Comparison of the Solubilization Effect of Micronized Poloxamers, on a poorly water-soluble model drug in capsule formulation by dry Granulation

Charles Onyiuke
BASF Corporation, Pharma Ingredients and Services, 500 White Plains Road, NY 10591

Abstract
Dry blend granulations lower the fastest and most economical methods of solid oral dosage manufacture in the pharmaceutical industry. This study investigated the effect of micronized poloxamers on the solubility of poorly water soluble drugs in capsule formulation using dry blended powder.

Introduction
The ideal method of solid dosage formulation and manufacture has always been by granulation where the active ingredient(s) and the excipients are blended to achieve homogeneity of the mixed particles. This method allows particles to be sized to achieve a desired mass based on the size distribution. This also allows the desired density of drug on the granule to be achieved. The efficiency of this process is the mixing time of the dry particles which needs to be long enough to achieve homogeneity. This is necessary to achieve adequate drug release and stability.

Materials
Carbamazepine was obtained from BASF Corporation.
Micronized Poloxamer 407® (F108 Micro), Poloxamer 237 (Lutrol® F87 Micro), Poloxamer 338 (Lutrol® F127 Micro), the non-ionic surfactants of poly(oxyethylene)poly(oxypropylene) (POE-POP) were obtained from BASF Corporation.
Crospovidone (Kollidon® CL) was obtained from BASF Corporation.
Calcium Carbonate was obtained from Particle Dynamics.
Pro-Solv (SMCC), Calcium Carbonate, and Silicified Microcrystalline Cellulose were obtained from Acme (Canada). Polyethylene glycol (PEG) 400 was obtained from J.R. Kosher (Canada). Size 0 Empty Capsule Shells were obtained from Capgo.

Methods
Poloxamer 237 (Lutrol® F87 Micro), and Poloxamer 338 (Lutrol® F127 Micro) were micronized in-house using Freon™/SF6/CO2. The Sprayed Pellet method is a fast and economical process; but it is the most challenging method in terms of achieving a high degree of homogeneity. For this reason, it is necessary to establish guidelines for processing conditions that may subsequently be used to achieve adequate quality control.

Carbamazepine Formulations with Different Lutrol® Micro Grades in 1:5 ratios

Carbamazepine Formulations with Different Lutrol® Micro Grades in 1:10 ratios

Results

Table II
Carbamazepine Formulations with Different Poloxamer Ratio (w/w %)

Discussion
Physical mixture of Carbamazepine and different Lutrol® F micro grades in capsule formulations increased Carbamazepine solubility remarkably. The capsules from the 1:5 ratios formulations have been tested. The solubility enhancement is a simple, fast and economical process; but it is the most challenging method in terms of achieving a high degree of homogeneity. This is necessary to achieve adequate drug release and stability.

Conclusion
Micronized grades of Lutrol® F88 and F127 improved the solubility of carbamazepine when compared to control capsule formulation.
Carbamazepine was more soluble in micronized Lutrol® F88 than in Lutrol® F27 micro, F87 and F108 micro pld.
The small particle size of the micronized Lutrol® grades ensured optimum ingredient miscibility and blend homogeneity.
The gelling property of Lutrol® F127 micro can be utilized in Dry Blend formulations to provide sustained or delayed drug release.
Dry blend granulation where micronized Lutrol® F88 and F127 are used to solubilize poorly water-soluble drugs, such as Carbamazepine, is a robust and economical method of solid dosage manufacture.
The solubilization effect of Poloxamers studied decreased from F108 > F127 > F87 > 108.

References
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