INGREDIENT DISPERSIONS BASED ON PHYSICOCHEMICAL PARAMETERS

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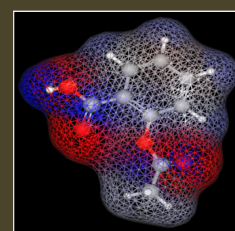
Introduction

Current information lacks richness in systematic methods that may give an indication as to the effectiveness of a specific set of dispersing conditions prior to their application, particularly for dispersions in hydrophobic media. This study addressed the possibility of constructing a **predictive model that may indicate the effectiveness of a specific set of dispersion conditions prior to their application**, particularly for **dispersions in hydrophobic media**. In particular, the objectives were to determine the physicochemical characteristics of the dispersing media that are potentially influential in the dispersability of powders, to characterise the properties of the active pharmaceutical ingredients that could contribute to the ability to form stable dispersions, and to characterise the dispersions of the active pharmaceutical ingredients (APIs) in the dispersing media or dispersing media-surfactant mixtures.

acetylsalicylic acid

ciprofloxacin HCl

disulfiram

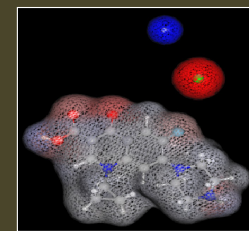**etidronate disodium**

salicylic acid

Methodology

Five APIs were analysed: **acetylsalicylic acid**, **ciprofloxacin hydrochloride**, **disulfiram**, **etidronate disodium** and **salicylic acid**. Molecular surface areas were computed using MarvinSketch (ChemAxon Ltd.). The dispersing liquids were paraffin, vaseline, cornflower, sunflower, olive and rapeseed oils, while the dispersing agents were Span 20, Brij 30 and lecithin.
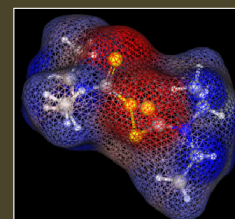
- The densities and surface tensions of the dispersing media were determined using a Sigma 701 Tensiometer (KSV Instruments Ltd.). Kinematic viscosity measurements were performed using U-Tube Ostwald Viscometers operated as per ASTM methods D446-004 and D445-01.
- The wetting profile of each API was characterised by monitoring the rate of permeation of each dispersing solution into the pores of the solid powder using the Sigma 701 Tensiometer fitted with a glass powder wettability measuring device. The relative efficacy with which each dispersing solution wetted the active ingredient particles was statistically analysed using a 2-Segment Piecewise Linear Model.
- The dispersion stability was evaluated by using a method analogous to that employed when using a turbidimeter. The propensity of the primary particles to settle to the bottom of the containing vessel was monitored as a function of time by quantifying optical density in terms of the absorbance of the particulate sample at 600 nm.
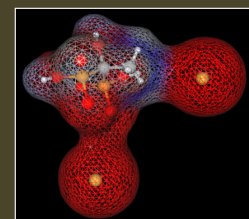
Results and Discussion
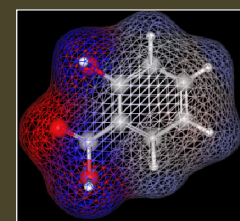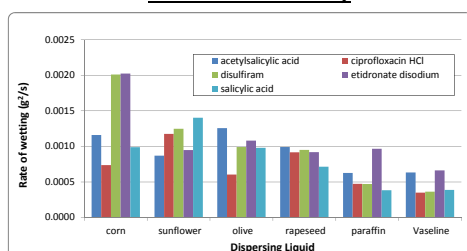
Physicochemical Properties of Dispersing Media

|	sunflower oil	corn oil	rapeseed oil	olive oil	paraffin oil	Vaseline Oil
Kinematic Viscosity (mm²/s)	64.125	63.011	70.605	75.571	140.376	145.955
Density (g/mL)	0.845	0.840	0.834	0.836	0.772	0.804
Surface Tension (dynes/cm)	32.580	32.645	32.580	32.250	31.005	30.785

API Powder Wettability

Powder wettability results indicated that as the attractive forces between molecules increased in magnitude, the *more viscous oils were impeded from flowing freely and penetrating into the API powder bed*. Thus, the rate of wetting of the powder surfaces was relatively slower in the case of Vaseline Oil and paraffin oil, and particle settling could have commenced prior to complete wetting.

API Powder Dispersion Stability
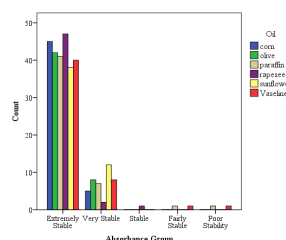
The use of oils as dispersing liquids resulted in **extremely stable dispersions**. These dispersing liquids were taken to provide the framework for *extended dispersion stability*.
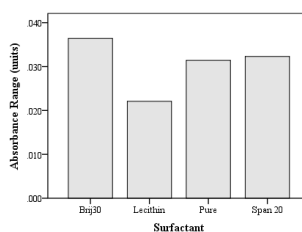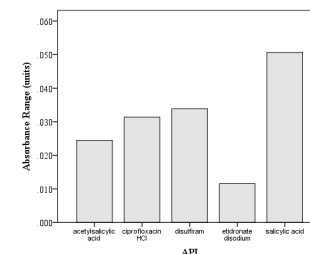
However, the *API dispersion stability in paraffin and Vaseline Oil was not infinite*. Rather oils with lower viscosities exhibited more extended dispersion stabilities.
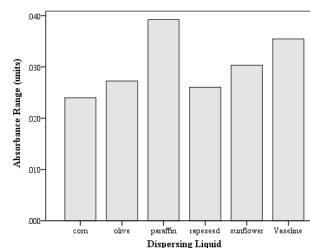
Conclusions

1. With regards to the *dispersing medium*, the optimised sample preparation was related to the interplay between the dispersing medium's ability to affect powder wetting in a relatively short period of time and to confer resistance to settling, both processes significantly dependent on viscosity.
2. While **surfactants** are usually chosen because of their stabilising effects on the dispersion stability, the study indicated that differences in the *hydrophilic-lipophilic balance* of these surface active agents were related above all to the rate of wetting of the API, rather than to the rate of settling.
3. As regards the *active pharmaceutical ingredients*, the physicochemical property *percentage polarity* was the only parameter which was correlated to dispersion stability. This was taken to be indicative of the strength of intermolecular forces of attraction between API molecules.

References

Ellul, M. Optimisation of Sample Preparation in the Particle-Size Characterization of Active Pharmaceutical Ingredients by Laser Diffraction. B.Sc. Thesis, University of Malta, May 2010.

Acknowledgements