POLYOX™

Water Soluble Resins

Colorcon

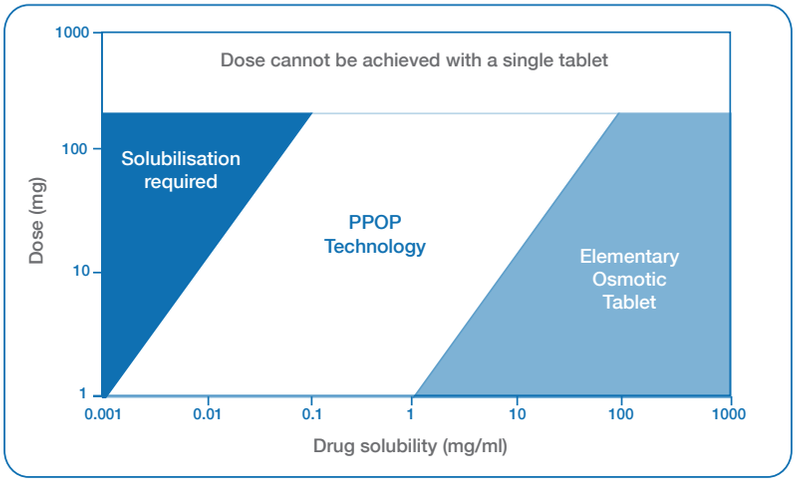
DUPONT

CONTROLLED RELEASE ALLIANCE

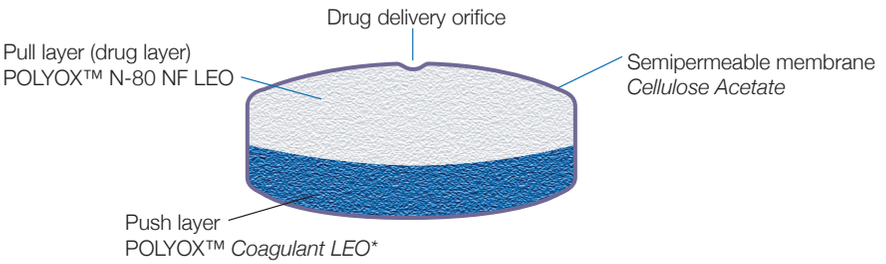
Technical Bulletin

Push-Pull Osmotic Pump (PPOP) Formulations

Selection of suitable drug candidates: osmotic technology on dose-solubility map



PPOP Technology



*LEO - Low Ethylene Oxide

POLYOX™ Grades

POLYOX™ Grades	Approx. Molecular Weight (Daltons)	Function
WSR N-80 NF LEO	200,000	Pull layer
WSR Coagulant NF LEO	5,000,000	Push layer

Key Formulation Considerations

Key Considerations	Purpose	Typical Working Range
Orifice dimension	Delivery of drug	500 to 1000 µm
Drug layer: Push layer ratio	To achieve desired release	2:1 to 3:1
Total tablet weight	Tablet size	100 to 700 mg

PPOP Technology and Recommended Ranges

Pull Layer (Drug Layer)

Ingredient	Purpose	Typical range
Drug	Active	1-30%
POLYOX™ N-80 / 205 LEO	Polymer entrainer	70-95%
HPMC or PVP	Granulation binder	2-5%
Magnesium stearate	Lubricant	0.5-1%

Push Layer

Ingredient	Purpose	Typical range
POLYOX™ coagulant LEO	Swelling agent	50-70%
Sodium chloride	Osmogen	30-40%
Pigment	Colorant	0.2%
Magnesium stearate	Lubricant	0.5-1%

Semipermeable membrane (SPM)

Ingredient	Purpose	Typical range
Cellulose acetate (CA398-10)	Continuous polymer phase	5-8%
PEG 3350	Pore-former	1-3%
Water	Solvent	3-6%
Acetone	Solvent	87-90%

Material Considerations

- Particle size and distribution (PSD) of drug
- PSD of granules (if granulated)
- POLYOX™ viscosity grade

Processing Considerations

- Content uniformity of drug
- Good excellent flow of material

Material Considerations

- PSD of osmogen (NaCl)
- PSD of granules (if granulated)
- POLYOX™ viscosity grade

Processing Considerations

- Content uniformity of osmogen (NaCl)
- Color uniformity

Material Considerations

- PEG molecular weight / grade
- Cellulose Acetate : PEG ratio
- Acetone : Water ratio
- % Solid content of dispersion

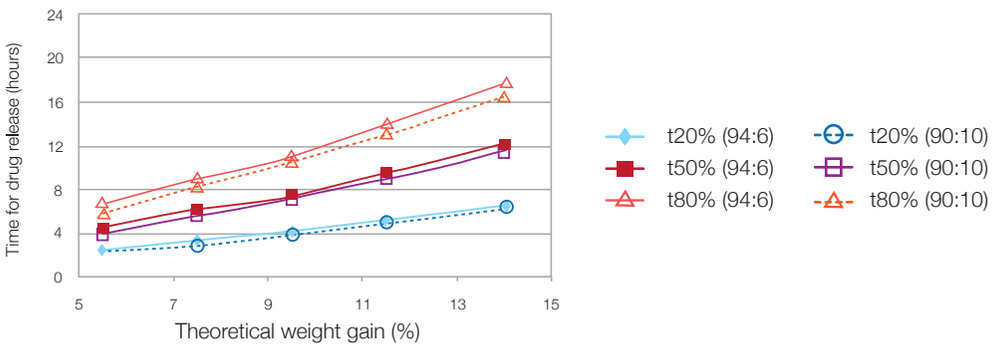
Processing Considerations

- Content uniformity of PEG
- Transparency of film (affects detection system on laser drill equipment)
- Residual solvent within ICH limits for solvents
- Orifice diameter and aspect ratio

PPOP Regulatory Considerations

Dissolution	Target Specification
Multi-pH dissolution	0.1N HCl, pH 4.5, pH 6.8, and water
Release profiles	% Drug release at (min) 3 time points e.g., t10, t50, t80
Alcohol Study	No dose dumping; release lower or comparible with reference listed drug (RLD)

Effect of Acetone:Water ratio (CA Coating) on % Drug Release



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