Improved Dissolution and Micromeritic Properties of Ibuprofen by Continuous Twin Screw Hot Melt Granulation Using Kolliphor P 188 Micro as Meltable Binder

R. G. Narkhede¹, J. N. Pawar², V. M. Tawde¹
¹BASF India Ltd., ²Institute of Chemical Technology

Purpose
Ibuprofen possess challenges of low dissolution, poor flow properties and sticking tendency during commercial operations. Kolliphor P 188 micro (microp制led grade of Poloxamer 188) is an amphiphilic surfactants, having low melting point and also acts as hydrophilic lubricant. The objective of the present study was to develop solid oral formulation of Ibuprofen using twin screw granulation technology. The granules can be processed at relatively higher speeds compared to traditional hot melt extrusion process indicating commercial viability of process along with improved blend properties. The surfactant properties of poloxamers helps in achieving superior dissolution as compared to conventional formulations.

Methods
The ibuprofen granulation was carried out using 11 mm twin screw hot melt extruder. The experiments were designed by central composite design (CCD) using DOE software 9.70. The variables were polymer and drug ratio. Ibuprofen (Ibuprofen 70- BASF) and Kolliphor P 188 micro are sifted through 30 mesh and mixed using double cone blender. The extruder had eight zones, out of which zone 4 and 6 possessed the mixing elements with temperature of 55 ºC, additionally Zone 1 and 8 were having the temperature of 40 ºC. The extrusion was studied at different screw speeds without die assembly. The granules were prepared at different concentration of drug and polymer (drug loading 93-97%). The granules obtained were allowed to attain room temperature and passed through 20# sieve. The granules were characterized for micromeritic properties, in vitro dissolution testing and optimized batch was evaluated for DSC and XRD studies. The granules were filled into hard gelatine capsules and analysed for dissolution using USP Type I dissolution apparatus.

Results
Marked improvement was observed in micromeritic properties of the hot melt granulated product as compared to API alone, physical mixture and conventional RMG granules. The process run at different screw speeds has given reproducible results in terms of dissolution and improved micromeritics. The granules obtained at all the variables of screw speed were highly dense as compared to granules obtained by conventional high shear granulation. In vitro dissolution in pH 7.2 has revealed improved dissolution as compared to conventional tablet formulation. Central composite design infers optimized batch containing 95 % API and 5 % polymer ratio. DSC and XRD study has confirmed no change in crystallinity, which is desirable attribute of typical continuous granulation process.

Conclusion
Kolliphor P 188 micro is found to be an excellent hot melt granulation binder for formulating denser and free flowing granules of Ibuprofen. From the various improvement outcomes of this study, it can be concluded that Kolliphor P 188 micro acts as an excellent binder for continuous hot melt granulation, acts as surfactant and also shows lubricating effects in the granules as compared to conventional binders. The process is found to be commercially viable with respect to high output and easy processing steps. This novel approach of continuous melt granulation using twin screw extruder along with Kolliphor P 188 micro as meltable binder can be utilized at industrial scale for the high volume drug candidates.