Foam granulation: new developments in pharmaceutical solid oral dosage forms using twin screw extrusion machinery

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Abstract
This paper investigates foam granulation in a twin screw extruder as a new continuous wet granulation technique for pharmaceutical powder drug formulations. Foamed aqueous binder has a reportedly lower soak-to-spread ratio than drop or spray liquid addition in batch granulation. This work demonstrates a twin screw extruder configuration for foam granulation and subsequently compares the new approach against liquid injection in the granulation of α-lactose monohydrate with a methylcellulose binder. Trials were conducted at high powder output rates (20–40 kg/h) and high screw speeds (220–320 RPM) with two screw configurations. Process stability improved with the new technique allowing granulation with less binder. The extruded mass maintained a low exit temperature, being insensitive to operating conditions unlike the liquid injection approach, where temperatures rose significantly as flow rate increased. The particle size distribution by foam granulation reflected a more uniformly wetted mass with larger granule growth noted even for conditions where dry powder exited by liquid injection. Other factors were found similar between the two binder delivery methods such as consumed mechanical energy, as well as fracture strength and compressibility of produced granules.

Keywords: Foamed aqueous binder, lactose, methylcellulose, cellulose ether, twin screw extrusion, wet granulation, continuous granulation, continuous manufacturing

Introduction
High-shear wet granulation by twin screw extrusion machinery is an emerging continuous manufacturing technology for solid oral dosage forms¹–¹⁴ which is receiving considerable attention by the pharmaceutical industry. The technology has the capacity to produce a well-mixed granular product of excipients and active ingredients with high consistency in a relatively short span of time (in the order of seconds). The approach requires less binder in order to produce a granule of equivalent properties compared to the standard high-shear wet granulation process¹⁵, necessitating less energy consumption for drying and less milling in downstream steps. In addition, there have been studies examining the capacity to localize more of the subsequent processing steps of tabletting within the extruder, including drying and compaction¹⁶,¹⁷. Wet granulation in a twin screw extruder is particularly useful with many of the hydrophobic materials that the industry has current interest in processing¹⁸. An attractive feature of the machinery is its offer of a flexible production platform that is readily configured in-house to different products and different scales of manufacturing (laboratory to pilot-scale and, in some cases, even full production outputs are possible on the same machine). The work of Shah¹¹ was particularly illustrative in displaying the broad capacity of the machinery and the interests of pharmaceutical companies regarding the technology. Developing this technology requires thorough studies on all operational factors, including screw design¹¹,¹², machine type, auxiliary equipment configuration¹¹, and feeding strategies of all formulation components. Though the current research looks at immediate release applications, the process is well suited to controlled release as well. For this paper, the focus will be upon the issues with binder addition to the extruder.

The metered addition of a liquid binder solution facilitates agglomeration of the conveyed powder