of MPharm results and the final degree classification. In investigating the effect A-levels have on degree outcomes, A-level chemistry and pharmacy practice modules in the first year of MPharm were found to be particularly good predictors of the final degree classification.

Although critics argue that undergraduate selection should not rely solely on A-level achievement[2] and universities should commission tests based on their course contents in addition to A-levels,[3] this study has shown statistically significant variation in performance on the MPharm course dependent upon A-level grades.

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Patient satisfaction with the community pharmacy seasonal influenza vaccination service in Wales

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Community pharmacies in Wales have great reach and are widely used by the population. The seasonal influenza vaccination uptake target is 75% for those aged 65 years and older and those aged six months to 65 years in clinical at risk group.[1] Pharmacists are ideally placed to identify and initiate an intervention with at-risk patients which can encourage vaccine uptake.[2] The aim of this study is to determine why different patient groups use the community pharmacy influenza vaccination service and identify their satisfaction with the service.

This was an observational study using (i) questionnaires distributed by Public Health Wales to pharmacies providing the service and (ii) demographic data of 7851 patients collected from pharmacies involved in the influenza vaccination service through the reimbursement process.

7851 patients were vaccinated in pharmacies across seven Health Boards in 2013-2014, an increase of 80.4% vaccines from year 2012-2013. The most frequent eligibility was for those aged 65 years and over (n= 4079, 51.96%) followed by chronic respiratory disease (n=1558, 19.8%). Some patients said they would not have been vaccinated (18%, n=587/3219) if it was not for the community pharmacy service. Not having to book an appointment for a flu jab in pharmacies was the most frequent reason patients gave for using the service. Nearly all the patients were very satisfied with the service (99.3%, n=3742/3768).

The initiation of the influenza vaccination service in community pharmacies in Wales was mainly to help vaccinate hard to reach and at clinical risk populations, which is mostly those under 65 years of age (1). However, results show that most people vaccinated were 65 years and over which means more health campaigns are needed to encourage hard to reach groups to be vaccinated. Patients find the pharmacy vaccination service accessible and very convenient and is associated with high patient satisfaction.

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Patient Satisfaction Survey: satisfaction with medicines management and information about medicines during hospital stay and discharge

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All health professionals have a duty to their patients to provide the best possible care and patient satisfaction levels is a good indicator of how well patients feel that they have been treated.[1] Patient satisfaction levels in terms of the quality and quantity of the medical information that they have received is an important aspect that may often be overlooked; this is suggested as limited research is found about the topic. The aim of this research is to investigate whether patients were receiving sufficient medical information.

A bilingual questionnaire to assess patient satisfaction pertaining to medical information received during their stay and upon discharge was designed. After obtaining necessary ethical approvals from the School of Pharmacy and Cwm Taf University Health Board (CTUHB) Research and Development Department, this study was conducted in the Royal Glamorgan hospital and Prince Charles hospital under CTUHB. Patients' demographics were noted and the questionnaire was sent to 285 patients who were recently discharged and they were carefully selected according to inclusion and exclusion criteria. Responses were entered into a SPSS database. Kruskal-Wallis and Chi-square tests were then carried out as appropriate.

100 questionnaires were returned. 84% of the respondents had the opportunity to discuss their medicines with at least one staff member, majority of them discussed it with a nurse. Only 17% of patients experienced problems with their medications during their discharge. Majority of the patients, 88 out of 96 patients did not experience any problems with their medicines upon leaving the hospital. Overall, 87%-97% of patients were satisfied.

The findings from the research show that while most of the patients were satisfied with the information they received, there is still room for improvement for example: reducing waiting times and providing more information such as side effects to patients to help improve patient's experience.

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Does inhibition of Src improve the response to chemotherapy in breast cancer?

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Triple-negative breast cancer (TNBC) is a sub-type of breast cancer understood to have a particularly poor prognosis.[1] It is an aggressive sub-type typically treated with chemotherapy due to a lack of defined drug targets making targeted treatments, used to treat other sub-types of breast cancer, ineffective. The activity of Src family kinases has been linked with cancer aggression and metastases.[2] Recent research has demonstrated the potential use of Src inhibition as an approach to improve the response to chemotherapy.[3,4] The aim of this project was to investigate the efficacy of this approach in a cellular model of TNBC.

MDA-MB-231 cells were used as a model of TNBC, and MCF7 cells (model of ER+ breast cancer) were used as a comparison. Cell lines were treated with epirubicin chemotherapy ± Src inhibitor, saracatinib. MTT and Ki67 assays were used to analyse how treatments affected cell proliferation alone and in combination. Western blotting was also used to analyse Src activity and levels of Poly ADP Ribose Polymerase (PARP) cleavage, used as a marker of apoptosis.

Initial analysis suggested insensitivity of MDA-MB-231 cells to Src inhibition with saracatinib. Despite this, further investigation showed a modest trend for improvement in response to epirubicin when given alongside saracatinib, illustrated by decreased cell proliferation with the combination treatment. However, this trend was not statistically significant. Data on PARP suggested a role for apoptosis in the mechanism of combination treatment with epirubicin and saracatinib.

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Calcium phosphate stability in parenteral nutrition

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Parenteral nutrition (PN) is given to patients who are not able to get full nourishment from the enteral or oral route.[1] There are a number of essential components needed in PN to achieve total nutrition.[2] One of the main concerns with PN is the precipitation of calcium phosphate since it can lead to catheter occlusion or even death from respiratory distress, leading to multi organ failure.[3] The mixing order of the PN can alter the amount of precipitation formed. The aim of this investigation was to attempt to identify the nature and cause of any precipitate and the influence of the mixing order and components on the stability of the proposed formulations.

2-in-1 PN (in which the main constituents are glucose and amino acids without lipids) was made up in 100ml sterile glass multidose vials on day 0 of each week using the three different mixing orders given: the original Cardiff order, the original Fresenius Kabi order, and the new Fresenius Kabi order. Tests for precipitation were

then carried out on days 0 – 3 to observe changes over time. These tests involved visual inspection, turbidity measurements, and pH measurements. Mean values were calculated for these values and compared.

The results showed that the new proposed mixing order was still capable of producing a precipitate, as these bottles showed the largest increase in visual precipitation and in turbidity measurements.

The mixing order of the components is able to affect the stability of PN mixtures. The precipitate formed in the experiments during this investigation can be assumed to be calcium phosphate, but further tests and chemical analysis on the precipitate would be needed to confirm this. Future experiments could be carried out to investigate the effect of different storage temperatures and times on precipitation formation.

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Design of a computer aided package to educate undergraduate pharmacy students about dyslipidaemia

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Computer aided packages also known as computer assisted learning (CAL) packages are used for interactive learning. CAL employs multimedia (such as animations and hyperlinks), interactive tasks and self-assessment tests.[1] CAL is a flexible learning resource which can be used as an alternative to or, supplementary to lectures where students can work through the package independently at their own pace.[2] The aim of this study was to evaluate the opinions of second year pharmacy undergraduate students, at Cardiff University, on a CAL package about dyslipidaemia.

A CAL package about dyslipidaemia was designed in Microsoft PowerPoint. Content included the pathophysiology, evidence-based management and the role of the pharmacist. Students were able to assess their knowledge through interactive quiz questions. Presentation techniques such as animations and diagrams were used to explain scientific concepts and the actions of lipid-regulating drugs. An online, anonymous questionnaire was distributed to evaluate presentation, content and overall opinions of the CAL package. The questionnaire included 5-point Likert scale statements and open-ended questions.

A response rate of 19% (n=21) was achieved. Respondents positively accepted the use of CAL. Students agreed the package was easy to use and presented well. They found content was appropriate for MPharm II, improved their knowledge and quizzes were a suitable way to test their knowledge. All of the students agreed the CAL package was engaging. Students (81%) reported they would prefer CAL in addition to a lecture.

Findings of this study replicate similar findings where CAL has been evaluated as a useful resource but to be used as a supplementary teaching aid.[3] Low response rate was a limitation to this study; investigating reasons for this is recommended before more CAL packages for MPharm II are designed at Cardiff University. Further studies could evaluate the use of CAL in postgraduate pharmacy education.

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Review of errors made in Medicines Administration Record (MAR) charts

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Care home residents are among the most vulnerable in the population to medication related harm due to their prevalence of comorbidities and polypharmacy. A report on medicine usage in care homes found that 22.3% of residents had at least one administration error.[1] Medication administration in care homes is recorded on

Medicines Administration Record (MAR) charts. This study aims to assess MAR charts to identify the most common types of errors as well as to determine effect of factors such as drug type and resident characteristics on the presence of errors.

Errors were categorised through consultation of published guidelines and preliminary assessments of care homes.[2] Individual care homes were randomly assigned and distributed, this study reviews MAR charts for Care Home 10. Charts were assessed for errors which were entered into Excel and SPSS spreadsheets to allow for computer-driven statistical analysis.

MAR charts for one month were received for 41 residents. 71.3% (n=610) of medication entries had at least one error. 'Cannot Assess' errors, assigned to inconsistencies in 'when required' medication, were the most common types of error, 52.8% (n=8106). This was followed by 'Controlled Drug (CD) witness signature missing' (22.0%, n=8106) and 'Omission' (12.3%, n=8106). Non-opioid analgesics and compound analgesic preparations and Anxiolytics were the most common drugs of error, 27.6% (n=8106) and 18.3% (n=8106) respectively.

A high prevalence of errors was found in the study, particularly with PRN medications the majority of which were Non-opioid analgesics and compound analgesic preparations. This can be attributed towards the lack of any standardised procedures for administering PRN medications. Lack of appropriate record keeping was also exemplified by the high frequency of 'CD witness signature missing' errors. Improvements to staff training would help reduce the occurrences of these errors and lead to safer resident medication administration.[3]

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"Stepping into the patient's shoes": pharmacy students' views on medication adherence

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Adherence is defined as "the extent to which the patient follows medical instructions". It has been estimated that 30-50% of medication prescribed for long term conditions are not used as prescribed.[1] A week long medication simulation activity took place in the 1st semester of 2013/2014 with first year MPharm students followed by an hour lecture on the patients' perspective on medicines taking. The aim of the study was to evaluate students' experience of taking medicines including the extent of adherence and to gain feedback on the value of this teaching method on the 'patients' perspectives of medicine-taking'.

A standardised form was used to collect students' adherence to one of five dosing regimens of a mock medicine (Tic Tacs®). This was completed and collected after the lecture alongside a teaching evaluation form. Quantitative data were analysed using IBM SPSS statistics 20. A total percentage adherence was calculated and Kruskall Wallis and Mann-Whitney U statistical tests were used to assess differences in adherence with regards to gender and dosing regimen. Thematic analysis was used to identify emerging themes from students' comments and teaching evaluation forms were reviewed for strengths and weaknesses of the teaching method. Semi-structured interviews were planned for further feedback. Ethics approval was obtained.

75% of students were 80% adherent or more. Through thematic analysis 12 themes emerged, these mainly related to challenges found. The use of resources was also mentioned. The activity was well received as student engagement was good. The interviewee concluded the activity was more challenging than first thought but was beneficial and relatable to pharmacy practice.

This mock medicine activity was successful in teaching students about the patients' perspectives on medicines taking.[2,3] Further research is needed in this area of student learning to allow opportunities for enhancing teaching empathy in undergraduate pharmacy education.

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The incidence of depression in Parkinson's disease and non-parkinsonian tremor

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Although Parkinson's disease (PD) and non-parkinsonian tremor (NPT) are movement disorders, non-motor symptoms occur.[1] Depression is of great interest as it significantly reduces a patients' quality of life and whilst recognised in NPT, is probably the most common non-motor symptom in PD.[1,2] However, factors linked to the incidence of depression in these conditions have not been studied in detail.[3] This study aimed to explore the basic demographics of depression in PD and NPT and to determine if high rates of polypharmacy correspond with a high incidence of depression

This retrospective study included PD and NPT patients from two movement disorder clinics in South Wales. They were grouped by their depression classification: depressed with mood comments, depressed taking antidepressants or no depression. Class of antidepressants, polypharmacy data (including number of drugs patients' were taking) and L-DOPA equivalents (which express dosage of antiparkinson medication on a single scale) were extracted and analysed using descriptive and inferential statistics.[4]

Depression prevalence in PD was 52.6% compared to 28.4% in NPT. A wider range of antidepressants were used in PD, whilst TCAs were used more frequently in NPT. There was a significantly higher number of drugs used in depressed patients taking antidepressants compared to those with mood comments or no depression. Interestingly, the results were replicated in both movement disorders. In PD, L-DOPA equivalents were significantly higher in both depressed patient groups compared to patients with no depression.

In carrying out this study valuable results were discovered. Of particular importance was the comparison made between L-DOPA equivalents and number of drugs taken by PD patients. This suggested that patients with mood comments had the same severity of motor dysfunction as those taking antidepressants, but were using a lower number of drugs which may be related to their lack of antidepressant medication.

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A community–based cardiovascular risk assessment: analysis of pilot data

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Pilot data was obtained from a Health Check Campaign conducted by Mayberry Pharmacy in October to November of 2013 which assessed subjects' risk of developing CVD. Risk factors, such as blood pressure, physical inactivity, smoking and existing medical conditions, were reported on a standardised form. Interventions included lifestyle advice and referral to a GP.

The data was refined and analyses were conducted which looked for 1) the prevalence of hypertension and other risk factors amongst the subject group and 2) possible correlations between the risk factors and blood pressure (BP) using a range of statistical tests including Spearman's, Pearson's, t-tests and ANOVA tests.

Results show that almost two-thirds (64%) of those over 61 years had hypertensive readings. Highly significant differences were found in both SBP and PP because of age ($p<0.001$). The DBP was the only BP that did not show a significant difference from either age or gender. The modifiable factors assessed in the Health Check did not seem to have any effect on the BP.

Similar studies have been carried out [1, 2], however this is the first where a CVD risk assessment has been made available in a pub. A longitudinal study would have provided more data on the efficacy of such a service but no follow-up was attempted. There are several improvements which could be implemented to a future CVD screening tool, including the use a CVD risk calculator (e.g. QRISK®2)[3] which would enable the calculation of 10 year risk of CVD.

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Review of Medication Administration Review (MAR) charts from care homes

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There is a growing focus on improving resident safety in care homes; more specifically, reducing the number of administration errors associated with medication administration record (MAR) charts.[1-3] MAR charts are prone to medication administration errors; thus replacing MAR charts through innovative solutions, like barcode-scanning technology, could reduce the number of errors.[4] A collaboration involving ABMU Health Board, are working to introduce barcode-scanning technology into selected Welsh care homes. The project aim was to investigate the types and frequencies of medication administration errors occurring on MAR charts. Eventually, this baseline data could be used as a measure of comparison to establish if there is an overall reduction in errors, after implementing the technology.

Ethical approval was obtained to conduct a cross-sectional analysis on MAR charts from selected Welsh care homes. Each member of the research team received MAR charts from individual care homes to analyse, using the finalised categories from 'test' MAR charts, which were part of the validation process. Excel and SPSS were used for collating quantitative data.

Analysis of 26 residents' MAR charts showed the mean age of a resident was 86 years old with an average of 10 medicines. The mean number of administration errors per resident was found to be 72 over a 28-day period. This equates to approximately 2 to 3 errors a day. The most common type of error was omission. Results have shown the vast range of medication administration errors associated with MAR charts. However, further research is required because issues such as polypharmacy, were not captured within this project.

This research has demonstrated the problematic nature of MAR charts, when used for administration. Hence, a technology-based solution would be well placed in care homes, as it would replace MAR charts and contribute to making medication administration more safe and efficient.

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Effect of biocide exposure on emerging antimicrobial resistance in bacteria

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Biocides are used in vast array of environments as preservatives, disinfectants and antiseptics. The main function of biocides is to kill or inhibit bacteria from multiplying in these environments.[1, 2]. The aim of this study was to investigate the effect of antimicrobial resistance and cross-resistance caused by biocide used in consumer products.

The study was carried out to find changes in Minimum Inhibitory Concentration (MIC)/Minimum Bactericidal Concentration (MBC) and Antibiotic Susceptibility profile in enterobacteria exposed to chlorhexidine (CHX) or triclosan (TRI). MIC was determined by using a 96 well microtitre broth dilution method. MBC was then carried out by plating two concentrations above MIC, the MIC and two below MIC on Tryptone Soya Agar (plates containing a neutraliser. Finally, antibiotic profiling was performed by placing antibiotic disks on plates swabbed with bacteria and measuring zones of inhibition around the disks to see for any changes in susceptibility.

A single 24 hour exposure to CHX at a sub-MIC concentration resulted in an increase in MIC for both *Escherichia coli* and *Klebsiella pneumoniae*. An increase in MBC for *E. coli* following exposure to CHX was also observed. No significant results obtained for TRI in this study. Antibiotic profiling results depicted a change in susceptibility profile in *E. coli* following exposure to CHX. There was no change in antibiotic susceptibility profile for *K. pneumoniae*. There was nom change in antibiotic susceptibility profile following exposure to TRI.

Repeated exposure to low concentrations of biocide results in resistance being developed as bacteria get used to the biocide being applied. Biocides have many uses to society and they are precious resources which need to be managed properly. The benefits of using biocide outweigh the risks.[3, 4]

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Clinical monitoring of home parenteral nutrition

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Home parenteral nutrition (HPN) is a specialised branch of artificial nutrition that serves to nourish patients suffering with intestinal failure or other gastrointestinal disorders who are unsuitable for enteral or oral feeding and is therefore a life-saving treatment. HPN lacks the intense clinical support that is available within a hospital setting. Ensuring the safety and efficacy of HPN is therefore inherently complex and relies on solid patient and carer education in conjunction with appropriate monitoring of biological, biochemical, physical and psychological parameters. In the UK, there are just two nationally funded specialist intestinal failure units; this has resulted in many smaller centres being forced to cater for the surplus of patients requiring treatment. Little is known about current monitoring practice in the UK for these patients. The aim of this study was therefore to gather information relating to the current practices of monitoring patients receiving HPN in UK. Data gathered by the survey should illustrate the extent to which monitoring practice varies between centres and should highlight deviations from published European guidelines.

A web link to an anonymous, online survey consisting of 16 questions covering numerous aspects of HPN monitoring practice was emailed to members of the British Pharmaceutical Nutrition Group (BPNG). Despite every effort, response rate was poor and the sample size was comparable to that of previous studies.[1]

Centre size and monitoring practice was found to vary considerably between centres. However, most centres were operating to the standards outlined by the European Society for Clinical Nutrition and Metabolism (ESPEN).[2] Sepsis was the most common HPN-related complication encountered by centres and concurs with findings from similar studies.[3]

HPN in the UK is predominantly provided by small centres catering for low volumes of patients, with monitoring practice varying considerably between centres. Centres appear to operate a two-tier system in which unstable patients are monitored more frequently.

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Patient satisfaction survey: satisfaction with the information and management of medicines in hospital

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The pharmacy department plays an important role in managing and informing patients about their medications in hospital.[1] It is important that hospital pharmacy continues to uphold its standards and show continuity of care.[1,2] When assessing the quality of medicines information and other services, patient perceptions and satisfaction are important factors to consider.[3] The aim of this study was to evaluate patient satisfaction levels regarding medicines management and the medicines information provided in ABMU hospitals.

This cross-sectional study was carried out at Morriston Hospital and Princess of Wales Hospital within the ABMU Health Board. A postal questionnaire was developed to assess clinically important areas and was designed for self-completion by recently discharged patients. SPSS was utilised to analyse quantitative data. Chi-square tests were applied to satisfaction scores across different variables. Thematic analysis was used on the qualitative data obtained.

A 33% response rate was achieved. Both hospitals engendered patients with high levels of satisfaction regarding medicines information. Patient demographics and clinical factors showed no significant differences in satisfaction, with levels remaining high regardless of age, gender and number of medicines. Satisfaction levels were found to be higher for patients who reported no problems with their medicines during their stay (P=<0.001) or on discharge (P=0.012). The performance of clinicians providing medicines information was rated highly by patients within both hospitals. However, 30% of patients did not receive information in the format they preferred. Analysing patient comments indicated important areas in need of attention, including, delayed or omitted doses of medicines, long waiting times for discharge medicines and insufficient medicines information.

Whilst patients were on the whole satisfied, areas for improvement have been identified and it is important that the two pharmacy departments continue to develop the standards of their services in an attempt to further improve their quality of care.

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Experiences of prescribing advisors involved in a social prescribing initiative in Cwm Taf

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Social Prescribing is the process of referring people with health problems to non-medical sources of help and support in the community.[1] In 2013, an initiative driven by Public Health Wales (PHW) was implemented in Cwm Taf, which involved pharmacists and pharmacy technicians within the Prescribing Advisory team providing advice GPs on Social Prescribing. The aim of the initiative was to implement Social Prescribing into the wider prescribing agenda.[2] The purpose of this study was to collect feedback from the Prescribing Advisory team involved in the imitative.

Ethical approval was granted by the SPPS Research Ethics Committee. A sample size of 6 was achieved through purposeful sampling. Semi-structured interviews were conducted to collect data and thematic analysis was used to identify patterns in the results.

Six main themes were identified in the results. The Prescribing Advisors were confident advising GPs on prescribing of medicines but less so when it came to Social Prescribing. A lack of knowledge on the available services, and unfamiliarity to the term were noted as the main reasons for this. All participants suggested that more training sessions should be provided throughout the initiative to improve knowledge and resultantly increase the confidence of Prescribing Advisors. Another issue raised was the infrequency of the Annual

Prescribing Meetings. This meant that the topic was raised with GPs a maximum of once a year and resulted in a 'stop-start' execution of the initiative.

The main conclusion was that the initiative should continue into 2015. However, a number of changes were required in order to improve it. As well as PHW providing more training sessions, other suggestions included holding separate, more frequent meetings with GPs away from the Annual Prescribing Meetings. Some participants also suggested dividing the role amongst other healthcare professionals and allocating more time for Social Prescribing specifically during consultations with GPs.

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Exploring the downstream signalling effects of zinc transporter ZIP7 and the implications for cancer

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Zinc is an essential trace element that has many biological roles in humans.[1] It has been characterised as a second messenger and is capable of transferring an extracellular stimulus into an intracellular signalling cascade.[2] As zinc cannot passively cross plasma membranes it utilises transporters, such as the ZIP7 transporter, which is found on the ER membrane[3] to transport zinc. ZIP7-mediated zinc release occurs after the phosphorylation of ZIP7 on residues Ser275 and Ser276 by CK2[3]. The aim of this study was to investigate if any alternative residues are also phosphorylated and essential for ZIP7-mediated zinc release, and to explore the downstream signalling effects, which may impact cancer progression.

MCF-7 cells transfected with wild type ZIP7 and mutant S275A/S276A ZIP7 were treated with 20μM of zinc and ionophore, for 0, 2, 5, 10, 15, and 20 minutes before lysis. Western Blotting analyses were undertaken on three separate samples for each condition and probed for activation of downstream signalling molecules and $pZIP7^{S275/S276}$ and developed onto film. Densitometry was performed and normalisation was made to V5. Statistical analysis was performed using a two-way ANOVA with a Dunnett's post hoc test. Significance was assumed if $P<0.05$.

AKT was confirmed as activated by ZIP7-mediated zinc release, which occurs due to phosphorylation of Ser275 and Ser276 residues. Two novel phosphorylation sites on ZIP7 were investigated and results suggested some form of hierarchal phosphorylation mechanism. Following ZIP7-mediated zinc release, a number of downstream signalling pathways were activated which are known to lead to the migration of cells.[4]

A CK2 inhibitor could potentially inhibit the phosphorylation of $Ser^{275/276}$ inhibiting ZIP7-mediated zinc release leading to reduced cell growth and migration. This novel pharmaceutical agent could potentially inhibit the metastasis of cells, which could slow the progression of some cancers.

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Changes in monitoring and prescribing practices of lithium subsequent to the NPSA safety alert

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Lithium is a clinically effective long term treatment for bipolar disorder, however its use is limited by its narrow therapeutic index and metabolic adverse effects.[1] In response to 567 incident reports and findings from the POMH-UK baseline audit, an NPSA alert 'Safer Lithium Therapy', was released in December 2009, reiterating

the need to comply with 2006 NICE lithium guidelines.[2] These state that lithium serum levels should be monitored every 3 months and thyroid and renal every 6 months. The aim of this study was to assess whether the rate of lithium prescribing and the frequency of monitoring changed following the NPSA alert.

An Interrupted Time Series analysis was undertaken to assess whether a change in the rate of lithium prescribing 24 months post alert was different to the 24 month period prior to alert. National lithium and Depakote prescribing data were obtained from all seven of Wales's health boards. Monitoring data was collected from Whitchurch Hospital using a retrospective case note review to discover the proportion of patients compliant with the NICE 2006 guidelines pre intervention compared with those post intervention.

The difference between the lithium and Depakote prescribing rate change pre and post intervention was not statistically significant (p=0.779, p=0.134). Renal monitoring saw the greatest increase from 37% pre-intervention to 78% post-intervention (p=0.0005). There was a statistically significant increase between the frequency of lithium and thyroid monitoring pre and post intervention (p=0.0041, p=0.0374).

Despite other trials reporting an increase in the use of Depakote compared to lithium, no statistically significant difference was seen in both their prescribing rate change in response to the NPSA alert.[3] Improvements in monitoring reflect the results of the POMH-UK supplementary audit,[4] however despite relative improvements, compliance in practice remains inadequate and falls short of NICE 2006 guidelines.

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A review of Medicines Administration Record (MAR) charts in the Abertawe Bro Morgannwg University (ABMU) Health Board locality

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There are currently 22,179 spaces for older adults[1] in care settings across Wales, with all of these service users requiring medication via MAR charts. It's known there are issues with this tool of administration and research has already been completed in England[2]. The aim of this project was to collect and review information relating to use of MAR charts. Specifically, we sought to identify errors and the frequency they occur; investigate whether there is a link between controlled drugs and regulatory errors; investigate errors with medication that aren't deemed vital to service user but may improve their quality of life when used.

To meet these aims and objectives, errors were defined and categorised and an error rule book was created to review MAR charts. This was created by performing a critical review of the available literature. Service providers were chosen based on strict inclusion criteria and data collected was analysed in Microsoft Excel and SPSS. Ethical approval was gained.

25 service users were enrolled with them collectively having 51 MAR charts. 2692 errors were identified with each of these errors fitting into, administration (683), regulatory (488), risk (84), stock (286) and cannot assess (1151). 217 medicines were reviewed with 12 being controlled drugs. A positive correlation was identified between controlled drugs and the number of regulatory errors with a correlation coefficient of 0.701 (significance 0.024). 67 medicines were identified as to improve the service users' quality of life when used as prescribed with 1248 errors being identified.

Overall, a high number of errors were identified. It must be noted that the majority of the errors recorded would not put service users at risk of serious harm. The data collected can be used as part of wider research into the state of care in the service provider setting.

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Depleting endocytic proteins to analyse cellular uptake of macromolecular therapeutics

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The plasma membrane is impermeable to most molecules >1kDa hence creates a problematic barrier for delivery of hydrophilic and large macromolecular therapeutics into cells.[1] Endocytosis is often used as a delivery route and represents a mechanism common to all eukaryotic cells and encompasses various pathways. It is important to characterise what pathways are used by drug delivery systems and this calls for further studies on the pathways themselves. This study focused on attempts to deplete AP2-µ2 and GRAF-1 endocytic proteins that regulate the clathrin-mediated endocytic pathway and a subclass of the clathrin independent endocytic pathway termed CLIC/GEEC[2] siRNA[3] targetting was employed as a method of depleting AP2-µ2 and GRAF-1 in HeLa cells.

Cells were cultured under tissue culture conditions and siRNA transfection was performed targeting the proteins at two concentrations: 183nM and 100nM. Cell lysates were then collected and a BCA assay was carried out for protein quantification. SDS-PAGE was used to separate the proteins based on their molecular weights followed by protein transfer onto PVDF membranes and detection with HRP labelled antibodies to monitor protein depletion.

AP2-µ2 was successfully depleted using optimised methods of siRNA targeting at 183 nM. Despite numerous attempts GRAF-1 could not be depleted using this methodology. It remains to be determined whether this was due to the nature of the siRNA or the dynamics of the protein inside the cell.

Overall the data collected confirms siRNA as a successful method for endocytic protein depletion, however off target effects still remain a challenge. Further work is clearly required to optimize conditions to achieve effective depletion of GRAF-1 and inhibit the CLIC/GEEC pathway. Here, the choice of cell line, cell passage number and other factors need to be analysed closely.

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Preparation and characterization of titanium based nanoparticles loaded with anti-inflammatory drug

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Nanoparticles are defined as particles that have “at least one dimension in the size range 1 nm – 100 nm”.[1] They are being used as a drug delivery system for orthopedic applications, where medical implants may be required. Titanium is a commonly used implant material due to its superior properties; however post implantation, it could result to inflammatory responses.[2] Therefore the titanium implant surfaces are functionalized in order to achieve optimal performance.[3] Loading an anti-inflammatory drug - Dexamethasone (Dex) on titanium nanoparticles is thought to reduce inflammation and enhance bone growth by osteoblast differentiation.[4] The aim of this study was to prepare and characterize a drug delivery system by the functionalization of titanium based nanoparticles (TiO_2) loaded with Dex.

TiO_2 nanoparticles were functionalized via silanization using mercapto (–SH) groups. Dex was loaded on functionalized TiO_2 nanoparticles in two different ways: conjugate (via covalent bonds) and adsorbed (via weak van der Waals forces). The functionalized nanoparticles were then characterized using TGA, particle size, particle charge and drug release, as a function of pH.

TGA results indicated the presence of organic material, and showed that more organic material was present in the conjugate compared to the adsorbed Furthermore, the zeta potential and HPLC data confirmed the presence of Dex in the conjugate and adsorbed. The drug release profile showed promising results with regards to release of Dex at pH 4-7. At pH 7, maximum release of Dex was observed in both conjugate and

adsorbed. The release profile of the adsorbed was better than the conjugate. The method used to investigate particle size was less effective as indicated by relatively high PdI and high agglomeration.

These results confirm the presence of Dex on the surface of TiO_2 nanoparticles. However, appropriate approaches to reduce agglomeration, long-term and in-vivo studies need to be considered.

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Evaluation of inhaler technique in patients of the Cardiff and Vale University Health Board

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Inhaler technique is of great importance in patients with respiratory disease as inhalers are the primary method to deliver drugs to the lungs.[1] The main drawbacks of inhalers is that it requires accurate use of the device by the patient to ensure that as much of the dose reaches the lungs as possible to provide good disease management.[2] Poor Inhaler technique is a cause for concern as there was such a high percentage of errors recorded with inhaler use.[3] The aim of this study is to evaluate inhaler technique in the patient population of the Cardiff and Vale University Health Board, particularly focusing on differences in metered dose inhaler (MDI) technique compared to dry powdered inhaler (DPI) technique.

Ethical approval was granted for both arms of the study. The first arm of the study involved the use of a semi-structured interview to question pharmacists in the Cardiff and Vale University Health Board about advice they provide to patients that use inhalers and their opinion on inhaler technique. The data was analysed with use of a coding sheet to identify frequencies of common themes. The second arm involved patients completing a short questionnaire about their inhalers and then the patients were assessed on their inhaler technique using an Aerosol Inhalation Monitor. Analysis of this data was carried out using Microsoft Excel, Access and Graphpad prism6.

MDI technique was statistically worse than DPI technique. Those that use spacers also have statistically better technique than those that use MDI alone. Pharmacists also believe that inhaler technique is bad with several pharmacists emphasizing that MDI technique is worse than DPI technique.

MDI technique is poor, however DPI technique could also be improved. Pharmacists and other health care professionals should make more of an effort to provide advice and training to patients that use inhalers

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Review of Medicines Administration (MAR) charts in care homes

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Over 400,000 people over 65 years old reside in care facilities in the United Kingdom[1], with the median period from admission to death being 15 months.[2] Medication errors may be a contributing factor to this statistic, with literature showing 69.5% of patients have at least one error.[3] Medicines Administration (MAR) charts are produced by pharmacists, and are used in care homes to provide a formal record of administration. The aim

of the study was to identify the number, and types of errors made in one care home in the Abertawe Bro Morgannwg University (ABMU) Health Board.

Eleven care homes were recruited, with one care home allocated to each of the ten MPharm students. A retrospective review of MAR charts was undertaken, with errors identified and allocated into broad and sub-categories. The care home investigated was a residential facility with thirty residents.

A total of 25 charts were analysed, with residents taking a mean of 7.4 (SD+/-4.45) medications. Allergy information was missing in 20/25 (80%) of charts. The total number of errors identified was 433. Nearly all charts (24/25, 94%) contained at least one error (Mean=17.44; SD+/-21.36). Administration errors were the most common error (n=107, 25%) with 82 (77%) of these omissions. Emollients were the BNF category with the most errors (n=140), with 103 (74%) of these omissions. A positive correlation (Spearman rho=0.49, $p<0.05$, n=25) was found between number of drugs prescribed and number of errors.

A large number of errors were identified, with errors in administration being the most commonly observed. Emollient non-compliance was frequently captured, which could exacerbate the symptoms of patients' dry skin conditions. Further research into the potential consequences of these errors is recommended, and changes need to be made to improve patient safety.

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A review of Medication Administration Record (MAR) charts from residential and nursing homes within the Abertawe Bro Morgannwg University Health Board

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In 2009 Alldred et al found that almost 70% of care home service users experience at least one error in their medication.[1] Not all errors are considered serious, however previous systematic reviews have shown that "4.3% of (hospital) admissions are considered to be drug related and preventable".[2] This study specifically examined record keeping and administration of medicines via Medication Administration Records (MAR) charts (n=229), from one nursing home, to ascertain the types, frequency and patterns of errors within the care home environment.

As a quality assurance measure, two validation stages were built into the study. Subsequently an error classification scheme was agreed. This scheme was then used to review the medication records on the MAR charts from the participating nursing home. Data from the study was analyzed in SPSS. Clinical assessments were outside the scope of this investigation.

The study revealed that 98.7% of service users at the participating home experienced at least one error during the study cycle. Administration errors, associated with the delivery of medicines to service users, accounted for the greatest proportion of incorrect entries or omissions identified. Nutritional supplement medicines, vital for maintaining health and wellbeing and extremely important in promoting service user dignity[3] were those most frequently omitted. It was also found that there was a correlation between the number of medications prescribed and the propensity for errors ($p=0.002$ $\varrho=0.352$).

All errors highlighted in this review can potentially put the service users' health, safety and quality of life at risk. Further research is needed to establish whether these results are an anomaly or whether they reflect systemic issues. This study would also benefit by inclusion of a clinical appraisal and a larger sample population.

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Development of community-based cardiovascular risk screening service: analysis of cross-sectional pilot data

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Cardiovascular disease (CVD) caused over 160,000 deaths in the UK and cost more than £6.8 billion in 2012.[1] Evidence has demonstrated that the risk of developing CVD largely depends on modifiable risk factors such as hypertension, obesity, smoking and physical inactivity.[2] It has been proposed that the idea of implementing cardiovascular risk screening service in community pharmacies to identify patients at risk is both feasible and desirable.[3] A health campaign was conducted to assess the potential of this service. The main aim of this study was to evaluate the feasibility of conducting cardiovascular risk screening service in community settings in Wales.

Participants were interviewed by a pharmacist to complete a questionnaire. The pharmacist then conducted blood pressure measurement and provided lifestyle advice to the participants. Data collected from the campaign were analysed to identify the prevalence of hypertension, obesity and smoking in the population. GraphPad Prism software was used for statistical analysis to investigate association between blood pressure and different cardiovascular risk factors.

24.4% of participants were hypertensive and those aged over 60 were more prevalent in isolated systolic hypertension (ISH) than the younger participants. 31.4% of participants were overweight and 28.5% were obese. The ratio of total smokers to non-smokers was 1:3. Study found that systolic blood pressure, pulse pressure and mean arterial pressure increased with age. However, it was observed that obesity, smoking and exercise did not increase the risk of hypertension.

This study demonstrates that pharmacist can successfully identify those at risk of CVD and provide patients lifestyle advice accordingly. Pulse pressure screening targeting population aged over 60 might be beneficial to control prevalence of ISH and stroke in the elderly. In conclusion, it is feasible to conduct cardiovascular risk screening service in community settings. Future work needed to develop a standardised screening protocol.

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Evaluation of inhaler technique in patients of the Cardiff and Vale University Health Board

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Inhalers are commonly used to treat respiratory conditions such as asthma and COPD which combined caused 24,000 deaths in the UK over a 12 month period (2012/13).[1] The NHS spends £1 billion annually on asthma treatment with an estimated 80% being spent on the 20% of the most symptomatic patients.[1] It is well documented that inhaler technique in the patient population,[2] and in healthcare professionals is poor.[3] The aim of this study is to assess and survey the inhaler technique of patients in the Cardiff and Vale University Health Board.

The study had two branches; a semi-structured interview with pharmacists, and a patient questionnaire and assessment of their inhaler technique. The interview covered how pharmacists guide patients in the use of inhalers. 45 pharmacists were convenience sampled throughout the health board. Data was analysed using content analysis. Quantitative data were analysed using Graphpad Prism. All data was anonymised. Ethical approval was granted. Permission was also granted to be run as part of an NHS service evaluation.

89 patients were recruited. Only 3% and 29% of patients demonstrated correct inhaler technique using the pMDI (n=67) and DPI (n=48) inhalers respectively. Of the HCPs studied, nurses gave advice most frequently (52%) and pharmacists least frequently (6%). 11 patients had never been given advice. Pharmacists mentioned a number of issues that hindered their ability to offer advice. Examples include time (n=15), dependant on the patients' inhaler type (n=9) and patients not willing to listen to advice (n=29).

Patients' inhaler technique was generally poor. Healthcare professionals need to receive more training in order to educate and reinforce correct technique in their patients. They also need to motivate patients to become more involved in their own treatment, as a barrier to the provision of advice was a lack of interest.

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Patient satisfaction survey: satisfaction with medicines management and information about medicines during hospital stay and on discharge

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Providing "timely and accessible information to patients regarding their condition, care, medication and treatment"[1] is a standard for health services in Wales and is a crucial aspect of patient safety. We have also become increasingly aware of the need to involve patients in the development of pharmacy services.[2] This is especially since reports of failures in hospitals have been highlighted.[3] The aim of this study was to assess patient satisfaction with the management of their medicines in hospital and their satisfaction with the information received about their medicines.

This is a follow-up to the earlier research carried out in the four hospitals within Hywel Dda Health Board as part of an All-Wales study, which began in January 2014. The questionnaire (used in January 2014) was adapted to overcome some of the issues raised and extended to include additional questions. Hospital pharmacists selected recently discharged patients' discharge summaries according to specified criteria. Codes were assigned to patients, their demographics were inputted to a database and bilingual questionnaires along with cover letters were sent out to their homes.

Of the 344 questionnaires sent, 124 replies were received (36% response rate). Responses were recorded and analysed in SPSS. Results showed that the overwhelming majority (82.3%) spoke to a member of staff about their medication during their stay in hospital. However, significantly fewer patients spoke to pharmacists compared to nurses and doctors, both during their stay and on discharge. Problems experienced were varied but commonly featured were: delays in receiving medicines and lack of information provided about medicines.

With only a few patients experiencing problems since leaving hospital and with such high levels of satisfaction, we can say that the overall outcome was positive. Nevertheless, improvements can be made to enhance services for the future, e.g. introduction of electronic discharge summaries.

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The interactions between complement and neutrophil extracellular traps (NETs) in sepsis

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Sepsis is a fatal, inflammatory disorder characterised by an over-exaggerated response of the host immune system to an invading pathogen.[1] Within this condition, neutrophils are excessively activated and produce

NETs, which are protruding web-like structures, mainly composed of DNA and histone.[2,3] Classical complement proteins have been found to interact with NETs via C1q and C3b deposition,[4] thought to be important in sepsis. As such, our project aimed to study these interactions in detail.

Neutrophils were isolated from whole blood from 3 healthy donors and activated to produce NETs using 25 ng/ml phorbol 12-myristate 13-acetate. NETs were quantified using an extracellular DNA stain (Sytox Green). Haemolytic assays were used to establish the effect of NETs and NET components on complement. Serum complement was incubated with one of our test reagents (DNA, histones, 'NET model' or NETs) and added to IgG-activated sheep erythrocytes (ShE). Serum titration curves and % lysis were produced. T-tests or ANOVA were used to assess statistical significance.

Results showed that, in the presence of DNA, histones and 'NET model', the ability of serum complement to lyse ShE via the classical complement pathway is decreased ($p<0.05$). This indicates that complement proteins deposited on NET components. A decrease in lysis occurred with DNA after an extended incubation period, however histones showed this after shorter incubation. The 'NET model' produced a bigger effect than either DNA or histones alone. A large decrease in haemolysis (and hence complement deposition) was observed in the presence of NETs from donor 1 ($p<0.05$), however this was not shown with donors 2 or 3.

NETs and NET components can interact with the classical complement cascade, demonstrating cross talk between these two systems of innate immunity. This project will contribute towards the increased knowledge of sepsis pathophysiology, to hopefully uncover novel drug targets and therapeutic interventions.

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Questionnaire development of local infiltration analgesia in knee replacement service evaluation

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Enhanced Recovery After Surgery (ERAS) is a programme focusing on patient care. In the United Kingdom, it is delivered by the National Health Services with the aim to improve patients' recovery after surgery.[1] ERAS is divided into pre-operative, intraoperative and post-operative care.[1] Anaesthetic is one of main factor to be considered in intraoperative and post-operative care.[1] Local Infiltration Analgesia (LIA) had emerge to be a popular anaesthetic method in elective surgery such as orthopaedic. LIA involves infiltration of a mixture of anaesthetic agents and adjuvants into the surgical site prior to closure of the wound to reduce inflammation.[2] The aim of this project is to pilot an online questionnaire developed during summer 2014 and make sure that the design of the questionnaire is appropriate for future use. The objective of the research is to improve the validity and logic of the questionnaire by piloting work.

The questionnaire was piloted with five subjects from different backgrounds. Sample of questionnaire was sent to them via email. Their comments and feedback were collected and the questionnaire were modified following discussion.

Feedback resulted in hip replacement related questions being removed from questionnaire. Some spelling and grammatical errors were also picked up by the pilot subjects. Issues related to the use of the online questionnaire were also raised up by one of the pilot subjects.

The hip replacement related questions were removed as it is a more complex surgery and therefore it was felt it would be better to focus on one area rather than two areas. Spelling and grammatical errors may affect the presentation and quality of the questionnaire thus it is important to address these errors. Issues raised regarding online questionnaire were probably due to the type of internet browser being used but should be noted as possible issue for future use of the system. Piloting is an important process as it helps to identify any underlying problems with the questionnaire, the pilot results showed that the questionnaire was well designed and relevant to the service evaluation.

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Stakeholders' perceptions of the inclusion of prescription prices on dispensing labels

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Medicines wastage is a huge problem within the NHS, costing an estimated £50million a year in Wales.[1] Causes are numerous and could be related to medicines being provided free of charge, and patients being unaware of medicines costs and extent of wastage. Informing patients of cost through inclusion of medicine price on the dispensing label may encourage patients to reconsider wasting their medicines. The aim of this study was to explore stakeholder views of the proposal to include cost on dispensing labels, and to consider its potential impact in practice.

Ethical approval was granted by the SPPS Research Ethics Committee. Stakeholder analysis was used to identify key stakeholders who were invited to interview via a gatekeeper. Data was transcribed verbatim and thematically analysed which generated codes. These were grouped into themes forming the results.

Ten stakeholders were invited of which seven agreed to participate. Stakeholder professions included; GP (n=1), community pharmacist (n=1), health board member (n=1), pharmaceutical industry representative (n=1) and health representatives within Welsh Government (n=3). Five key themes were generated; recognition of problem, perceived benefits of proposal, perceived barriers of proposal, patient-centred care and suggestions for model. Overall, 72% of stakeholders were in favour of the proposal.

Stakeholders felt medicines wastage was a significant problem and avoidable wastage needed recouping in order to save money. Benefits of the proposal included improved awareness of cost burden to the NHS and the majority felt the proposal would improve patient adherence and therefore wastage. However, ethical concerns such as patients being discouraged from taking medicines were identified. All emphasised that for the proposal to be successful it must be patient-centred and encourage ownership of their medicines. Before implementation, ethical concerns will need addressing and the proposal piloted.

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Potassium permanganate wound lavage: investigations into reactions with simulated chronic wound bioburden

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Permitabs (KMnO4) are used clinically in the treatment of chronic wound infections; one 400 mg tablet is dissolved in 4 litres of water to create a pink/purple soplution.[1] Research into the antimicrobial activity of KMnO4 is largely based on clinical evidence, with focus on its ability to decrease bioburden and the enabling of the establishment of normal wound healing. This study analyses the oxidation mechanism of KMnO4 with respect to both Pseudomonas aeruginosa and an artificial wound fluid (AWF); representing the exudate present in a chronic wound environment.[2]

UV-Vis spectrophotometry was used to analyse the changes in KMnO4 oxidation state at 529 nm after its reaction with organic matter. The antimicrobial effect of KMnO4 was analysed via suspension tests, with analyses of both AWF and bacterial reactions occurring over two temperature increases (5 oC and 10 oC). A contact time of 20 minutes and the recommended concentration (63 mM) were selected; 50 mM and 70 mM were also tested.

Combinations of KMnO4 and AWF produced a decrease in KMnO4 concentration within the first 12 seconds. Subsequent tests confirmed an initial decrease followed by a plateau in concentration. Increases in temperature accelerated the rate of permanganate reduction. However, bacterial analyses did not show an observable change in activity upon increasing temperature due to the complete eradication of all bacteria.

An accelerated rate of KMnO4 reduction signifies a greater oxidation rate; results using AWF show an increased rate when the temperature is increased and when concentration is increased to 70 mM from 63 mM. Although not proved in this study, it is hypothesised that an increase in oxidation rate would increase rate of bactericidal activity.

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Review of Medicines Administration (MAR) charts from care homes

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Care homes currently use paper-based medicines administration records (MAR) to document the administration of medicines. The Care Homes Use of Medicines Study (CHUMS) found that 69.5% of residents in England experienced one or more errors related to their medication.[1] To date there have been no studies assessing errors that occur when using MAR charts in care homes in Wales. The aim of this study was to investigate administration errors in one care home. This was part of a larger project to evaluate errors in 11 care homes in South Wales.

MAR charts from participating care homes were reviewed retrospectively. Errors were defined and categorised by group consensus based on Care Quality Commission (CQC) guidance.[2] Descriptive data were assessed using Microsoft Excel® and frequencies of error types were assessed using SPSS®. Spearman's rho correlations and Mann-Whitney U tests were carried out to identify relationships between variables.

A total of 183 medicines were prescribed for 24 residents. The three most commonly prescribed groups of medicines were for the cardiovascular, central nervous and gastro-intestinal systems. In total, 1367 errors were identified over 17 days in October 2014. Stock errors were present for all but one medication. A high amount of omissions (n=397) were identified. The use of a "when required" (PRN) medication showed significantly higher rate of administration errors (p=0.012). There were significant positive correlations between total number of medication and total errors (rho=0.882, n=24, p<0.001), administration errors (rho=0.572, n=18, p<0.05) and stock errors (rho=0.979, n=24, p<0.001).

Based on the findings of this one small care home, the current system of paper MAR charts allows for many errors, since CQC standards are not being met. These baseline data allow for comparison of errors following introduction of new systems, such as clinical reviews by pharmacists[3] and eMAR with barcode scanning[4].

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Pharmacists' use of a professional development framework to identify learning needs

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In 2014, the Royal Pharmaceutical Society (RPS) introduced the Foundation Practice Framework[1] as a structured method for pharmacists to assess their own learning and identify areas for improvement. The framework was based on the General Level Framework[2], which has been used as part of the Diploma in Pharmacy Clinical Practice (Community and Primary Care) at Cardiff University since 2005. Pharmacists were asked to self-assess their skill level over 107 competencies at four timepoints throughout the course. The aim of this study was to identify trends in pharmacists' self-assessment of their competency levels and types of evidence used to support this

A retrospective review of all frameworks completed between 2008-2014. Pharmacists rated themselves using a 4-point scale ("never" to "always"). These answers were given corresponding numerical codes, where the higher the number, the higher the competency level. Quantitative data were analysed using SPSS© and *student t-tests* used to explore changes over time. Students provided supporting comments which were reviewed and "Wordles"©[3] of the most common words were created.

A total of 38 students' frameworks were reviewed (38 at timepoint A and B, 27 at C and 26 at D). A total of 16,264 individual self-ratings were inputted. Students showed a mean improvement of 29.7% over the course. Varying rates of improvement were seen over each of the four clusters. The ratings for "Personal Competencies" were consistently the highest, whereas pharmacists reported the least confidence in "Problem Solving Competencies". The greatest improvement was seen in "Delivery of Patient Care". Supporting comments suggested that frameworks were used appropriately.

The findings indicate that the use of a professional development framework provides an effective tool to support pharmacists' learning. Further research is needed to establish whether this is also true for those using a framework outside of a formal education programme.

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Should patient's Discharge Advice Letters (DALs) be sent to community pharmacists: the views of the public in Wales – development and piloting of the questionnaire

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Improving continuity of care of patients moving between healthcare settings is currently a priority within the National Health Service[1] helping to avoid hospital re-admissions and reduce morbidity and mortality. The Discharge Medicines Review service, led by community pharmacists in Wales, was created to help improve the continuity of care for patients moving from hospital into community. A proposal was received to have hospital Discharge Advice Letters (DALs) sent to community pharmacists helping them to carry out the Discharge Medicines Review (DMR) service. The aim of this study was to develop and pilot a questionnaire to establish the views of the public on this.

Using themes from Rowlands'[2] qualitative study on this topic, an anonymous, self-administered questionnaire was developed to establish the views of the wider public in Wales. The questionnaire used closed and open-ended questions and a 5-point Likert scale. An additional double-sided proforma was provided to guide participants' feedback. Two pilots were carried out using convenience sampling; pilot 1 (n=18) was distributed by hand, pilot 2 (n=60) by mail. Feedback collected from pilot 1, was used to improve questionnaire before pilot 2.

Pilot 1 reached 100% response rate; pilot 2 achieved 45%. Comments made included that language used was too 'scientific' for the general public (n=2) and the meaning of 'community pharmacist' is unknown (n=4). After pilot 2, significantly fewer comments were made; only minor revisions were required to produce the final copy of the questionnaire.

The pilot stage has proven crucial to the successful development of the questionnaire. It identified issues with terminology and fundamentally the lack of understanding of the public about what a community pharmacist is. The questionnaire is now ready to be sent out on a larger-scale to the wider public in Wales.

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Synthesis of ^{18}F-ProTide precursors for Positron Emission Tomography (PET) imaging

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Positron emission tomography (PET) is a molecular imaging technique which uses positron-emitting isotope labelled biomolecules for cancer diagnosis and treatment follow up.[1] ^{18}F is the radioisotope of choice due to its favourable half-life (110 minutes).[1] Although [^{18}F]-FLT is a promising tumour proliferation radiotracer, its use is limited by poor membrane permeability and the rate limiting monophosphorylation step.[1] However, a ProTide approach has the potential to circumvent these problems. The aim of this study is to synthesise 3'-fluorinated thymidine pro-nucleotides (ProTides) using methods applicable to ^{18}F radiochemistry. The objectives include development of an efficient chemical synthetic route for the production of FLT based ProTides and first trial of late stage fluoride introduction on FLT-ProTide precursors using cold fluorination.

A 2,3'-anhydrothymidine was first synthesised using the Mitsunobu reaction followed by hydrolysis reaction at the 3' position of thymidine.[2,4] Next, the 5'O-position was protected with a phosphochloridate to furnish the ProTide precursor which was then subjected to a mesylation at the 3'-OH group to obtain the FLT-ProTide mesyl precursor.[3,4] Late stage fluorination with non-radioactive ^{19}F was carried out on the precursor as proof of concept prior to radiosynthesis. Purification and charactherisation techniques were also carried out in between each step.

The mesylated precursor was successfully synthesised via a shorter and effective route compared to previous studies with a yield of 30%.The fluorination was unsuccessful due to absence of peak on ^{19}F NMR and decomposition of starting material.

Further testing and optimisation would still need to be done to improve the yield and stability of the precursors. Failure of the fluorination reaction suggested that the fluorinating agent used, TBAF was not nucleophilic enough to carry out the reaction. In conclusion, this project reflects that great progress has been made in synthesising a ProTide precursor for PET imaging.

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The potential link between ageing, clathrin-independent endocytosis and Alzheimer's disease

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Alzheimer's disease (AD), an age-associated neurodegenerative disorder, is characterised by accumulation of amyloid-β (Aβ). Aβ is derived from amyloid precursor protein (APP) after it enters cells via endocytosis.[1] Recent studies suggested that clathrin-independent endocytosis (CIE) is crucial in the production of Aβ.[2] CIE involves the internalization of molecules via caveolins and flotillins.[3] I examined the expression of CIE proteins in wild-type (Wt) and transgenic (Tg) mice of different ages that overexpress APP to compare and determine the effect of ageing (a major risk factor) on the expression of these proteins.

Western Blotting was performed on cortex from 3-, 9- and 18-month old Wt and Tg mice. 10µg of samples were resolved on 10% polyacrylamide gels, before incubating in relevant antibodies. Western blots were quantified using Image J. Protein bands were expressed relative to GAPDH levels. Results were analysed by using two-tailed Student's t-tests, or one-way ANOVA and Tukey's post hoc test.

APP levels were increased in 9 and 18 month Tg mice compared to Wt mice confirming the validity of the Tg mouse model. A significant increase in caveolin-1 was seen at 9 months in Tg compared to Wt mice but no

significant changes were seen at other ages. No changes in flotilin-1 and -2 levels were seen between Tg and Wt mice. In the age comparison study, there were no significant changes in the expression of APP and caveolin-1 with age in either Wt or Tg mice.

Caveolin-1 and -2 are known to be protective against Aβ accumulation.[4] The upregulation of caveolins in younger Tg mice suggests that this protective effect could be a result of increased APP levels. Caveolin levels appeared to be decreased as animals grew older implying that this protective mechanism is lost with age in Tg mice. My results suggest that CIE is not greatly affected by ageing and may not be critical for the development of amyloid pathology.

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Evaluation of the inhaler technique in Cardiff and Vale University Health Board

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Inhaler technique is important for the clinical outcomes of inhalers.[1] Many studies have concluded patient's technique is inadequate. Guidelines suggest counselling should be provided before a new device is prescribed and assessed regularly.[2] Pharmacists are ideally placed to provide this advice.[3] This study aims to give an insight into pharmacists' views surrounding inhaler technique and find out how effective the inhaler technique is in Cardiff and Vale Health Board.

This observational study was carried out in two arms. The first arm included a patient questionnaire and a Vitalograph Aerosol Inhalation Monitor (AIM) test to evaluate patients' inhaler technique. The second arm involved a semi-structured interview on pharmacists which contained key questions including how often advice is given, prompts and barriers to providing advice and who they believe is the most appropriate person to provide advice.

A total of 89 patients and 45 pharmacists participated. Results show that 85% of patients did not use their inhalers correctly. Dry powder inhalers (DPI) resulted in better technique in contrast to metered dose inhalers (MDI) (29% vs 3%, $p<0.0001$). 60% of pharmacists believed that they were the most appropriate person to provide advice and 51% stated that they were always able to offer advice. A common barrier to offering advice was pharmacists' lack of time (25%).

Overall, inhaler technique was poor. Nurses were the most common professional to counsel patients, although pharmacists believe they could do more. A multi-disciplinary approach would probably be best to ensure patients can adequately use their device. Future interventions need to be implemented to ensure inhaler technique can be improved.

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Review of drug stability in elastomeric devices

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Elastomeric devices are portable, lightweight infusion pumps that do not require any programming or the use of batteries.[1] Home infusion therapy using these devices has become increasingly popular over the years.[2] However, there is a general lack of drug stability data in these devices. Hence, the purpose of this study is to gather available information on drug stability in elastomeric devices and to identify if there is a need for further studies on this subject.

A literature search was carried out on seven different electronic databases. Eleven manufacturing and/or distributing companies were also contacted in an effort to obtain drug stability data for the devices.

Fifteen published studies and a guideline published by one of the manufacturers were found that met the inclusion criteria. Drug stability data was found for five different elastomeric devices. The Homepump device had the most amount of drug stability data published while antibacterials had the highest amount of data among the different classes of drugs. Ceftazidime was identified as the drug most frequently studied for stability in these devices.

This study suggests that there is a reasonable amount of published data on drug stability in these devices. However, most of the data was extracted from a single guideline and not all papers that were reviewed provided sufficient information. Manufacturers and/or researchers should identify the information that users require in order for them to provide relevant information in the publications. The general lack of data could also be due to the fact that manufacturers involved are not obliged to provide the information. This review suggests that drug stability data in elastomeric devices should be more accessible to healthcare professionals. Furthermore, future publications should provide more relevant information. These efforts will assist healthcare professionals in selecting the most appropriate device for the drug required by the patient.

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Solid-phase natural product extraction from Greek marine sponges

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Drug discovery from marine sponges has shown potential by the current approval of three drugs on the market.[1] However, extraction yields of natural product are tremendously low and causes difficulties in mining potential drugs from natural resources.[2] Chemoselective isolation strategies has been developed to isolate compounds according to functional group compositions from complex biological matrix using polystyrene-based resin beads with a chemoselective reactive group that act as immobilised support.[3,4] It was hypothesized that many natural products from marine sponges contain nitrogen and hydroxyl-containing molecules and these resins are capable of capturing these functional groups. This study was to develop a method to extract natural compounds from Greek marine sponges using isothiocyanate and sulfonyl chloride functionalised resins by solid-phase extraction.

Solid phase extraction using electrophilic resins has been used to isolate compounds from a *Sarcotragus* species and *Crambe crambe.* Mass spectra of the extracted compounds provided their molecular weight. Possible compounds were found using MarinLit, a database of marine natural products.

The isothiocyanate functionalised resin showed better extraction for both marine species as it has higher percentage recovery compared to the sulfonyl chloride resin. Different resins are capable of extracting different types of compounds. 31 possible compounds were found from the *Sarcotragus* species while only eight compounds were isolated from *Crambe crambe*.

Resins with different functionality can extract different types of compounds from a complex mixture. Both marine species may contain more nitrogen containing compounds. The Isothiocyanate and sulfonyl chloride resins used in the solid phase extraction proved to be a successful method for extracting compounds from Greek marine sponges but it is not an efficient method due to extremely low yield of extraction.

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Exploring pharmacists' views on community pharmacy placement schemes

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Experiential placements are fundamental part of University pharmacy programs, providing students the opportunity to consolidate knowledge attained during their studies and develop skills and attitudes of the profession; hence placements are mandatory by many accreditation bodies.[1,2] Supervising pharmacists play a large part in the success and quality of placements and are an essential asset to the pharmacy curriculum.[3,4] This study aims to explore the views of community pharmacists on current placement schemes organised through Cardiff university MPharm to improve the quality of placements. Objectives are to identify aspects to support their supervisory roles and facilitate student learning, formulate suggestions to improve schemes and identify current issues and barriers.

A series of one-on-one semi-structured interviews were undertaken, audio-taped and transcribed verbatim. Transcripts were analysed thematically and analysed for themes relating to experimental placements.
Nine community pharmacists participated in the interviews, representing varied workplace settings. Pharmacists positively rated the support from the university and reported enjoying the supervisory role. Major concern reported was difficulty managing their own workload whilst facilitating for students. Students' motivation and willingness to learn were specified as important contributors to the success of placements. Mechanisms to improve placement schemes were generated.

Findings from this study were in line with existing literature in this area of work and across various disciplines. Overall placements were considered useful and valuable by community pharmacists for students. Pharmacists' attitudes showed a solid commitment to the supervising role, the appreciation of the potential professional and personal gain and were aware of the limitations associated with their role. The study highlighted issues that can be addressed and suggested improvements, which can be used for future initiatives to improve the quality of placements.

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The following abstracts have been withheld as they have been or will be published elsewhere, and/or due to intellectual property or confidentiality issues:

Enhancement of particles diffusion through intestinal mucus by Self-MicroEmulsifying Drug Delivery (SMEDD) System

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An investigation into the stability and in vitro microbicidal efficacy of a pomegranate rind extract-based handrub

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Pomegranate-based handrub: probing the need and microbiological evaluation against *Pseudomonas aeruginosa*

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Probing mathematical models for determining tannins/metal ion binding constants and stoichiometry

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The effect of different formulations of self-microemulsifying drug delivery systems (SMEDDS) to improve nanoparticle permeability through intestinal mucus

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Awareness of sickle cell trait status: a cross-sectional survey of antenatal women in Ghana

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Sickle cell disease (SCD) is a hereditary blood disorder, characterized by red blood cells that assume a rigid, sickle shape leading to pain, infection and other complications. Nearly one third of Ghanaians have the trait and about 2% of babies in Ghana are born with the disease. A recent study of Ghanaian women of childbearing age indicated they did not realize the significance of testing for the sickle cell trait (SCT) before conception, and how this could impact their family planning decisions. Awareness of sickle cell relies on healthcare providers (HCPs) providing accurate patient information.

To evaluate pregnant women's awareness of SCD and SCT and the factors that contributes to it. Methodology: Adult antenatal patients who were at least 20 weeks gestation answered a questionnaire regarding awareness of their trait status and questions to test their knowledge of sickle cell.

Although the majority of patients were aware of their trait status (87.4%), only 29% of knowledge questions were answered correctly; patients who self-identified as having SCT did not do better. Patients who responded that they knew a lot about SCD scored on average 3.5 points more than individuals who responded that they knew nothing ($p<0.001$).

Individuals who knew they had been tested for the SCT scored approximately 2 points higher than those who did not know whether they had been tested ($p=0.004$). Respondents with at least secondary education scored on average 1 point higher on the knowledge test than those with less education ($p=0.004$). Knowing someone with SCD was associated with a mean score 1.25 points higher than individuals who did not know an affected individual ($p=0.000$).

The patients' awareness of SCT and SCD was poor. Perceived knowledge, knowledge of trait status, education and prior personal experience of sickle cell were correlated to knowledge.

Are schizophrenic, adult, out-patients more compliant to long-acting injectable antipsychotics compared to oral antipsychotics in long-term clinical trials? A systematic review

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Schizophrenia is an acute mental disorder suffered by more than twenty-one million people globally. The World Health Organization (WHO) (2014) state that approximately 1% of the global population experiences a severe episode of schizophrenia at some point in their lifetime. There is an ongoing difficulty to treat patients with schizophrenia which is likely to be due to the complexity of the symptoms and the varying degrees of psychosis suffered from one individual to another. Treatment regimens have to be tailored to the individuals needs and constantly monitored for adjustment.

Compliance to medication is an ongoing battle for physicians and the individuals suffering with schizophrenia and are probably non-compliant to their medication due to the burdensome nature of the positive and negative symptoms of the disease, the side effects associated with antipsychotic medication. The overall aim of this research was to advance an understanding of non-compliance to long acting injectable antipsychotics compared to oral antipsychotic drugs in a clinical trial environment to provide answers to the study endpoints. Primary endpoint: is there a statistically significant difference in compliance to long-acting injectable antipsychotics vs oral antipsychotic medications. Secondary endpoint: are patients more compliant to typical or atypical antipsychotics. A systematic review, using the PRISMA statement, of 18 completed studies was performed to determine treatment compliance rates of schizophrenic outpatients participating in clinical trials. The search was performed using Trial Trove. A meta-analysis of the quantitative data was performed and complemented with a meta-synthesis of the qualitative information.

A meta-analysis of the empirical data was performed. A random effects model was adopted. Each effect size(es) was represented in the overall summary estimate. es (random) = 22.7% with the lower and upper

confidence limit. Primary endpoint: Oral vs LAI: Odds ratio 95% CI = 0.9703 (0.8710-1.0809); p=0.5844. df 1 Secondary endpoint: Typical vs Atypical: Odds ratio 95% CI = 0.9703 (0.8710-1.0809); p=0.5844. df 1. p>0.05 was observed for both endpoints.

There was no significant difference in the rates of compliance for any treatment group. However, meta-synthesis of the studies stimulated argument of a clinical significance for treating schizophrenia with long-acting injectable antipsychotics accompanied with cognitive behavioural therapy.

Clinical research and risk in a UK university: a case study

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Clinical research is a core research function of most research-intensive universities in the UK. Academic-led (non-commercial) clinical research attracts millions in research income each year and is considered an important aspect of maintaining a position in increasingly competitive times, as universities struggle for research funding and high positions in league tables.

Despite decades of increased research and ethical governance, academic clinical research can still present a degree of risk to universities. Unlike Clinical Trials of Investigational Medicinal Products (CTIMPs), clinical research that is not classified as a drug trial, is not governed by any one legal framework or legislation. Therefore, universities must effectively manage any risks associated with academic clinical research.

Focusing on Cardiff University as a case study, this exploratory work utilised a mixed methods approach to data collection. Using the data from a questionnaire conducted with academic clinical research staff and a series of interviews with staff involved in the management and governance of clinical research, the study begins to look at the complexities of defining what is meant by 'high risk' academic clinical research.

It also considers the gaps in the University's current approach to risk management of clinical research and discusses the differences in perceptions of clinical research risk, existing between academic clinical research staff and the University as a corporate entity. Finally, the components of a potential University tool for the risk assessment of clinical research are considered.

The UK primary care system: prime location for clinical drug trials or research backwater?

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The UK National Health Service delivers healthcare to a million patients every thirty-six hours, ninety percent of these encounters taking place within the primary care system. These patients are efficiently managed by well-qualified and experienced teams of clinicians and their chronic disease information
effectively databased within this setting providing an excellent and timely source of relevant data, and yet the global pharmaceutical developers that sponsor clinical drug trials still appear to overlook this structure when identifying centres at which to site their drug trials, in favour of the secondary care, hospital setting.

In an effort to establish whether this avoidance was justified and whether there are any specific reasons that clinical trials placed in primary care were more likely to fail than those in secondary care, a search was conducted of the available literature. Publications for reasons of general failure in clinical trials
were also examined and a detailed examination of the primary care system was performed, looking at it's suitability as a drug research environment as well as it's advantages over a secondary care setting for the conduct of clinical drug research.

Seventy-seven patients who had participated in a clinical drug trial in primary care completed a questionnaire providing feedback about their motivation and general experiences. The findings showed significant positive expression about taking part in a clinical trial in a general practice with clear evidence of trust in their general practitioner in the role of clinical investigator. The data suggests patients felt they had been well looked after in their clinical trials with a distinct majority expressing that they would be happy to consider future participation.

Clearly, fundamental to this process is the choice of the patient however, and without their motivation to support clinical research in any setting, this discussion would be redundant.

The atypical nature of the UK primary care system represents a degree of risk to some global drug developers and despite considerable Department Of Health initiative, the real merits of primary care as a clinical research host are still being overlooked. Whilst acknowledging that certain types of clinical research are clearly unsuitable for primary care, many studies that are being undertaken in UK hospitals would be far better placed in a primary care setting. This is not good for researchers in either clinical environment and much needs to be done to enhance collaboration and trust between primary and secondary care clinical trialists, in order that a greater understanding of relative strengths can be recognized. As a key part of this effort, bodies such as the National Institute of Health Research must provide a much clearer picture for prospective pharmaceutical sponsor companies of where patients 'reside' in terms of key disease management and which researchers are best placed to access them.

Identification and management of treatment induced sexual dysfunction in breast cancer patients receiving adjuvant endocrine therapy

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This service evaluation explored the support offered at a district general hospital, to women with hormone receptor positive breast cancer on adjuvant endocrine therapy in relation to sexual dysfunction as a quality of life issue. The evaluation was concerned with examining the structure and appropriateness of the information, advice and management women were offered and at what time points in their pathway of care opportunities to identify and address sexual dysfunction on endocrine therapy occurred. The concept was highlighted by two patients who separately disclosed sexual dysfunction. It emerged that the pathway for identification and management of sexual dysfunction for breast cancer patients on endocrine therapy at the evaluation site was poorly defined.

The aim was to engage the Breast Cancer Multi-Disciplinary Team (MDT) in a process, which would inform and improve joint working from within so that it consistently provided cohesive, evidence based support to the patients in their care.

The evaluation comprised semi structured interviews with 3 key stakeholders and subsequent questionnaire to the wider Breast Cancer MDT. All 9 team members who had direct patient contact participated. The results from the questionnaire concurred with the findings of the literature review in that it identified a well-defined hierarchy of side effects on endocrine therapy, which take precedence over sexual dysfunction symptoms when clinicians talk to patients. This is despite the literature indicating that the incidence of sexual dysfunction is significant and can negatively impact on quality of life to such an extent that patients become non-compliant in taking their medication.

The evaluation informed improvements in the management of sexual dysfunction, including the prescribing formulary for supportive products being extended and led to consideration of a more robust and unified approach to the identification and management of sexual dysfunction on endocrine therapy for breast cancer patients.

Complete comprehension of the impact of eczema on children and their parents could not be established, further research into this area needs to be carried out, a larger sample population may show the differences/similarities between parent and child. Introduction of a control group would be of benefit in comparing a 'healthy' child's responses against those with more complex health needs.

Interactive drug-design: using advanced computing to evaluate the induced fit effect

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This thesis describes the efforts made to provide protein flexibility in a molecular modelling software application, which prior to this work, was operating using rigid proteins and semi flexible ligands. Protein flexibility during molecular modelling simulations is a non-trivial task requiring a great number of floating point operations and it could not be accomplished without the help of supercomputing such as GPGPUs (or possibly Xeon Phi).

The thesis is structured as follows. It provides a background section, where the reader can find the necessary context and references in order to be able to understand this report.

Next is a state of the art section, which describes what had been done in the fields of molecular dynamics and flexible haptic protein ligand docking prior to this work. An implementation section follows, which lists failed efforts that provided the necessary feedback in order to design efficient algorithms to accomplish this task.

Chapter 6 describes in detail an irregular – grid decomposition approach in order to provide fast non-bonded interaction computations for GPGPUs. This technique is also associated with algorithms that provide fast bonded interaction computations and exclusions handling for 1-4 bonded atoms during the non-bonded forces computation part. Performance benchmarks as well as accuracy tables for energy and force computations are provided to demonstrate the efficiency of the methodologies explained in this chapter.

Chapter 7 provides an overview of an evolutionary strategy used to overcome the problems associated with the limited capabilities of local search strategies such as steepest descents, which get trapped in the first local minima they find. Our proposed method is able to explore the potential energy landscape in such a way that it can pick competitive uphill solutions to escape local minima in the hope of finding deeper valleys. This methodology is also serving the purpose of providing a good number of conformational updates such that it is able to restore the areas of interaction between the protein and the ligand while searching for optimum global solutions.

The exploration of CD44 as a mediator of a drug resistant phenotype in ER+ breast cancer

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The majority of breast cancers express the oestrogen receptor and are potentially amenable to endocrine therapy, however the clinical effectiveness of these agents is limited by the phenomenon of acquired resistance which is associated with disease relapse and poor prognosis. It has been previously demonstrated that the CD44 receptor is overexpressed in acquired tamoxifen resistance where it associates with an enhanced migratory phenotype, however little is known regarding the effects of CD44 splice variants in this context. This thesis aimed to explore the role of CD44 variant isoforms in a model of ER+ breast cancer derived tamoxifen-resistance (Tam-R cells) and expand these explorations into an additional model of acquired fulvestrant-resistance (Fas-R cells).

Multiple CD44 isoforms were found to be upregulated in resistance although a differential expression profile was observed between Tam-R and Fas-R cells. Inhibition of global CD44 expression in both endocrine resistant models led to a loss in their migratory, proliferative and invasive capacity and attenuated their responses to the CD44 ligand, hyaluronan. Overexpression of CD44v6 in endocrine sensitive MCF-7 cells induced EGFR pathway activation leading to enhanced cellular invasion, and attenuated response to fulvestrant. Accordingly, CD44v6 suppression in Tam-R cells resulted in a loss of EGFR pathway signalling and reduced invasion. Preliminary clinical analysis revealed that co-expression of CD44v6 and EGFR associated with a trend for worsened outcome in ER+ breast cancer patients treated with tamoxifen.

These data suggest that upregulation of CD44v6 may contribute to an aggressive phenotype in tamoxifen resistant cells through a mechanism involving the EGFR. Future use of CD44v6 and EGFR as biomarkers may have potential therapeutic value to predict a cohort of ER+ breast cancer patients which relapse earlier on tamoxifen and may thus require more aggressive treatment strategies.

Computer-aided design, synthesis and evaluation of novel antiviral compounds

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RNA viruses are a major cause of disease that in the last fifteen years counted for frequent outbreaks, infecting both humans and animals. Examples of emerging or ri-emerging viral pathogens are the Foot-and-Mouth disease virus (FMDV) for animals, Chikungunya virus (CHIKV), Coxsackie virus B3 (CVB3) and Respiratory Syncytial virus (RSV) for humans, all responsible for infections associated with mild to severe complications.

Although both vaccines and small-molecule compounds are at different stages of development, no selective antiviral drugs have been approved so far, therefore for all four these viruses improved treatment strategies are required. Promising targets are the viral non-structural proteins, which are commonly evaluated for the identification of new antivirals.

Starting from the study of different viral proteins, several computer-aided techniques were applied, aiming to identify hit molecules first, and secondly to synthesise new series of potential antiviral compounds. The available crystal structures of some of the proteins that play a role in viral replication were used for structure- and ligand-based virtual screenings of commercially available compounds against CVB3, FMDV and RSV.

New families of potential anti-CHIKV compounds were rationally designed and synthesized, in order to establish a structureactivity relationship study on a lead structure previously found in our group. Finally, a *de-novo* drug design approach was performed to find a suitable scaffold for the synthesis of a series of zinc-ejecting compounds against RSV. Inhibition of virus replication was evaluated for all the new compounds, of which different showed antiviral potential.

Investigations into the pharmaceutical issues associated with the provision of micronutrients to parenteral nutrition (PN) patients

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In recent years, there has been an increased emphasis on treating patients with parenteral nutrition (PN) at home in an attempt to reduce costs and improve clinical outcomes. This increased interest in home parenteral nutrition (HPN) has stimulated researchers to investigate potential sources of instability. One of the more unstable groups in PN is micronutrients, which can be divided into two groups: vitamins and trace elements. This research investigates the effects of artificial light sources (cool white, warm white and UVA) on the physico-chemical stability of vitamins. Vitamins were chemically analysed using a novel stability indicating HPLC assay that could quantify five water-soluble and three fat-soluble vitamins simultaneously in one run. Samples were physically analysed by visual analysis, microscope analysis, laser diffraction, pH and osmolality.

Initial experiments investigated the physico-chemical stability of vitamins exposed to artificial light sources over a period of 24 hours. In cool and warm white light there was approximately a 20% loss of riboflavin and 10% loss of retinol. In UVA light there was approximately a 20% loss of retinol. All other analysed vitamins were stable in these artificial light sources for the time period. Further experiments investigated these conditions following 6 days of storage between 2-8°C. These experiments revealed similar results in the three types of artificial light source.

The protective effects of lipid emulsions on retinol were then investigated in containers and administration sets. Samples containing lipid emulsions in syringes and administration sets allowed a statistically significant increase in retinol stability. Nevertheless, degradation in excess of 10% still occurred in these groups. The protective mechanism of lipid emulsions was primarily thought to be a result of light obscuration. However, soybean oil (SBO), a clear liquid, provided unexpected obscuration of UVA light suggesting it may reflect or absorb damaging rays thereby improving retinol stability.

PhD

Bacterial resistance to biocides: development of a predictive protocol

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In the last 10 years biocides have been used increasingly and questions have been raised about their contribution to the reported increase in biocide and antibiotic resistance in pathogenic bacteria. The EU Biocidal Product Regulation (BPR) now requires information on the risk of resistance development in organisms targeted by the biocidal product. There is no current protocol available to predict the likelihood of bacteria becoming resistant to a biocidal product or biocides contained therein.

This study aimed to identify useful markers of biocide resistance and develop a step-by- step protocol predictive of bacterial biocide resistance and antibiotic cross-resistance following biocide exposure.

A range of experimental techniques with the potential to generate markers of biocide resistance were explored. These included minimum inhibitory concentration (MIC)/minimum bactericidal concentration (MBC)/antibiotic susceptibility determination, flow cytometry, efflux activity measurements, outer membrane protein changes, real-time PCR and microarrays. *Salmonella enterica* serovar Typhimurium strains SL1344 and 14028S, and *Burkholderia lata* strain 383 were exposed to low concentrations of chlorhexidine gluconate and benzalkonium chloride as test biocides. Baseline and post-exposure data were then compared. Techniques used to understand any change in antimicrobial susceptibility were assessed in terms of practicality, cost and ease of use, and a step-by-step protocol was put together accounting for each of these factors.

Increases in biocide MIC and MBC of up to 100 fold were observed in SL1344 and 14028S after exposure to both biocides. However these changes were not stable after subculture of surviving organisms in the absence of either biocide. No such dramatic changes were observed within *B. lata*. Up-regulation of efflux activity was observed as a result of CHG/BZC exposure and the efflux regulatory gene *acrR* underwent a >100 fold down-regulation in both *Salmonella* strains after CHG exposure. Flow cytometry experiments performed using SL1344 and 14028S indicated that at low CHG/BZC concentrations (0.0001 – 0.0004 %) greater than 50 % of the population were not killed and that these organisms could be sorted and further investigated to determine the mechanisms behind their survival. Reduction in the expression of two outer membrane proteins was observed in strain SL1344 after exposure to 0.0004 % CHG but further protein sequencing would be required to identify these.

Changes in phenotype and genotype of biocide-exposed bacteria were identified using different experimental techniques. Some of these changes e.g. increased MIC/MBC values, altered antibiotic susceptibility, up-regulated efflux activity, alterations in the expression of specific genes and surviving organisms identified by flow cytometry represent useful markers of biocide resistance. A preliminary step by step protocol incorporating these techniques was successfully developed and allows for the rapid identification of biocide resistance and antibiotic cross-resistance as a result of biocide exposure, and will prove particularly useful in light of the recent changes to the BPR.

Biocide impregnated surface materials for use in clinical areas – under what conditions do they work?

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The survival of microorganisms on surfaces is well documented, potentially acting as a reservoir for the dissemination of healthcare-associated infections (HCAIs). Antimicrobial surfaces aim to control surface bioburden and lower HCAI rates. The existing antimicrobial surface efficacy test (JIS Z 2801) is an initial screening test; however, its set up (35°C, >90% relative humidity (RH)) bears little relationship to conditions in practice. This study aimed to develop new surface efficacy tests using wet and dried microbial inocula, reflecting conditions within a healthcare setting.

Changes in surface RH, temperature and bioburden were measured over one year at a hospital, allowing realistic parameters to be set for the new tests. Wet and dry inocula tests were developed and validated to mimic aerosol deposition and dry-touch contamination on surfaces, respectively. Aerosols of *S. aureus, A. baumannii* and *B. subtilis* spores and dry inocula of *S. aureus* and *A. baumannii* were tested against copper alloys and control stainless steel surfaces. Surviving bacteria were enumerated after varying contact times,

and under in-use and JIS Z 2801 test conditions. FACS experiments were conducted to understand the mechanism of action of copper against dried microbial inocula.

Wet inoculum testing showed copper alloys presented significantly reduced activity against *S. aureus* aerosols at in-use conditions (>4 log10 after 60 min) compared to JIS Z 2801 test conditions (>4 log10 after 30 min). A >4 log10 reduction in *A. baumannii* was observed within 30 min but copper alloys were not sporicidal at in-use conditions. Dry inoculum testing showed a <2 log10 reduction in *S. aureus* and *A. baumannii* after 24 h at in-use conditions with potential mechanisms of action including; membrane damage, DNA damage and arrested cellular respiration.

The new tests developed provide realistic, second-tier tests to the JIS Z 2801. Copper was antimicrobial against both wet and dry inocula but was overall more efficacious against a wet inoculum, which suggests a liquid interface enhanced antimicrobial activity. It is recommended that antimicrobial surfaces are tested under in-use conditions against both wet and dry inocula to confidently predict their performance in practice.

The role of BCA2 in receptor tyrosine kinase endocytosis and breast cancer

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Breast Cancer Associated gene 2 (BCA2), is a little-studied E3 ligase that is overexpressed in 56% of all primary breast cancers and has been linked with increased cell proliferation and invasion *in vitro*. BCA2 has been implicated in EGFR degradation however there is conflicting evidence surrounding its function and effect on receptor biology. This project aimed to elucidate the role of BCA2 in EGFR endocytosis and downregulation and to determine its link with breast cancer survival.

Data generated with online mRNA analysis tools indicated that high BCA2 levels were often associated with improved breast cancer prognosis. *In silico* studies also demonstrated that many genes coexpressed with BCA2 were regulators of membrane trafficking and suggested that BCA2 expression was repressed by HER2/EGFR/Ras signalling.

Experimentally, it was shown that siRNA depletion of BCA2 led to increased EGFR protein levels while transient BCA2 overexpression reduced levels of the receptor. It was found that BCA2 overexpressing, EGF stimulated cells demonstrated reduced lysosomal degradation of both receptor and ligand. Associated with this, downstream EGFR signalling in BCA2 overexpressing cells was reduced in magnitude but prolonged in duration and ultimately cell viability was impaired.

These findings support a role for BCA2 in the endolysosomal system. In agreement with this it was shown that BCA2 overexpression inhibited the vesicle membrane association of Rab7, a regulator of late endocytosis and reported BCA2 interactor.

Transferrin receptor levels and transferrin uptake were unaffected by BCA2 overexpression suggesting trafficking effects may be restricted to EGFR, a distinct class of receptor and/or to later (degradation) stages of endocytosis.

This thesis provides a detailed exploration of BCA2 biology and presents evidence of a functional role for the protein in the endocytic regulation of EGFR. The mechanism(s) underlying the complex relationship between BCA2 and breast cancer outcome have yet to be fully determined.

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