EXPERIMENT 1

TABLET FORMULATION & POWDER CHARACTERIZATION

Safety information

The chemicals listed below will be used in this experiment. The likely hazards associated with each of the chemicals are noted and recommended procedures for handling are given. You must read this page and the experimental description carefully before starting the experiment and before coming into the laboratory. Note any potential hazards and adopt precautions as your safe lab practice. When you are satisfied that you understand any possible difficulties that might arise and the recommended procedures for dealing with them, sign the declaration and have it initialled by a demonstrator. This must be done prior commencing lab work. At the beginning of the lab session demonstrators will quiz you about the safety information and experimental procedure in order to identify your ability to work safely and efficiently. If you fail to prove ability for safe and efficient work you will not be allowed to start lab practical. Please note, that it is your own responsibility to complete the lab practical during time that is allocated to you. Be sure to request information or help if you are in doubt on any point.

Chemical	**Hazard**	**Precautions**
Paracetamol tablets	Toxic if swallowed	Do not ingest

Declaration - I have read and understood the contents of the safety information sheet and the script for the experiment

Signed (student): .....

Checked (demonstrator): ..... Date: .....

EXPERIMENT 1

TABLET FORMULATION & POWDER CHARACTERIZATION

SAFETY

This experiment involves use of a moving machine which is potentially dangerous. Ensure hands are dry before equipment is switched on/off. Take great care when compressing powders to produce tablets. Avoid your fingers, clothes or hair getting caught anywhere on the machine.

All the materials used are in powder form and most are from everyday food substances which are not toxic. Do not however, taste any material as it may not be food grade and minimize contact with bare skin. Avoid inhaling the powders. Clean up any spillage of powder immediately.

Dispose of all used materials in designated waste containers / areas. Clean and replace equipment after use. Wash all glassware after use

INTRODUCTION

Tablets are the most common dosage forms employed for oral administration of drugs. A single tablet will under normal circumstances contain different excipients each performing a specific function, for example, bulking agents (or fillers), binding agents, disintegrating agents, lubricants, and active pharmaceutical agents.

Different mixtures of these constituents will affect the final properties of the finished dosage form and their ultimate performance in the body. The properties of the tablets produced are also affected by manufacturing process variables such as the force used to compress the powdered excipients. Various tests need to be performed in order to characterise the properties of tablets. These tests provide information on the effects of the different formulation and manufacturing variables used. Such information will aid the decision for the best formulation and set of conditions for producing an ideal tablet that will be safe, effective and durable. Common tests include size (thickness and weight uniformity), hardness, friability, disintegration time and tablet dissolution.

The main aims of this experiment are the preparation (formulation) of tablets by directly compressing the constituent materials using a tablet press and investigating the effects of

varying the tablet constituents and the manufacturing process on the properties of the tablet produced.

METHOD

Please follow these instructions carefully and check the diagrams overleaf for details of the tablet press and to familiarise yourself with the various parts and its operational principles. It is also of **UTMOST** importance, that all mixtures put through the press contain a minimum of 1.0 % magnesium stearate. This acts as a lubricant for the press, without which the lower punch will seize up and the die does not fill with mixture, which results in the tablet production coming to a stop.

1. Preparation of powdered / granular mixture (Mixing)

Follow the formulations shown in table 1 below to prepare the mixtures as follows:

1.1 Weigh out the powders separately. Mix thoroughly lactose, starch and talc in a mortar.

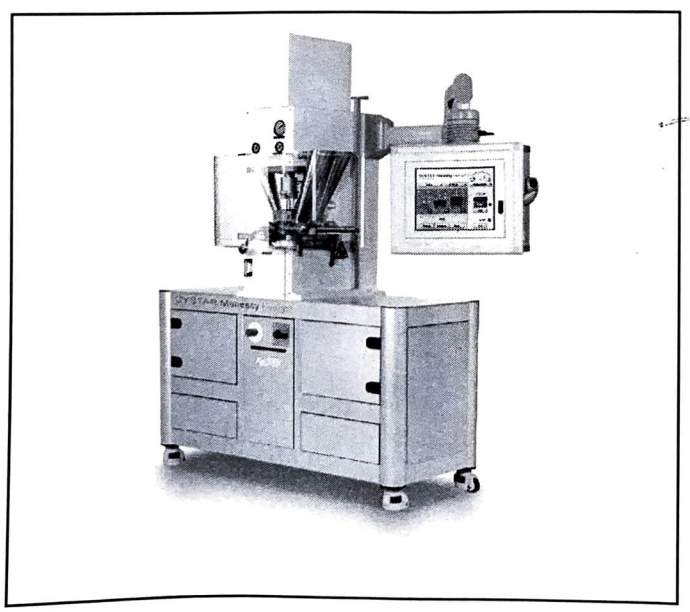
1.2 Add all of the excipients on a 250μm mesh and pass them through the mesh gently and pure the powder in a plastic container. Mix the powders well for 5min and label each formulation as Batch A or Batch B.

Table 1: Tablet formulations

Ingredient/Formula	Formulation/Weights	
	A (g)	B (g)
Lactose	50	37.5
HPMC	12.5g	25.0
Talc	1.25	1.25
Magnesium stearate	0.625	0.625

2. Production (compression) of tablets

2.1 Place the powder in hoper No 1 and compress the tablets as indicated in Table 2. The specifications for each tablet should be 10mm diameter and 300 mg weight. The first two groups should carry out the compression studies for batch A1 and the rest two for batch A2, respectively. As it depicted in Table 2 the tablet compression force and dwell time are the variables for the powder studies.



2.2 Tablet characterization

a. Weigh together 5 tablets from each Batch (now A1 – A20) and record the total weight.
b. From this total weight of 5 tablets, calculate the mean (average) weight per tablet and the standard deviation (SD).
c. Determine tablet hardness by measuring the force required to fracture a sample batch of 5 tablets using the Hardness Tester provided. Calculate the mean hardness (force) and the SD for each batch.

d. Determine the thickness of each tablet using the calliper provided and calculate the SD for each batch.

e. Provide three Tables including the average weight, hardness and thickness of each batch.

Table 2: Setting of compression force and dwell time for studying the compression behaviour of Batches 1&2.

	Tablet Compression Force (mPa) Kn Kn				
Dwell Time (msec)	**30**	**50** 40	**100** 50	**150** 60	**200** 70
5	A1/B1	A2/B2	A3/B3	A4/B4	A5/B5
10	A6/B6	A7/B7	A8/B8	A9/B9	A10/B10
5K	A11/B11	A12/B12	A13/B13	A14/B14	A15/B15
10K	A16/B16	A17/B17	A18/B18	A19/B19	A20/B20

*The tablet press settings will be adjusted by the demonstrators responsible for the practical.

3.1. Tablet weight uniformity and hardness

This is an official method and described in the Tablet Monograph (p459) and Appendix (p A211) of the British Pharmacopoeia (BP 2000). The specification is dependent on the weight of tablet.

Questions

The BP specification states that for tablets weighing more than 250mg, not more than two out of 20 tablets should deviate by more than 5%. In addition, not more than 1 tablet should deviate by more than 12.5% from the mean.

a. How many tablets had deviations > 5%?

b. Did your batch pass the uniformity test?

c. How useful is your experimental test on 10 tablets as far as the BP specification is concerned.

3.2 Tablet hardness

Questions

a. What is difference in hardness between A1 and A2? Give a reason for the difference

b. What effect does increasing the compression pressure (or force) have on tablet hardness (F1 and F2)?

c. What are the implications of having too soft or too hard tablets?

3.3. Heckel Plots

Many methods have been used over the decades to study the volume reduction mechanism and bond formation of pharmaceutical powders. The most frequently used method for studying the powder volume reduction process is the Heckel equation, or the porosity–pressure function, which is based on the assumption that the process of pore reduction during compression follows a first-order kinetic (Heckel, 1961). The parameters concerning compressibility characteristics can be obtained from the porosity–pressure plot. Yield pressure (Py) is a measure of the plasticity of materials and can be used for relative comparisons between different material compression characteristics. A Heckel plot can be used to study plain materials, but it can also be used to study powder mixtures whose characteristics are usually a combination of plain material characteristics.

Questions

a. Use the Heckel equation to provide the plot for each formulations A and B (one plot for each dwell time).
b. Calculate constants K and A and discuss the powder properties based on the Heckel plots.
c. See APPENDIX A for Heckel plot equations.

References

M.E. Aulton. Pharmaceutics: The Science of Dosage Form Design. Churchil Livingstone Ed, New York, 2003.

EXPERIMENT 2

TABLET DISSOLUTION AND DRUG RELEASE

Safety information

The chemicals listed below will be used in this experiment. The likely hazards associated with each of the chemicals are noted and recommended procedures for handling are given. You must read this page and the experimental description carefully before starting the experiment and before coming into the laboratory. Note any potential hazards and adopt precautions as your safe lab practice. When you are satisfied that you understand any possible difficulties that might arise and the recommended procedures for dealing with them, sign the declaration and have it initialled by a demonstrator. This must be done prior commencing lab work. At the beginning of the lab session demonstrators will quiz you about the safety information and experimental procedure in order to identify your ability to work safely and efficiently. If you fail to prove ability for safe and efficient work you will not be allowed to start lab practical. Please note, that it is your own responsibility to complete the lab practical during time that is allocated to you. Be sure to request information or help if you are in doubt on any point.

Chemical	**Hazard**	**Precautions**
Paracetamol tablets	Toxic if swallowed	Do not ingest

Declaration - I have read and understood the contents of the safety information sheet and the script for the experiment

Signed (student): .....

Checked (demonstrator): ..... Date: .....

EXPERIMENT 2

TABLET DISSOLUTION AND DRUG RELEASE

LEARNING AIMS

- To gain familiarity with tablet testing
- To understand drug release profiles
- To assess tablet dissolution

DIRECTED READING

Assessment of Dosage Forms. Physicochemical Principles of Pharmacy. Florence & Attwood, MacMillan 1988

INTRODUCTION

A dissolution test is a mean of identifying and proving the availability of active drug materials in their delivered form. Many active materials are only required at the milligram or even microgram level in order to achieve the desired pharmacological effect. As the delivery of a mg amount of active material to the subject is not realistic, we have to employ bulking agents in order to present medication in a form which is easy to administer. These non-active bulking agents such as microcrystalline cellulose (e.g., Avicel) and silica (e.g., Aerosil) can have an effect on the way that the active material is released or what is referred to as its bioavailability.

We need to define the availability of the active material as this will have a bearing on the dosage available after ingestion. A dissolution test simulates this availability and allows the prediction of the time for complete release of the material from the dosage form. It also gives important Quality Control information as to how much of the active material was in the dosage form and whether this concentration conforms to the expected dosage.

METHOD

1. Switch on the dissolution apparatus with the water bath. Ensure temperature is set at 37°C.
2. Fill three dissolution flasks with 900 ml of distilled water and allow to warm up to predefined temperature.
3. Lower the paddles into the dissolution solution until they come to a stop. They should not be touching the tablet or the base of the flasks.
4. Set the paddle rotating speed at 50 rpm.
5. Make sure the UV-spectrophotometer is switched on and is fully initialised before taking any readings. Set the wavelength to 242 nm in fixed mode.
6. To begin the test, drop one of the three paracetamol formulations provided into the three flasks respectively (NB: there should be only one tablet in each flask).
7. Start sampling immediately by pipetting 2 ml of the solution into clean cuvette and measure the absorbance on the UV. Pour the solution back into the flasks after each measurement to keep volume constant.

8. Take further samples at 5 minute intervals for 60 minutes. Remember to rinse the cuvette with clean distilled water three times and shake out any water droplets before the next measurement.

NB: ***The UV absorbance range is linear up to about 1.2 so please ensure your readings falls below this value. If they are not, you may need to dilute the solution before taking your readings. Carry on as follows.***

9. Dilute exactly 1 ml of each of the samples to 10 ml with distilled water and mix thoroughly.

ATTENTION: further dilution may be required.

10. For each diluted solution, pipette 2 ml of the dilution into the silica cuvette. NB: Do not pour diluted solution back into the flasks. 1 ml should not affect the total volume significantly.

RESULTS

Record your results as shown in the Table 1. Assume each tablet contains 500 mg of paracetamol. Use 648 as the A1 % 1cm for paracetamol.

Table 1: Dissolution results

Time (mins)	Absorbance		Concentration (mg)	% Release
	Tablet 1	Tablet 2		
0	- 0.04	-0.036		
5	0.029	0.0220		
10	0.220	0.720		
15	1.071	0.751		
20	1.0012	1.055		
25	0.872	0.683		
30	1.061	0.284		
35	0.309	0.532		
40	0.293	0.309		
45	1.078	0.227		
50	0.886	0.756		
55	1.012	1.01		
60	0.698	0.511		

Plot data as % release versus time on the same graph. See the examples at the end of this script.

QUESTIONS

Comment on your results by answering the following questions. You are looking for trends/changes in the release rate and release profiles with variations such as tablet hardness/ dosage form.

- Which of the batch of tablets had the highest dissolution rates? Give reasons for the difference. See the formulation constituents in Table 2 to inform your answers.

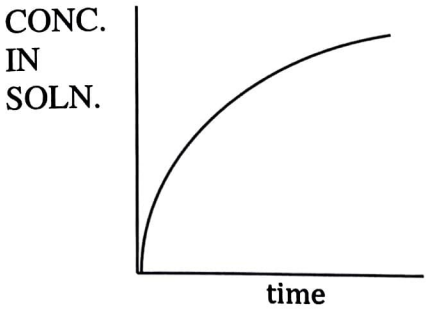
- What is the difference between prolonged, modified and sustained release dosage forms? What are the specifications for the above dosage forms and fast disintegrating forms in terms of in vitro dissolution points and pH settings?
- What is the meaning of the term sink conditions?

References

Table 2: Master formula for the formulations of paracetamol used

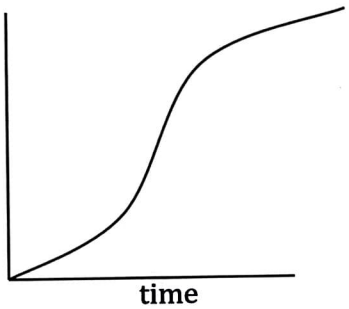
Caplets	**Panadol Tablets (Film coated)**	**Panadol soluble tablets**	**Capsules**
Paracetamol	Paracetamol	Paracetamol	Paracetamol
Maize starch	Starch	Sodium bicarbonate	Starch glycolate
Sodium metabisulphite	Potassium sorbate	Sorbitol powder	Gelatine
Magnesium stearate	Polyvidone	Sodium lauryl sulphate	Magnesium stearate
	Talc	Citric acid	Sodium lauryl sulphate
	Stearic acid	Sodium carbonate	
		polyvidone	
	FILM COATING		**CAPSULE SHELL**
	Hydroxypropylmethyl cellulose		Gelatine
	Triacetin		Titanium oxide
	Propylene glycol		

Typical dissolution profile



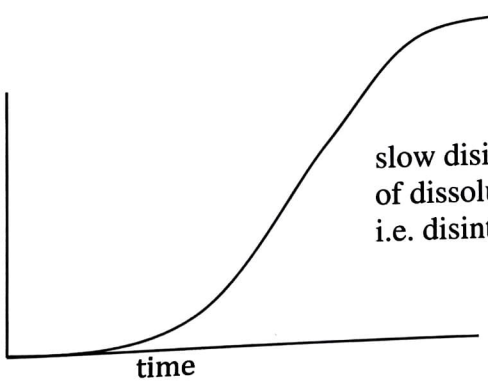
rate of non-disintegrating tablet

dissolution determined by process of dissolution and diffusion.



disintegrating tablet

rapid disintegration follow process of dissolution and diffusion
i.e. dissolution is rate-limiting.



slow disintegration/rapid process of dissolution and diffusion
i.e. disintegration is rate-limiting.

EXPERIMENT 3

INVESTIGATING POLYMERS

Safety information

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Chemical	Hazard	Precautions
Poly (ethylene glycol) (PEG)	Not classified as hazardous material	Do not ingest, avoid skin/eye contact, wear gloves
Poly(N-vinyl-2-pyrrolidone) (PVP)	Not classified as hazardous material	Do not ingest, avoid skin/eye contact, wear gloves
Glycerol	Not classified as hazardous material	Do not ingest, avoid skin/eye contact, wear gloves

Declaration - I have read and understood the contents of the safety information sheet and the script for the experiment

Signed (student): .....

Checked (demonstrator): ..... Date: .....

EXPERIMENT 3

INVESTIGATING POLYMERS

LEARNING AIMS

- To determine the viscosity of material
- To understand rheological behaviour of polymer on their own
- To understand rheological behaviour of polymer as a function of added plasticizer.

INTRODUCTION

Polymers are extensively used in the formulation of products ranging from paints, plastics and inks, to gels, creams and thin films. Different formulations use different polymers that act in different ways depending on the desired properties for the final product. Viscosity is an important characteristic for all materials, especially polymers. For liquids (solution or melt), viscosity influences flow characteristics, heat transfer, and mass transfer. The flow behaviour of a solution or melt is also responsive to properties such as molecular weight and molecular weight distribution.

Viscosity is defined by Webster's Dictionary as "the study of the change in form and the flow of matter, embracing elasticity, viscosity and plasticity." It can also be described as "the internal friction of a fluid caused by molecular attraction, which makes it resist a tendency to flow" *(Brookfield)*. A viscometer measures the friction that is created when an external object (spindle) attempts to cause a fluid to flow (stirring). The friction is between the 'layer' of a fluid that is made to move in relation to another 'layer'.

When investigating viscosity, the following key terms need to be considered (Table 3).

Table 3. Key parameters for the viscosity investigation

	Units	Description
Shear Rate γ	s^{-1}	measure of change in speed at which intermediate layers move with respect to each other
Shear Stress τ	dynes/cm^2 or N/m^2	force per unit area required to produce the shearing action
Viscosity η	centipoise (cps) or milli-pascal-seconds (mPa)	shear stress / shear rate

A material requiring a shear stress of 1 dyne per square centimetre to produce a shear rate of one reciprocal second has a viscosity of one poise or 100 centipoise. One milli-pascal-second is equal to one centipoise.

The 2 main classifications of polymer behaviour are **Newtonian** and **non-Newtonian**. Newtonian fluids, at a given temperature, have a viscosity that remains constant when shear rate is varied. A non-Newtonian fluid is one where the relationship between shear rate and viscosity is not constant. In practice, most fluids fall into this latter category.

Non-Newtonian fluids may be further subdivided into 3 categories: **pseudoplastic** where the viscosity decreases with increasing shear or show shear thinning *i.e* paint, **dilatant** where the viscosity increases with increasing shear or show shear thickening i.e., sand/water and **plastic** which acts as a solid under static conditions and a certain amount of stress must be applied to the fluid to induce flow i.e. tomato ketchup. Another factor to consider is that some fluids will display a change in viscosity with time under conditions of constant shear rate. Fluids that undergo a decrease in viscosity with time are termed **thixotropic** and those that undergo an increase in viscosity with time are termed **rheopectic**.

The use of hydrogel membranes usually demands polymers capable of forming films with high elastic and flexible properties besides having high water absorption. In terms of improvements of polymer plasticity, addition of specific plasticizers to polymers can produce promising results. The objective of this study is to evaluate effect of poly(ethylene glycol) (PEG) and glycerol as plasticizers on hydrogel membranes synthesized from poly(N-vinyl-2-pyrrolidone) (PVP) in aqueous polymeric solutions.

PVP is a highly hydrophilic polymer, biocompatible, and has considerably low toxicity. Throughout decades this polymer has been utilized in numerous applications in medicine, pharmacy, biotechnology, food, cosmetics and other industries. For example, its use as a synthetic blood plasma comes from World War II. Mixtures or blends of PVP-agar -PEG-water and PVP-agar-glycerol-water have been used in hydrogel preparation for diverse applications. Lower-molecular weight PEGs and glycerol are well-known plasticizers for various natural and synthetic polymers, for example, chitosan, poly(vinyl alcohol) (PVA) , PVP etc. Incorporation of a plasticizer in a given polymer mainly aims to lower the glass transition temperature (Tg). Plasticization of a polymer can impart improvements or adjustments in its original physical properties (film formation, higher elasticity and elongation at the rupture, more softness, etc.) and enables it to be used in various applications.

METHOD

The mixtures of PVP-PEG-water, PVP-glycerol-water and PVP-PEG-glycerol-water will be prepared using conventional method. Prepare 10 g of following solutions by weighing each component (PVP, PEG and glycerol) and dissolving them in water. Stir with a glass rode to obtain transparent solutions.

1. Prepare 10 % (w/w) PVP solutions
2. Prepare 10 % (w/w) PVP solutions + 5 % (w/w) PEG
3. Prepare 10 % (w/w) PVP solutions + 10 % (w/w) PEG
4. Prepare 10 % (w/w) PVP solutions + 5 % (w/w) Glycerol
5. Prepare 10 % (w/w) PVP solutions + 10 % (w/w) Glycerol
6. Prepare 10 % (w/w) PVP solutions + 5 % (w/w) Glycerol + 5 % (w/w) PEG

Draw a table in the lab book and note weights and solvent volumes.

Transfer 1.5 ml from prepared solution to lower Geometry and examine polymer viscosity as a function of shear rate from 0.1-100 s^{-1} using 4 mm Geometry at 25 °C.

You will be required to plot following graphs:

- Viscosity as a function of shear rate for each sample.
- Viscosity as a function of plasticizer concentration. Your graph should contain 3 data points (5%, 10% and 10% combined) and 2 data series (PEG and Glycerol).

QUESTIONS

- What is the rheological behaviour on polymer alone and after addition of plasticizer?
- List formulations in which plasticizer is incorporated and its role in formulation?
- Imagine you are preparing a polymer gel formulation to treat mouth ulcers. Describe what types of ingredient you would need to consider incorporating and why. Obtain the ingredient list of a commercially available mouth ulcer treatment and describe the role of each of the ingredients.

EXPERIMENT 4

SOLID LIPID NANOPARTICLES

Safety information

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Chemical	Hazard	Precautions
Poloxamers	Generally, they are not irritants to eyes, skin, and respiratory tract	Do not ingest, avoid skin/eye contact, wear gloves
Ibuprofen	Harmful if swallowed. Causes serious eye irritation. May cause respirator irritation. Suspected of damaging fertility or the unborn child.	Eye protection. Wear lab coat and gloves. Wash face, hands and any exposed skin thoroughly after handling. Don't eat, drink or smoke when using product. Avoid dust formation. (causes inhalation) – Avoid repeated or prolonged breathing of spray mist or dust.

Declaration - I have read and understood the contents of the safety information sheet and the script for the experiment

Signed (student): .....

Checked (demonstrator): ..... Date: .....

EXPERIMENT 4

SOLID LIPID NANOPARTICLES

LEARNING AIMS

- To gain familiarity with preparation and characterisation of Solid Liquid Nanoparticles

DIRECTED READING

Kocbek P, Baumgartner S, Kristl J. Preparation and evaluation of nanosuspensions for enhancing the dissolution of poorly soluble drugs. *Int J Pharm.* 312 (2006) 179-86.

Mehnert W, Mader K. Solid lipid nanoparticles Production, characterization and applications, *Adv Drug Deliv Rev.* 47 (2001) 165–196

Shah, R.; Eldridge, D.; Palombo, E.; Harding, I., Lipid Nanoparticles: Production, Characterization and Stability. 2015.

Müller R.H, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery: a review of the state of the art. *Eur J Pharm Biopharm.* 50 (2000) 161 – 177

Harms, M.; Müller-Goymann, C. C., Solid lipid nanoparticles for drug delivery. *Journal of Drug Delivery Science and Technology.* 21(1) (2011) 89-99.

Müller R.H, Mehnert W, Lucks J.S, Schwarz C, zur Mühlen A, Weyhers H, Freitas C, Rühl D. Solid lipid micronanoparticles (SLN) — An alternative colloidal carrier system for controlled drug delivery. *Eur J Pharm Biopharm.* 41 (1995) 62–69

Schwarz, C., Solid lipid nanoparticles (SLN) for controlled drug delivery II. drug incorporation and physicochemical characterization. *Journal of Microencapsulation.* 16(2) (1999) 205-213.

INTRODUCTION

Solid Lipid Nanoparticles (SLN) are particles made from solid lipids (i.e. lipids solid at room temperature and also at body temperature) and stabilised by surfactant(s). By definition, the lipids can be highly purified triglycerides, complex glyceride mixtures or even waxes. Recently, SLN based on para-acyl-calixarenes have been prepared and studied. Through the work of various research groups, the carrier system SLN has been characterised intensively. For detailed information on production, characterisation and application, the reader is referred to the main review papers up to date. Typical atomic force microscopy (AFM) image of SLNs is presented in Figure 1.

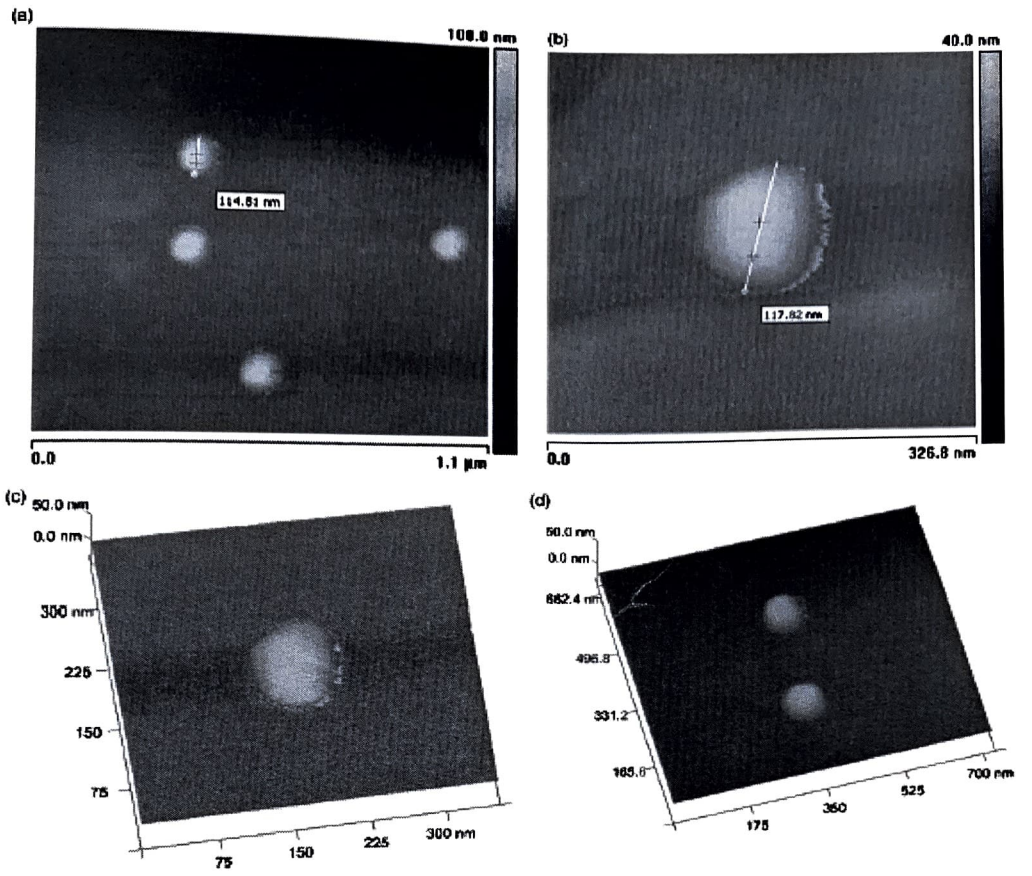

Figure 1. Typical atomic force microscopy (AFM) image of SLNs

Surfactants

In contrast to emulsions for parenteral nutrition which are normally stabilized by lecithin, the SLN can be stabilized by other surfactants or polymers and their mixtures. However, as a distinct advantage of SLN compared to polymeric nanoparticles they can be produced by high pressure homogenization identical to parenteral O/W emulsions. This is a technique well established on the large scale and already available in the pharmaceutical industry. The production lines for parenteral emulsions are in most cases equipped with temperature control units because an increased temperature facilitates emulsion production, this means that existing production lines can be used for producing SLN by the hot homogenization technique. Surfactants and co-surfactants include lecithin, bile salts, but also alcohols such as butanol. Excipients such as butanol are less favourable with respect to regulatory aspects. From the technical point of view precipitation of the lipid particles in water is a dilution of the system, that leads to a reduction of solid content of the SLN dispersion. For some technological operations it is highly desirable to have a high lipid solid content, e.g., 30%. An example is the transfer of the SLN dispersion to a dry product (e.g., tablet, pellet) by a granulation process. The SLN dispersion can be used as granulation liquid, but in the case of low particle content too much water needs to be removed.

Surfactants are compounds with two distinct regions in their chemical structure. One region has hydrophilic properties, the other having hydrophobic properties (Figure 2). The hydrophilic properties are usually conferred on molecule by the presence of ions, alcohol or carboxyl groups. Hydrophobic properties are due to long chain hydrocarbons which may also have a ring system attached to them.

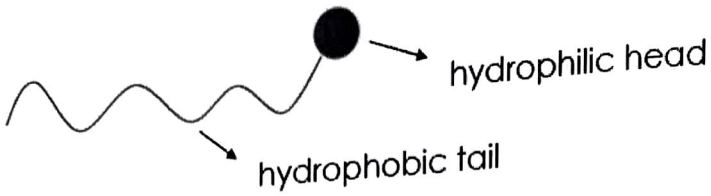

Figure 2. Typical structure of a surfactant

Surfactants can be defined into one of two categories; either ionic or non-ionic (Figure 3). The ionic group can also be sub-divided into cationic, anionic or zwitterionic (amphoteric) groups.

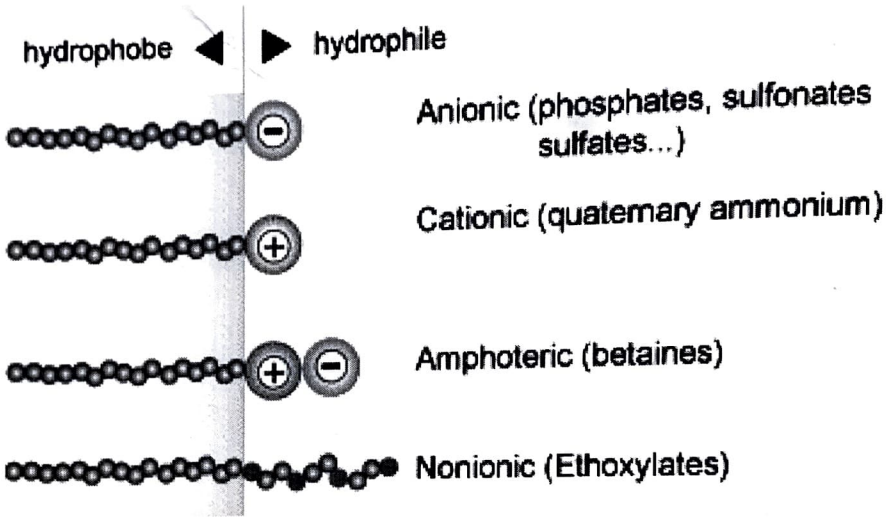

Figure 3: Different type of surfactants

Stability of SLNs

The measurement of the zeta potential allows predictions about the storage stability of colloidal dispersion. In general, particle aggregation is less likely to occur for charged particles (high zeta potential) due to electric repulsion. However, this rule cannot strictly apply for systems which contain steric stabilizers because the adsorption of the steric stabilizer will decrease the zeta potential, due to the shift in the shear plane of the particle. The physical stability of SLN dispersions can be investigated intensively, e.g., by measurements of particle size (photon correlation spectroscopy, PCS; laser diffraction, LD), charge (ZP) and thermal analysis (differential scanning calorimetry, DSC).

METHOD

Formulations by the HPH/Ultrasonication methods

Students will be divided in two groups and they will swap mid-experiment to use either HPH or ultrasonication to prepare SLNs.

The SLN samples loaded with IBU as the model pharmacological active ingredient will be prepared by the following methods:

- Prepare 50 ml of hot water in a tall-form 100 ml beaker by heating the water on a hot plate, do not add a magnetic stirrer bar.
- 1 g of the SLN components (IBU/tristearin/poloxamer 407) at a ratio of 10/20/70 (w/w/w) is placed in a separate container and heated to a temperature above the melting point of the lipid (above 70°C) allowing the IBU and poloxamer 407 to dissolve in the molten lipid.
- The drug-containing melt lipid is then dispersed in distilled hot water (50ml). This is done by, adding, with aid of a syringe, the melted SLN components to the bottom of the beaker of hot water while mixing the water with a homogeniser, keep the beaker of water on a hot plate at all times. This process has to be carried out quickly to avoid crystallisation.
- The sample needs to be homogenised (15,000 rpm) with an Ultra Turrax K25 homogenizer to form a pre-emulsion for 3 min. The homogenizer needs to be observed, as the solution can sometimes overflow from the beaker. A white milky solution will be produced.
- The same process will be repeated but this time the IBU/lipid components will be dissolved in 2 ml Et-OH while SLN components will be dissolved in hot distilled water. (Students will swap to conduct this part of the work i.e., HPH group will perform this step using ultrasonic horn and *vice versa*.)

Particle size measurements and zeta potential

The particle size distribution and the zeta potential of the produced preparations will be determined by dynamic light scattering (PCS) using a Malvern Zetasizer Nano-ZS. The determined particle size range is 0.6 nm – 6 μm.

QUESTIONS

- What are advantages of the SLNs compared to other drug delivery systems?
- Which preparation SLN method is most suitable for the formulation of IBU nanosuspensions and why?
- What is the effect of different surfactants on the obtained SLN particle size with the following characteristics: a) Higher surfactant amounts and b) surfactants with longer lipid chains?
- Can SLNs be used for the development of sustained release formulations and how?