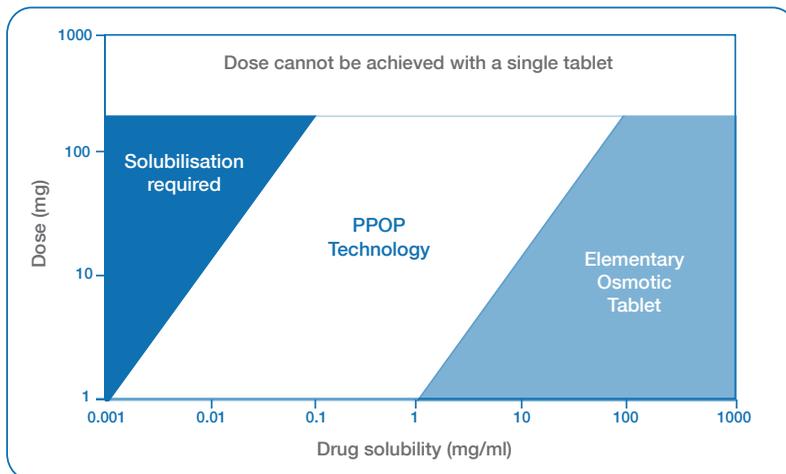
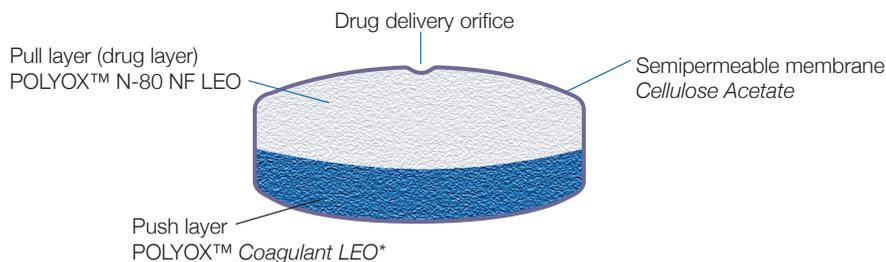


## Push-Pull Osmotic Pump (PPOP) Formulations

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
<ul style="list-style-type: none"> <li>Particle size and distribution (PSD) of drug</li> <li>PSD of granules (if granulated)</li> <li>POLYOX™ viscosity grade</li> </ul>
Processing Considerations
<ul style="list-style-type: none"> <li>Content uniformity of drug</li> <li>Good excellent flow of material</li> </ul>

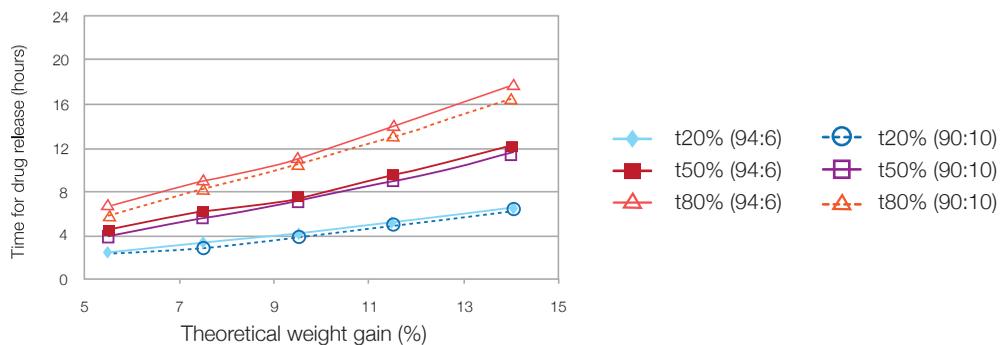
Material Considerations
<ul style="list-style-type: none"> <li>PSD of osmogen (NaCl)</li> <li>PSD of granules (if granulated)</li> <li>POLYOX™ viscosity grade</li> </ul>
Processing Considerations
<ul style="list-style-type: none"> <li>Content uniformity of osmogen (NaCl)</li> <li>Color uniformity</li> </ul>

Material Considerations
<ul style="list-style-type: none"> <li>PEG molecular weight / grade</li> <li>Cellulose Acetate : PEG ratio</li> <li>Acetone : Water ratio</li> <li>% Solid content of dispersion</li> </ul>
Processing Considerations
<ul style="list-style-type: none"> <li>Content uniformity of PEG</li> <li>Transparency of film (affects detection system on laser drill equipment)</li> <li>Residual solvent within ICH limits for solvents</li> <li>Orifice diameter and aspect ratio</li> </ul>

## 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 comparable with reference listed drug (RLD)

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



POLYOX™

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