Case Study

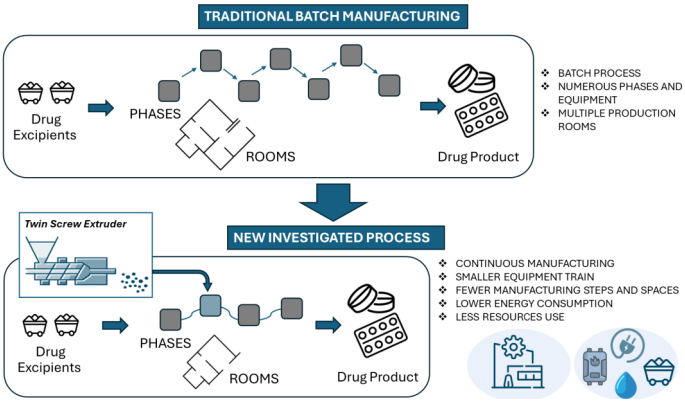
ETERNAL

CONTINUOUS PHARMACEUTICAL MANUFACTURING

SIMPLER, SAFER, FASTER

In the past, energy consumption and environmental impact were not considered major factors to be taken into account during the development of a manufacturing production line in the pharmaceuticals industry. Traditional batch manufacturing often involves long, discontinuous, multi-phase and energy-intensive processes that required facilities with a large physical footprint and, due to their high air-conditioning / environmental control service requirements, a correspondingly large energy consumption footprint.

Now, as they increasingly pursue sustainability in their operations, pharmaceutical companies are seeking to adopt innovative approaches and technologies enabling continuous manufacture, which improves efficiency and reduces environmental impact. One technology with exciting potential for enhancing downstream, drug product formulation is Twin Screw Granulation (TSG), a continuous technique capable of flexibly producing high-quality granular agglomerates with a range of properties. TSG can support dry, melt, or wet processes and the use of several excipients, further facilitating access to a range of final product performance profiles.



Twin screw extrusion offers the prospect of continuous downstream formulation. As well as potential material efficiencies, smaller equipment trains and fewer process steps means there is less need for expensive, energy-intensive environmentally conditioned manufacturing spaces.

Context

Until recently, pharmaceutical manufacturers have not considered energy consumption and environmental impact as major factors to be taken into account during the development of a manufacturing production line.

Challenge

Traditional batch manufacturing often involves long, discontinuous, multi-phase and energy-intensive processes that require large facilities. Pharmaceutical companies pursuing sustainability are now exploring innovative continuous manufacturing technologies, which can improve efficiency and reduces environmental impact.

Innovation

Twin Screw Granulation has been successfully used to produce granules for immediate-release tablets with fewer steps and less materials, avoiding water addition and energy-intensive phases, as a potential alternative to the current batch manufacturing process.

Next Steps

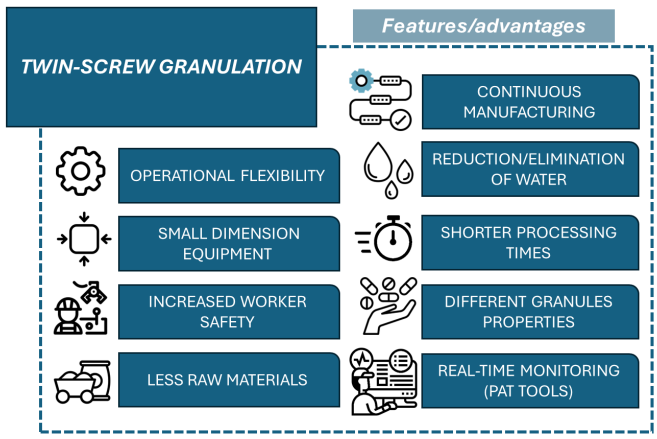
The positive results obtained at R&D lab scale are being tested and confirmed at a bigger scale using a pilot 18mm-extruder. The quality of the product granules from the pilot scale will be studied and the energy consumption measured and compared with the standard process to fully assess the improvements.

Features and Advantages

Twin-screw extrusion systems consist of a pair of co- or counter-rotating screws. The drug active and excipients are automatically fed as solid powders into the extruder, where the combination of mixing, kneading and controlled heating causes them to agglomerate into granules, suitable for further processing into the final product form.

Through twin screw melt granulation (TSMG), it is possible to obtain more uniform granules with better compressibility than is possible by conventional processing. Other advantages are

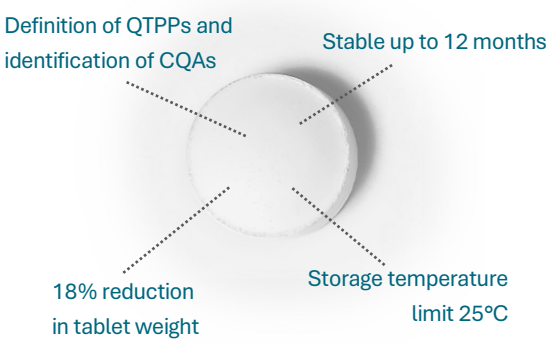
- Energy savings associated with the reduced number of manufacturing steps and the space-time efficiency of the process, which reduces the requirement for energy-intensive air-conditioning;
- Environmental impact reduction through optimised use of raw materials and water;
- Safer working conditions through automation; and
- Consistent product quality through real-time monitoring.



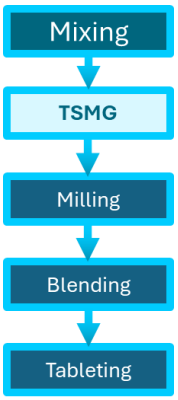
TSG accommodates many different excipients (e.g. thermoplastic polymers and meltable binders) offering great flexibility in targeting the desired type of granulation (wet, dry, melt) and product drug release profile. It can also handle both low and high drug content products and is advantageously compatible with real-time monitoring PAT (process analytical technology) tools.

Flexible, efficient, effective and safe operations with a small footprint

Prototype Defined



Process Streamlined



High energy consuming steps removed

Results and Benefits

During the R&D phase, TSMG has been studied in depth by Angelini Pharma for a selected target protype of interest, along with the associated process steps and parameters, establishing the Quality Target Product Profile (QTPP) and Critical to Quality Attributes (CQAs). A twelve-month stability study has been carried out to confirm the chemical-physical stability and microbiological quality of the product tablets, confirming the packaging type and storage conditions. Drug release and particle size have been explored extensively during initial scale-up trials, which are being extended into further phases of development.

Continuous production methods including TSG may be used to develop new drugs, to target and finely tune properties like immediate/prolonged release, to improve solubility or to mask taste without coating, and to produce pharmaceuticals in a greener way. Thanks to automation and real-time monitoring, operator safety can be enhanced while maintaining or even improving product quality, and raw material and energy consumption can be reduced, minimising environmental impact.

ETERNAL is contributing to the sustainable development of pharmaceutical manufacture, use and disposal, by using and promoting full life cycle approaches covering design, manufacture, use, and disposal through

- application-industry oriented R&D and scale-up;
- clear pathways to compliance;
- new scientific knowledge on the environmental fate and eco-toxicological effects of pharmaceuticals; and
- behavioural change for safe use and disposal.

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Find out more at: www.eternalproject.eu