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Planning and redesigning the laboratory component of a compulsory bachelor of pharmacy course

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Background

The study board, the teaching committee and the head of department launched the Farma2020 process in January 2014. The process consists in a complete redesign of the bachelor education in pharmacy. In the new overall course structure, all courses are worth 7.5 ECTS where 1 ECTS point equals a student workload of 30 hours. In this context, course development teams were formed in order to adapt the former courses to the new program. As a member of the course development team for the bachelor course "Instrumental Analytical Chemistry", I have been tasked with helping with the redesign of this compulsory course.

The Instrumental Analytical Chemistry course is a compulsory 8 ECTS course, which is comprised of lectures accompanied by a strong laboratory component. As seen in Figure 4.1, the course normally enjoys good ratings among the students. The most mixed feelings among the students relate to the course lectures, which was either the cause or the consequence of a very low student attendance (typically less than 50%). The results from the course evaluations have been more or less similar since 2006, with slight increases in satisfaction regarding the theory section of the laboratory manual, the description of the exercises in the laboratory manual, the usefulness of the exercise questions with helping to learn the theory, the usefulness of the student-teacher discussions upon returning of corrected reports and the use of English in the laboratory manual.

Even though the reviews from the students were generally positive, some improvements to the course are still necessary as in 2014, a signif-

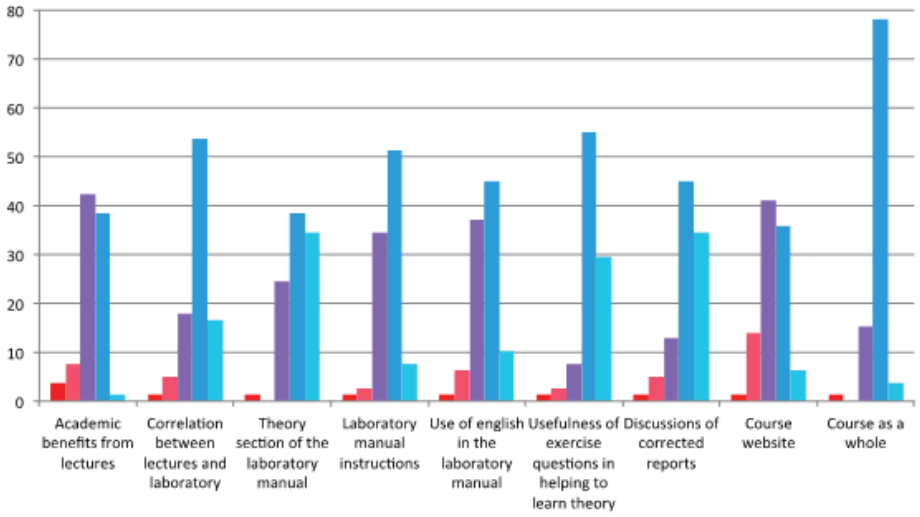

Fig. 4.1. Overview of student evaluations for Instrumental Analytical Chemistry (2014)

icant fraction of students failed the final examination and answers to the examination questions reflected that a good proportion of students could surprisingly still not perform rudimentary calculations related to basic laboratory tasks.

The "new" course – Pharmaceutical Analytical Chemistry

Despite the general satisfaction with the original Instrumental Analytical Chemistry course, especially its laboratory component, the whole course needs to be re-designed as part as the general re-design of the bachelor education. The re-design is characterized by a better communication among various course teams so as to avoid repetitions and/or glaring omissions in the curriculum material. Some of the subjects currently covered by the Instrumental Analytical Chemistry course are already or will be covered in different courses. A complete redesign of the laboratory component of the course is therefore required. In the new version of the laboratory course less subjects will be covered but they will be covered with more depth and the students will have more time to complete and reflect on each experiment.

The new course is tentatively re-baptized "Pharmaceutical Analytical Chemistry" (Farmaceutisk Analytisk Kemi) to better reflect its content and will be taught in the 4th semester. By then, the students are already quite mature in their education and have gained considerable laboratory experi-

Table 4.1. Comparison of the layout of the "old" Instrumental Analytical Chemistry with the "new" Pharmaceutical Analytical Chemistry

	Instrumentel Analytisk Kemi ("old course")	Farmaceutisk Analytisk Kemi ("new course")
Points	8 ECTS	7,5 ECTS
Structure	Lectures (3 ECTS) + laboratory (5 ECTS)	Lectures + laboratory (7,5 ECTS)
Experiments	12 "cookbook" experiments + 1 project based on the pharmacopeia	4 experiments requiring the students to participate in experiment design
Reports	Students fill out a questionnaire in lieu of writing a report	Students should write a laboratory report
Grading	Laboratory course: Pass/Fail (reports) Lectures: Graded (final examination)	Laboratory course: Graded (reports) Lectures: Graded (final examination)

ence. They have been taught to work with the diverse pharmacopeia methods (a compendium of analytical methods for pharmaceutical products) in two different courses during their first semester in the pharmacy education (Lægemiddeludvikling fra molekyle til menneske – oversigtkursus and Kemiske principper for de farmaceutiske videnskaber) and learned general laboratory practices in several other pharmacy courses (Kvantitativ Analytisk Kemi, Farmaceutisk fysisk kemi 1 & 2).

Table 4.2. Pharmaceutical Analytical Chemistry laboratory course overview

Farmaceutisk Analytisk Kemi – Laboratory component	
Exp 1: HPLC	6 x 4hr sessions
Exp 2: LC-MS	3 x 4hr sessions
Exp 3: GC-MS	2 x 4hr sessions
Exp 4: AAS	2 x 4hr sessions

The new course is scaled down from 12 experiments plus one final project to just four experiments as listed in Table 4.2. We focus here on the redesign of experiment 1 (HPLC). The original experiment, outlined in Table 4.3, is fairly standard for an Instrumental Analytical Chemistry course. Experiments are performed in teams of 2 to 3 students and only one form-based "laboratory report" is submitted for the team.

In the new course, the HPLC experiment will be now spread out over six 4-hour sessions to allow the students more time for preparation, reflec-

Table 4.3. Outline of the original HPLC experiment

Activity	Task
Experiment (One 4h-session)	Perform a "cookbook" type experiment with the aid of the laboratory manual
Laboratory report	Fill-in a report form and answer 11 post-lab questions. Only 3 questions can only be answered by looking at the students' experimental data. The students look for the answers to all other 8 questions in the lab manual and/or course textbook. The report is graded on a Pass/Fail scheme.

tion and experimentation. There is no laboratory manual, but instead, the students use the literature (the pharmacopeia) as a starting point to design their own experiment. The 6 sessions of the HPLC experiment are detailed below.

Prior to the first session: Reading and "pre-lab" questions

In order to prepare the students for the experiments, the students are required to perform some readings as well as to answer pre-lab questions. The answers to the pre-lab questions are not graded but will be discussed with an instructor prior to the beginning of the experiment. The pre-lab questions ensure the students have done the required readings, but also that important points related to the operation of the instruments are discussed prior to the beginning of the manipulations to avoid errors and/or damage to the instruments.

Session 1-3: Pharmacopeia methods

In the new course, we chose to part ways with the "cookbook" type laboratory manual. It has been observed that when the students follow detailed instructions, they tend to focus more on completing the activity then on trying to make quality observations or develop connections between their own experimental results and the related theory. Students from the pre-university programme in Malaysia who enrolled in the undergraduate pharmacy education were observed to have lost their skills of writing and analytical thinking as they depended much on the laboratory manual (Abidin et al. 2013). Also, in the absence of a "pre-lab" questionnaire, only a handful of

students will take the time to read and understand the laboratory manual prior to performing the experiment (Arnold et al. 2014, Parry et al. 2012).

There are two types of knowledge we desire the students to gain from the laboratory experiments: Substantive knowledge, which is "the understanding of scientific facts, concepts, laws and theories" (Arnold et al. 2014) and procedural, or epistemic, knowledge and understanding, which includes "knowledge about methods, when and how to use them, and their limitations" (Arnold et al. 2014). Problem-Based learning and Enquiry-Based learning are often recommended for teaching and learning in the laboratory (Abidin et al. 2013, Arnold et al. 2014, Moskovitz & Kellogg 2011). These teaching methods start with a question, or a problem, which needs to be solved with minimal guidance. Here, designing the experiments is key to the students' learning process. If the students are able to design a valid and reliable experiment to solve the problem or answer the question, they will be more likely to succeed in critically interpreting the data from their investigations (Arnold et al. 2014). However, Enquiry- or Problem-based learning is not easily implemented in a class with close to 200 registered students. Katherine C. Lanigan describes an alternative approach to helping students develop their problem solving skills through adoption and adaptation: method development of experiments from the literature (Lanigan 2008). This method represents a compromise between Enquiry/Problem-base learning and the traditional cookbook laboratory manual and is best suited for the new Pharmaceutical Analytical Chemistry course. Instead of basing the experiments on the scientific literature, the experiment will be based on the pharmacopeia, a compendium of analytical methods, which the students have learned to work with in previous courses of their bachelor education.

During the first laboratory session, the students are assigned a drug and should look through the various pharmacopeias to find the appropriate HPLC method and experimental conditions to perform an assay. The drug assigned contains an active pharmaceutical ingredient (API) as well as impurities (for example Lorazepam, monograph USP 3598 and USP 3602 in the United States Pharmacopeia). The students prepare an outline of the procedure they will follow, based on the pharmacopeia method, for the analysis and get it approved by a teacher. The second laboratory session is dedicated to preparing the samples, standards and mobile phase. In the third laboratory session, the students run the pharmacopeia method. Pharmacopeia methods for APIs and their impurities require efficient separation. The resolution, tailing factor and relative standard deviation should

be calculated as required by the pharmacopeia method. The percentage of each impurity in the tablet should be determined. The analysis should be performed completely and correctly, or repeated until satisfactory results are obtained.

Session 4: Introduction of information technology tools in the laboratory: HPLC simulation software

There are many interrelated experimental parameters that will impact the aspect of a chromatogram in HPLC experiments and it is unrealistic, both from a time and equipment perspective, to expect the students to explore them all in the context of a few laboratory periods. Information technology (IT) tools are ideal in this context to allow the students to learn and gain experience about the fundamental principles of chromatography without using too much time, solvent or damaging costly instruments.

There are many e-learning tools to help in teaching chromatography online. One option is the CHROMacademy website (www.chromacademy.com), an e-learning website developed by LC-GC magazine and Crawford Scientific. The CHROMacademy website is filled with information, tutorials, quizzes and webcasts to help in learning. The department of pharmacy already has a license for the use of the site and additionally, a 5 years free license is available for university students and staff, which would allow students to use the website also outside of the laboratory for the whole duration of their studies. However, true interactivity is missing and the website does not really constitute a true simulator which can also provide instant and unambiguous feedback.

Although several HPLC simulators are available on the market, they are often costly and platform specific. A tool commonly used in the industry is “DryLab”, developed by the Molnar Institute (http://molnar-institute.com/drylab/). DryLab is an HPLC optimization tool that predicts chromatograms under a much wider range of experimental conditions than would be possible to test in the laboratory. The software allows the user to vary multiple method parameters, such as pH, temperature, buffer concentration, and many more. Although probably one of the best tool available, the Molnar Institute does not offer a free license to university staff and students, making its cost a hurdle to its use in the teaching laboratory.

Boswell et al. (2013) have developed a free, open-source web-based HPLC simulator designed especially for the education community. Accessible at www.hplcsimulator.org, it is also available as an application for an-

droid smartphones and tablets. The simulator features controls for a wide range of experimental parameters and displays a graphical chromatogram to provide immediate feedback to the students. The software therefore offers an attractive alternative to its more costly competitors. With the HPLC simulator, the students can work on an exercise set with in the laboratory where they can get additional help from the instructors. The students also have access to the simulator at home to complete the exercise or review muddy points.

Session 5 & 6: Improvements on Pharmacopeia methods

Based on the experimental results obtained in session 3 and the knowledge gained from the simulations in session 4, the students devise a plan for improving the separation of the drug they have been assigned. The goal can be to improve resolution, shorten analysis time, improve peak shape, etc. The plan should be discussed and approved by an instructor. Discussion with the instructor will allow stressing out that pharmacopeial methods are standards and cannot be modified without validation. However, the pharmacopeia allows for certain adjustments to be made to the procedure. The acceptable range for modifications of HPLC methods without the requirement for validation is detailed clearly in the European Pharmacopeia 2.2.46. Other improvements possible to the method, aside from changing the separation conditions, could involve the construction of a calibration curve and the calculation of uncertainties, which are limited in the pharmacopeial methods but an important aspect of the course. The students should be encouraged by the instructor to construct a calibration curve and compare the results obtained with those obtained using the pharmacopeia method.

Evaluation of the student's performance in the laboratory: The lab report

Two types of evaluations are normally used to evaluate the students' performance in the laboratory. The students either get to write a standard lab report mimicking a scientific paper (introduction, methods, results and discussion, conclusions) or answer a set of post-lab questions. However, both these types of reports can easily become redundant with the material available in the lab manual. When there is a detailed lab manual to support an

experiment, writing an introduction and a methods section is often purposeless as the students lack a real research agenda and there is little for them but to parrot back selected details from the manual (Moskovitz & Kellogg 2011). Even when answering post-lab questions, students tend to not share the actual findings from the experiment, but instead use the ones found in books, on the internet or in the lab manual itself (Abidin et al. 2013). It is imperative that student writing be aligned with the lab activity. Method Development can alleviate this problem, as the students cannot just passively recopy the information available in the lab manual, textbook or from the course instructor. There is a real communication purpose behind the lab report, as the students should have substantially altered the standard pharmacopeia protocol and must scientifically justify the changes they made to the reader, who is not merely a grader anymore. However, the introduction section is still a very unproductive piece of work as the students at this intermediate level lack the breadth of knowledge needed to discuss their experiments in the context of the primary literature (Moskovitz & Kellogg 2011). It is therefore preferable to focus on tasks that are more productive to save both the students and instructors some time. Students will eventually get to write a full research report when they do their final pharmacy project. In the pharmaceutical analytical chemistry course, students should focus on a limited number of skills that are essential in science writing: how to decide which data to present, how to use graphs and tables to display their data effectively and how to discuss the presented data (Moskovitz & Kellogg 2011). This will allow us as instructors to request higher quality work and to provide more extensive feedback to the students, as the reports will be shorter. Therefore, the report should contain only a "Methods" section, a "Results & Discussion" section and a "Conclusions" section. The students should be evaluated on whether the data was handled with care and integrity, the clarity of the report and communication skills, and the quality of the results. The reports will be graded with extensive comments and will count towards the final grade of the course.

Handout

An example of the student handout accompanying the new exercise in shownbelow.

Experiment 1 - HPLC

Prior to the experiment:

Literature:

- Pharmacopeia Ph. Eur. 2.2.46
- Harris Chapter 23, 24, 25, 26

Answer the following pre-lab questions:

- Draw a schematic of an HPLC injection loop in the "load" and "inject" positions. How is the sample volume defined?
- How much sample do you need to inject into the loop in order to ensure repeatable injections?
- What are the basic components of a HPLC system?
- What is the difference between "reverse" and "normal" phase chromatography?
- Draw the chemical structures of the active pharmaceutical ingredient as well as the impurities expected in your assigned tablet.

First session:

- Review your answers to the pre-lab questions with an instructor.
- Find the monograph in the pharmacopeia for the drug/vitamin mixture your group has been assigned.
- Prepare a 1 page outline of the experimental procedure to follow in order to perform the HPLC analysis of your assigned mixture. Don't forget to take into account the number of replicate measurements you will have to do and your mobile phase flow rate to determine exactly how much sample and mobile phase you should prepare.

Second session:

- Prepare your samples and mobile phase.
- Note that you will have to degas your mobile phase for at least 15 minutes in the ultrasonic bath before running the experiment.

Third session:

- Run the separation according the pharmacopeia method.
- Calculate the resolution, tailing factor, relative standard deviation and percent impurities as required by the pharmacopeia method.
- Answer the post-lab questions:
  - What are the charges of your compounds at the separation pH?
  - Determine the amount of API as well as the percentage of each impurity in your tablet.
  - How do the results correspond with the claimed content? Is the tablet compliant?
  - Is the separation ideal?
  - Which aspects of the chromatogram obtained could be improved?
  - What else could be improved?

Fourth session:

- Go to HPLCsimulator.org
  - Draw the chemical structures of the components listed in the default separation mixture.
  - Change the pH/Temperature/solvent strength/particle size and observe the changes in the displayed chromatogram.
- Post-exercise questions
  - How does pH/Temperature/solvent strength/particle size influence separation? Why?
  - Based on what you have learned today, how could you improve the separation of the components in your tablet?
  - Prepare a revised outline of the procedure to improve the separation of your compound mixture.
  - Does your new method require validation?
  - How would you perform a validation?
  - Describe another method you have learned to determine the concentration of each analyte in your tablet, which is different from the method described in the pharmacopeia. Incorporate this to your revised analytical method.

Fifth session:

- Prepare your samples and mobile phase according to your revised analytical method.

Sixth session:

- Run the separation according to your revised analytical method.
- Calculate the resolution, tailing factor, relative standard deviation and percent impurity for your tablet. Report your results with a confidence interval.
- Answer the post-lab questions:
  - Which parameters did you change from the original method?
  - What was the impact of the changed parameters on the separation and why?

Instructions for the laboratory report:

- Your laboratory report should include:
  - A cover page
  - A detailed experimental section detailing the modifications you have made to the pharmacopeia method
  - A results and discussion section presenting your results in a clear and concise manner. Think about which results should figure in this section and what would be the best method (figure, table, etc.) to convey your results clearly to the reader. Discuss the presented data in relation with the theory. Do not forget error bars on your calibration curves and report results with a confidence interval when appropriate.
  - A short conclusion and possibly suggestions for future work and improvements.
  - A list of the cited references (Pharmacopeia methods, text book, websites...)

In summary

The laboratory portion of the Instrumental Analytical Chemistry course (now re-baptized Pharmaceutical Analytical Chemistry) will be modified to reflect current knowledge in teaching education. The number of experiments has been reduced and more time is allotted to the new experiments to allow the students more time for preparation, reflection and experimentation. Elements of Problem/Enquiry-based learning have been introduced in order for the students to be more involved in the design of the experiments,

instead of merely following a "cookbook recipe". The change from a traditional laboratory manual also enhances the value of the laboratory report, as without a manual to copy from, the report is rehabilitated and serves a real communication purpose for the students to present to their instructors what they have done in a clear and concise manner. Information technology tools are also introduced in the laboratory to enhance the students learning experience. The new course will be offered for the first time in 2017, at which point, an evaluation of the outcome of the new teaching methods in the laboratory will be possible.

All contributions to this volume can be found at:

http://www.ind.ku.dk/publikationer/up_projekter/2015-8/

The bibliography can be found at:

http://www.ind.ku.dk/publikationer/up_projekter/

kapitler/2015_vol8_nr1-2_bibliography.pdf/