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Ibuprofen ASD Production Using Fluidized Bed Coating

Introduction

Fluidized bed technologies are widely used to produce amorphous solid dispersions due to their improved coating abilities. Amorphous solid dispersions are desirable on account of their ability to improve the bioavailability and dissolution rate of poor water-soluble drugs.

API Selection

This project proposes the use of Ibuprofen as an API as it demonstrates poor water solubility and would benefit from an increase in bioavailability. Additionally, there is no energy required to break the crystal lattice as ibuprofen is in its amorphous state.

Desired Product

300 kg is the desired product load. This mass includes the microcrystalline particles, and the film however it is assumed that the mass of the film coat is negligible.

Design Objectives

Design a fluidized bed coating process to produce improved amorphous solid dispersion layering on inert microcrystalline cellulose particles.

Design objectives include the preliminary discussion on the following concepts:

1. Production cost evaluation for the chosen fluidized bed reactor technology
2. Design the scale-up of a fluidized bed reactor based on current market analysis
3. Consideration of equipment design including spray nozzle placement and pump sizing
4. Appropriate polymer selection for improved bioavailability

Design Process

What is an ASD?

Amorphous solid dispersions are mixtures that improve the bioavailability of poor water-soluble drugs, providing better dispersity due to the unsaturated drug state.[1]

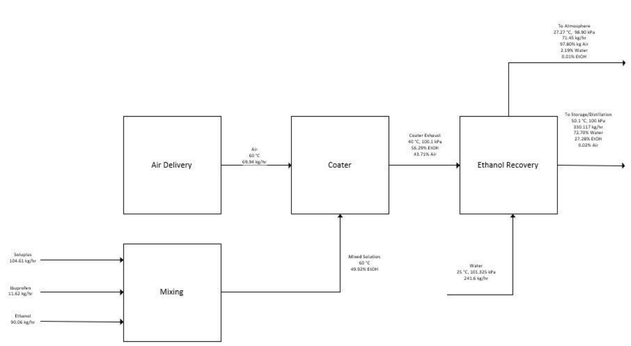
Production Methods

Spray drying and hot-melt extrusion remain the two most common amorphous solid dispersion production methods.[1] For this project, an intensified fluidized bed coating process was chosen. The process revolves around the simultaneous coating and drying of particles by spraying a polymer/solvent/API solution into the fluidized bed.

Production Challenges

ASD production using fluidized bed coating requires the use of a solvent, which requires proper filtration and consideration of add-on safety features as solvents are often flammable. Organic solvents can be difficult to evaporate completely and remove from the final product, making solvent selection a crucial production consideration.

Block Flow Diagram



Design Overview

1 Atomization Air

Air with 100% humidity enters the heating and drying system.

The air is at ambient conditions (i.e. 20 °C and 1 atm).

The heater/dryer is operating at 60 °C and moisture is removed until the air has 35% humidity.

2 Coating Solution Configuration

The coating solution consists of ethanol, IBU, and Soluplus®. Ethanol is 60% saturated with a mixture of 90% Soluplus® and 10% IBU by mass. The total amount of coating solution required for this process is 362 litres.

3 Particle Coating

The inert microcrystalline particles are fluidized in the Wurster column, the particles enter the spray zone and are covered with the coating solution.

After the particles have been sprayed with the coating solution, they enter the fountain region where the particle is dried and the ethanol is evaporated.

The coated particle falls through the down bed region, towards the horizontal transport region, and the particle repeats the cycle until a desired film thickness has been developed.

4 Ethanol Recycle

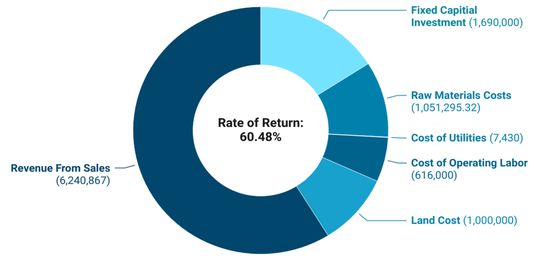
Evaporated ethanol is cooled and then recaptured using gas-liquid adsorption.

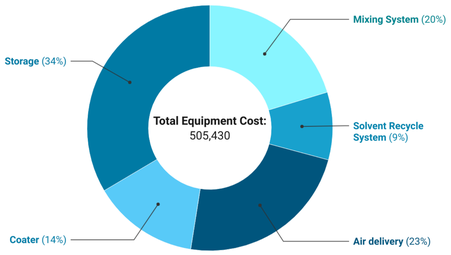
The EtOH/air mixture is cooled to 40 °C and enters the adsorption column.

The EtOH is adsorbed using process water and reduces the concentration of gaseous ethanol to the odor threshold of 100 ppm.

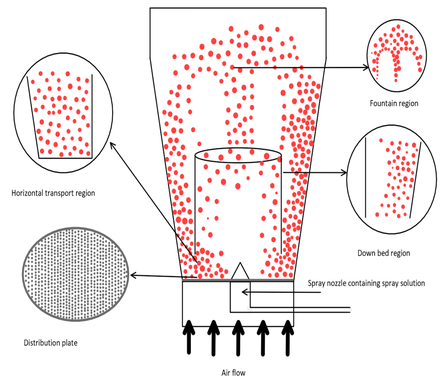
The Water-EtOH stream is then stored until enough has been collected for an extractive distillation to dehydrate the ethanol again.

Economic Summary





Fluid Flow Regions



There are three different flow regions present inside the fluidized bed reactor; the fountain region is located at the top of the Wurster column and is where particle drying occurs. The particles enter the down bed region, where they are fully dried before entering the horizontal transport region, which brings the particles back to the spray zone.[2]

Acknowledgments & References

[1]Bhujbal, S. V., Mitra, B., Jain, U., Gong, Y., Agrawal, A., Karki, S., Taylor, L. S., Kumar, S., & (Tony) Zhou, Q. (2021). Pharmaceutical amorphous solid dispersion: A review of manufacturing strategies. *Acta Pharmaceutica Sinica B*, *11*(8), 2505–2536. https://doi.org/10.1016/j.apsb.2021.05.014

[2]Li, L., Remmelgas, J., Wachem, B. G. M. van, Corswant, C. von, Folestad, S., Johansson, M., & Rasmuson, A. (2016). Effect of Drag Models on Residence Time Distributions of Particles in a Wurster Fluidized Bed: A DEM-CFD Study. *KONA Powder and Particle Journal*, *33*, 264–277. https://doi.org/10.14356/kona.2016008