Traditional capsules

Profession

Traditional capsules formulations Consists of a 2 piece hard gelatin shell, with a powder blend. Typical formulation would be:- Active Diluent Glidant Lubricant Wetting agent Capsules have advantages as oral dosage forms: Easy to administer, simpler formulations (Vs tablets-fewer stability problems) Taste/ odour masking Potentially good bioavailability Liquid filled capsules - Advantages 1. Dose Uniformity In a powder capsule for potent drug choice the problems are achieving homogenous mix at the required scale of scrutiny. To overcome this problem we could formulate as a solution; 100% homogenous.

Filling liquids also avoids problems of poor powder flow; if this occurs during filling, can lead to variation of fill weight. (with a 1% possible) . 2. Patient safety compliance/consumer preference Softgel capsule shel soft/flexlble; popular dosage form, due to ; Ease of swallowing Absence of taste Convenience (portable, robust) Soft gels capsules can be formulated to be taken In different ways; Chewable or lozenges Twist-offs (with a tag allows access to contents) 3. Increased Bioavailability Dissolution of drug from solid state (I. e formulated as an ordinary tab/cap) can be rate limiting step.

This often true for non-polar drugs. But In llquld fill cap, drug Is In a form from which It can be absorbed rapidly. Drug being In solution has additional advantage (I. e Vs tablet, fro low solublllty drug) Reduces varlablllty of drug plasma levels (between patients) 4. Safety Powder processing of very potent or cytoxlc drug hazardous; dust contamination avoided by solution. 5. Olly/low melting point drugs Dlfflcult to make Into " normal" tab/cap (drug could partly melt during compression) 6. Product stablllty Drug can be protected against 02/H20 by using llpld vehicle and soft gel shell.

Considerations for Capsule shell Having llquld In direct contact with the shell -more potential for formulation -pack Interaction, particularly affecting Integrity. Therefore, any trace of water cannot be used because water dissolves gelatin hence won't work. Llqulds can be filled Into Dotn sort ana nara cap- out OITTerent conslaeratlons apply. can't necessarlly Till same formulation into both types, need to think about composition of the shell itself (gelatin) Gelatin for Hard Capsules Main problem Liquid fill hard gel caps is; Residual moisture loss.... rom the shell into the formulation Hydrogels require 13% to 6% level of moisture, to retain strength. Hence hygroscopic solvents cannot be used as excipients in liquid filled caps since they might take up some water. E. g ethanol, liquid PEG, glycerol, PG. (all these cannot be used for hard capsule) During preformulations studies, we have to check that excipients are compatible with shell. Excipients that can be used for hard capsule; Lipophilic liquids/semi solids e. g arachis, castor, olive oils. Also some surfactants & emulsifiers. As an alternative, could consider HPMC (hydroxypropyl methylcellulose) caps.

Residual water not so important for integrity of shell, so wider range of olvents may be possible. Gelatin for soft capsules " Formulation" of soft gel caps themselves are different to hardgel . Typically the gelatin plus: Plasticiser (to give flexibility). Often 20-30% Glycerol is frequently used Water; lower residual level than hardcaps, 5-8% Colourant /opacifier Lower water level needed for the soft caps means ; hydrophilic solvents e. g. PEG 400can be used unlike for hard gels. (but need to be aware of migration into shell) Manufacture of Hardgel Caps In brief, Formulation is pumped into bottom half of shell, then cap is replaced.

Issues for manu. Hardgel caps Formulation viscosity (liquid & semi solid possible) Temperature of filling Sealing of capsule shell afterwards NB: Therefore need to consider physical aspects of formulation, as well as filling equipment available. Rheological Considerations Simplest formulation is a solution in which active dissolves, at room temp. Very precise control of filling possible. In-soluble active If active is not soluble, could consider using elevated temperatures, up to 70Deg. Celcius. (Above this could damage the shell) But when the temperature falls again, inside the shell drug would re-precipitate at RT.

As a consequence resulting particle size will be important (bioavailability). Another problem; Recrystallized/suspended drug inside capsule shell wil; have a potential to cake re " normal" suspension, could get crystal growth. t Is posslDle to Till a suspenslon out tnen anotner proDlem to solve; May oe a to keep homogenous, during filling. 2 Alternatives for insoluble drugs; 1 . Thixotrpic gel; Undergoes shear thinning during mixing/filling. so then enough to but gel resets in capsule Typical formulation- Lipophilic solvent (oil) *gel-former (e. g. silicon dioxide).

Silicon ioxide only forms a gel in a lipophilicenvironment. 2. Thermosoftened system Formulation is a liquid or suspension at (elevated) filling temperature, but solid or semi solid at RT. Typically based on a high molecular PEG, eg PEG 10, 000 (soft but solid) If drug crystallises, will need to consider resulting particle size as previously. Manu. Of Hardgell caps cont'd a)Filling- Hardgell caps On a development (small) scale, can use a syringe. Large-scale machines use volumetric pumps- hopper and nozzle can be heated. Up to 100, 000 caps/hr possible.