CASE STUDY

PHARMACEUTICAL

COUNTRY: Canada
PRODUCT: Twin Radial Xtruder, Marumerizer® Model QJ-700
KEY BENEFIT: Consistent quality and large capacity

Continuous Extrusion-Spheronization

Continuous Extrusion-Spheronization system solves quality and capacity issues at a major drug company

Background

A major Canadian pharmaceutical company, specializing in generic drugs, produces two drug formulations in pellet form using the process of Extrusion and Spheronization (ES).

The aforementioned drugs have been produced on two existing batch systems for the past several years. Each system is composed of an LCI twin screw Radial Xtruder® (extruder) Model EXDS-100 and a Marumerizer® (spheronizer) Model QJ-700. The products are first granulated using a high shear mixer in a separate suite, then manually transferred to the drug pelleting suite, where the wet granulation mix is extruded, spheronized, then transferred to the receiving pot of a fluid bed coater. The pellets are dried and coated for subsequent encapsulation.

Several concerns with pellet variability (primarily aspect ratio and particle size distribution), significant operator intervention, and increased market demands, prompted the client to contact LCI to explore options for a new, fully automated, and continuous pelleting system. LCI has been supplying Extrusion-Spheronization systems to the pharmaceutical and chemical industries in the Americas since 1983.

Problem

Extrusion is a continuous process, while spheronization is inherently a batch process. Given the manual nature of extrusion-spheronization systems, the extruder was being utilized intermittently. The operator fed the extruder with a scoop and collected a given weight of extrudates, which were then manually charged into the spheronizer on a batch basis and discharged after a set time. During the spheronization time, the extruder sat idle until the process was repeated.

Issues stemmed from the extrusion process such as inconsistent manual feeding (varied from operator to operator), variable extruder shaft speed (often controlled by operator), and material would dry and harden in the extrusion screen due to intermittent usage between spheronization batches.

Subsequent to extruder issues, the spheronization step incurred the following additional problems: spheronization parameters often controlled by operator (charge volume, spheronization time, and plate speed), frequent plate fouling due to sticky formulation (operators often had to stop

every two to three batches to manually scrape product off the spheronizer plate with a spatula), low capacity, and labor intensive process.

The spheronizer issue of frequent plate fouling is a common issue in the industry. The plate is typically cleaned by scraping product from the surface utilizing a spatula or brush. This cleaning method presents several issues in itself: the height of the grooves in the spheronizer plate can be damaged and diminished by utilizing a spatula, or, bristles of the brush may break off into the spheronizer bowl.

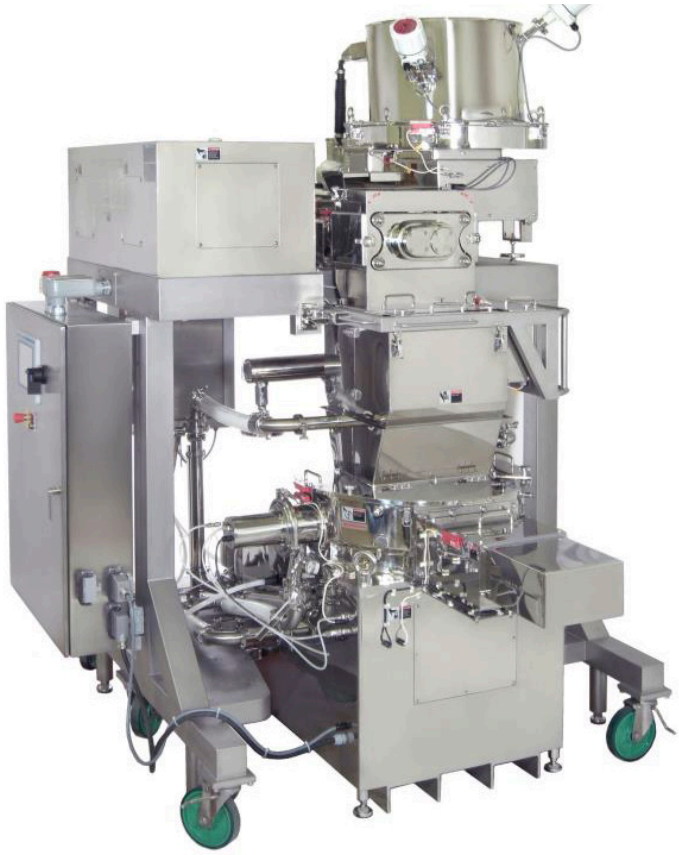
Solution

LCI designed and built a new Continuous Drug Pelleting System which fully integrated the extrusion and spheronization process to convert drug formulations into free flowing spheres of a controlled shape and size.

LCI has a test facility at its headquarters in Charlotte. A customer can send material to LCI, or LCI can send equipment to the customer for testing in their facility. Trials were performed at the client's facility with the laboratory equipment to optimize extrusion-spheronization parameters. Multiple trials with the client's material were also performed at LCI and the equipment manufacturer's facility (Fuji Paudal in Osaka, Japan) for the development of this new system.

A wet granulation batch is prepared in a high shear granulator and loaded into the hopper of the LCI Circle Feeder. The feeder continuously meters the wet granulation into the LCI Extruder forming cylindrical extrudates. The extrudates break off by their own weight and are collected in LCI's special discharging system. The wet extrudates are then charged to the LCI Spheronizer where they are converted into well-rounded spheres, which are subsequently dried/coated.

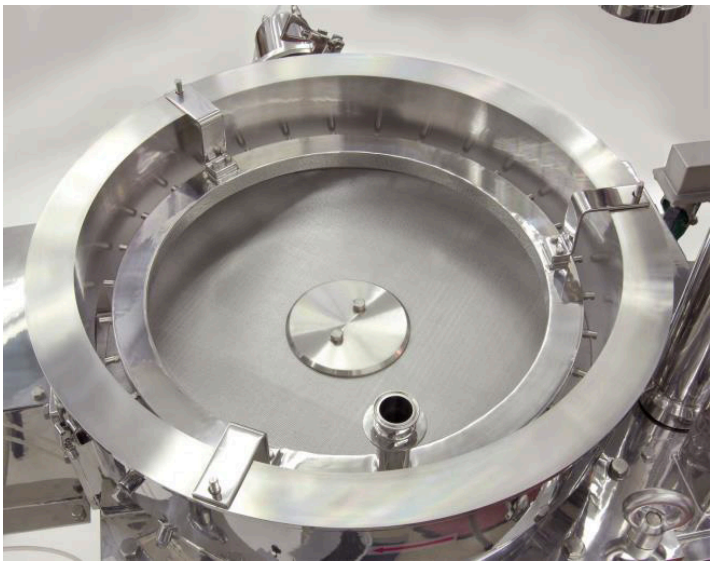
The Continuous Drug Pelleting System is a compact design and fit perfectly within the client's existing GMP suite. The high shear granulation suite was directly above the ES suite. A discharge chute through the floor with a transition hopper fitted to Circle Feeder hopper allowed for the flexibility of manually charging batches or fully automating feed all the way back to the high shear granulation.



LCI's NEW Continuous Drug Pelleting System which included patented GMP Circle Feeder Model CS-600, Radial Xtruder™ Model EXDS-100G, Discharge Device Model CD-30, Spheronizer Model QJ-700TG, and Wash-in-place (WIP) system.

In the new system, the spheronizer was equipped with wash-in-place (WIP) plate cleaning device. Since all pharmaceutical formulations differ in their dissolution characteristics, it was important to develop a flexible plate cleaning system. Using material sent by the client, LCI developed a wash-in-place (WIP) plate cleaning system that consists of

a water spray followed by an air purge to dry the plate and side walls. A vacuum system is utilized during this process to remove excess product and water. The parameters of the water and air flow rate and volume can be varied in this patent-pending WIP system to clean the plate for any pharmaceutical formulation. The WIP system for this application



Wash-in-place (WIP) spheronizer plate cleaning system consisting of water and air purges.

is utilized between every spheronization batch to clean the plate.

The CDP system was designed such that all system components are easily accessible for cleaning and maintenance. The Circle Feeder and Discharge Device swing aside; the Circle Feeder is a clamshell design such that hinged feed hopper is easily lifted for access. The Spheronizer is equipped with a plate lifting device to aid in the removal of the plate for complete cleaning. These features decreased the amount of time required for cleaning and maintenance.

The Continuous Drug Pelleting System was fully integrated and supplied with an Allen Bradley HMI (touch screen operator interface) and PLC. LCI's control system, XT-CDP, can be supplied as CFR 21, Part 11 compliant.
The CDP system can be supplied with LCI's patented Twin Dome Granulator™ or Radial Xtruder™

Results

Integration of the new LCI Continuous Drug Pelleting has greatly improved the quality of pellets by addressing several key issues.

- Reduced level of operator intervention and variability.
- Higher production throughput due to continuous processing.
- The extrudates produced are more consistent due to continuous and regulated feed by the Circle Feeder.
- The unique and patent-pending spheronizer Wash-In-Place system allows for plate cleaning after every batch. Utilizing a clean plate provides a better and more consistent particle size distribution.
- The client is able to improve their overall yield.
- The amount of time required for cleaning and maintenance is reduced.
- Greater safety with fully contained process

Discharge device swung aside and Circle Feeder swung aside and feed hopper open.