

Pilot Plant Scale-Up of Semisolid Products

- Pastes,Gels,Ointments and Creams-products with higher viscosities-certain aspects-more critical
- Natural turbulence created by mixers-not adequate for a homogeneous ointment or cream
- Mixing equipment-must be capable of effectively and continuously moving the semisolid mass from the outside walls of the mixing kettle to the centre and from bottom the top of the kettle
- This distributes the ingredients to bring about a rapid and efficient heat transfer to and from the product during the heating and cooling steps
- Power required-mixing operation-directly related to changes in the viscosity of the product

Pilot Plant Scale-Up of Semisolid Products

- Motors used to drive the mixing system-must be sized-handle the product at its most viscous stage
 - Motors-mixers-to disperse or dissolve components that have been added early in the manufacturing process- at low product viscosity-required to operate at slower speed-prevent splashing
 - Equipment-variable speed mixing
-
- Many processing steps-emulsification-homogenization-addition of active ingredient-product transfer-carefully predetermined temperatures-temperature range-critical-quality of final product
 - Cream-correct temperature-otherwise poor-quality product with improperly dispersed wax
 - Accurate understanding of heat transfer characteristics of the system and temperature gradient throughout the batch is important

Pilot Plant Scale-Up of Semisolid Products

- Temperature recorded by a single sensor-fixed point in the mixing vessel-misleading
- Unacceptable product viscosity range-inadequate temperature control-critical steps
- Improper temperature control-adverse effect-particle size of poorly soluble active ingredients
- If these added at too high temperature-solubility may be artificially increased-metastable product-on cooling-crystal growth or recrystallization from saturated solution
- Recrystallized material-different polymorphic form or a different crystal type or size
- Hence-change or particle size distribution-gritty,less elegant product or one with altered stability or biologic activity

Pilot Plant Scale-Up of Semisolid Products

- Many cream formulations and some gel products-shear sensitive
- Handling-transfer from manufacturing kettle to holding tanks or to filling lines-attention-amount of shear encountered
- Changes in viscosity-viscous products-pumped-long transfer lines or filtered to remove unwanted particulates
- Relationship between shear stress and measured viscosity values of the product must be understood
- Most viscometers-determine relative viscosity rather than absolute viscosity
- Accurate evaluation of the effect of process change on viscosity –recognize effect of sample conditions such as temperature, processing history of sample and age
- Such variables-properly controlled-accurate interpretations

Pilot Plant Scale-Up of Semisolid Products

- Cream-critical steps-emulsification of the two phases and dispersion of any suspended active ingredients
- Pharmaceutical equipments-homogenization of emulsion and dispersion of suspended API-various types of high-shear mixers,homogenizers, and colloid mills
- Colloid mill-fixed stator plate and a high speed rotating rotor plate-material drawn or pumped through adjustable gap set between the rotor and stator
- Sonic homogenization equipment-rapidly vibrating vanes

Pilot Plant Scale-Up of Semisolid Products

- Transfer pumps-semisolid products-move viscous material without applying excessive shear and without incorporating air
- Pumps-designed to meet these criteria-*positive displacement pumps*
- Operation-rotating member inside a close fitting stationery housing
- Self priming-create adequate head pressure-force product through long transfer lines and filtration equipment
- In choosing size and type of pump for a particular operation-*product viscosity,desired pumping rate,production compatibility with the pump surfaces and the pumping pressure required should be considered*

Pilot Plant Scale-Up of Semisolid Products (Positive displacement pumps)

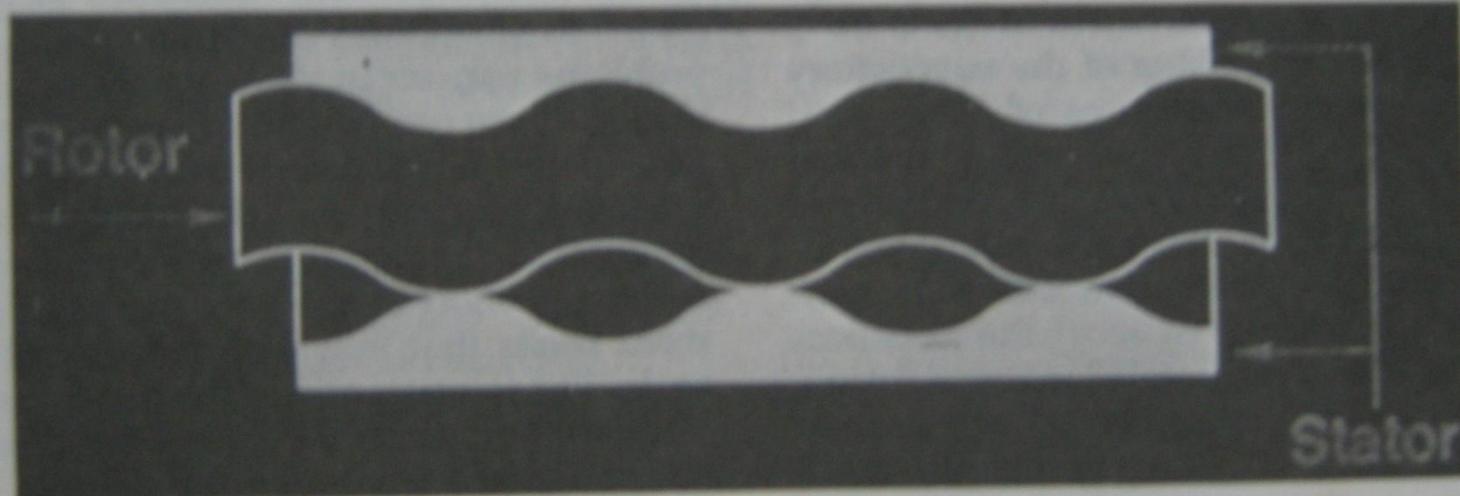


FIG. 23-15. Schematic representation of a positive displacement pump. The helical rotor moves inside the double helical stationary housing, creating a progressing cavity, which moves the material. (MOYNO Quick Displacement Progressing Cavity Pump, courtesy of Fluids Handling Division of Robbins & Myers, Inc.)

Pilot Plant Scale-Up of Emulsions

❑ EMULSIONS:Disperse systems

- Dispersed phase-oils or waxes-either liquid or semisolid state
- Liquid emulsions-special procedures- scale-up –production equipment-extensive process development and validation
- Processing parameters and procedures-adjusted and controlled –temperature,mixing equipment,homogenizing equipment,inprocess or final product filters,screens,pumps, and filling equipment
- Reduction of globule size of internal phase-affects physical properties of the emulsion-appearance and viscosity-physical stability of the product
- Manufacturing systems- high-shear mixers – likely to lead to air entrapment- adversely affect the physical and chemical stability

Pilot Plant Scale-Up of Emulsions

- Use of vessels-operated with contents under controlled vacuum avoids problem of unwanted aeration
- Filtration-remove particulates originating from raw materials or introduced during processing-affect quality of emulsion
- Unwanted particulates-efficiently removed by filtering separate oil and water phases before emulsification

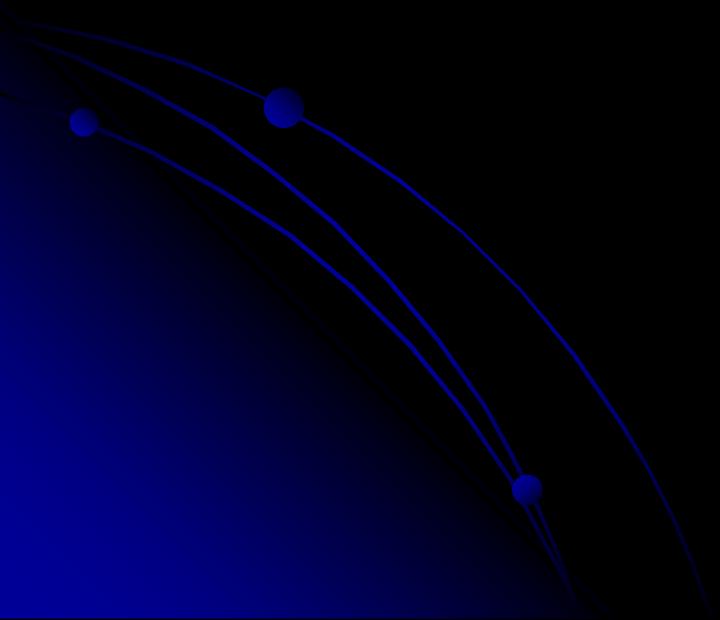
Pilot Plant Scale-Up of Suppositories

□ SUPPOSITORIES:

- Preparation Of The Molten Suppository Mass
- Molding and Packaging

Pilot Plant Scale-Up Studies

□ CONTRACT MANUFACTURE



Pilot Plant Scale-Up Studies

- ❑ Reference
 - The Theory And Practice Of Industrial Pharmacy

By LACHMAN AND LIEBERMAN