



An Interactive Software Tool for the Design of Pharmaceutical Products and Processes

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Background

1. Pharmaceutical process engineering is an important topic for current Chemical Engineering curriculum.
2. Design and development of the full-chain process require extensive and tedious calculations, which tend to stifle creative thinking of students.
3. A teaching tool with the proper GUI and engineering contents is needed.
4. In two years time, Kelvin Fung and 4 UG graduate students had developed a software tool, called ProWare. It can simulate the unit operations of “powder processing” in a pharmaceutical process.

Objectives

To design an interactive software tool to enhance teaching quality and raise students' interests on the design of pharmaceutical products and processes.

To modify the ProWare software by adding more unit operations of reactions, separations and purifications and final dosage form.

This talk will focus on the current development of ProWare and how it will help teaching and learning of the development of pharmaceutical process engineering.

A Generic Pharmaceutical Process

Raw Materials



Reaction Systems

Multiphase reactions, biochemical reactions,
asymmetric synthesis



Separation and Purification

Extraction, decantation, crystallization
&

Downstream Processing

Filtration, washing, deliquoring, drying



Bulk Solid Processing

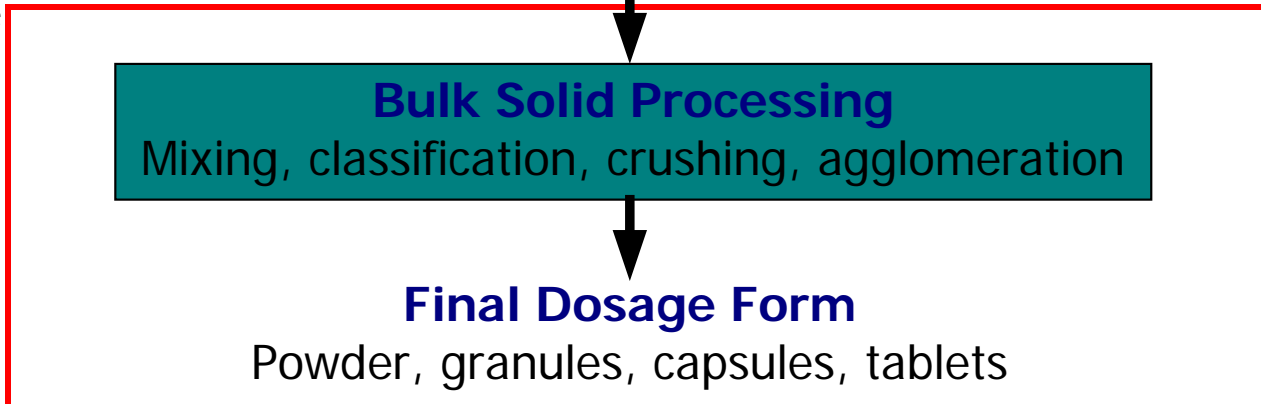
Mixing, classification, crushing, agglomeration



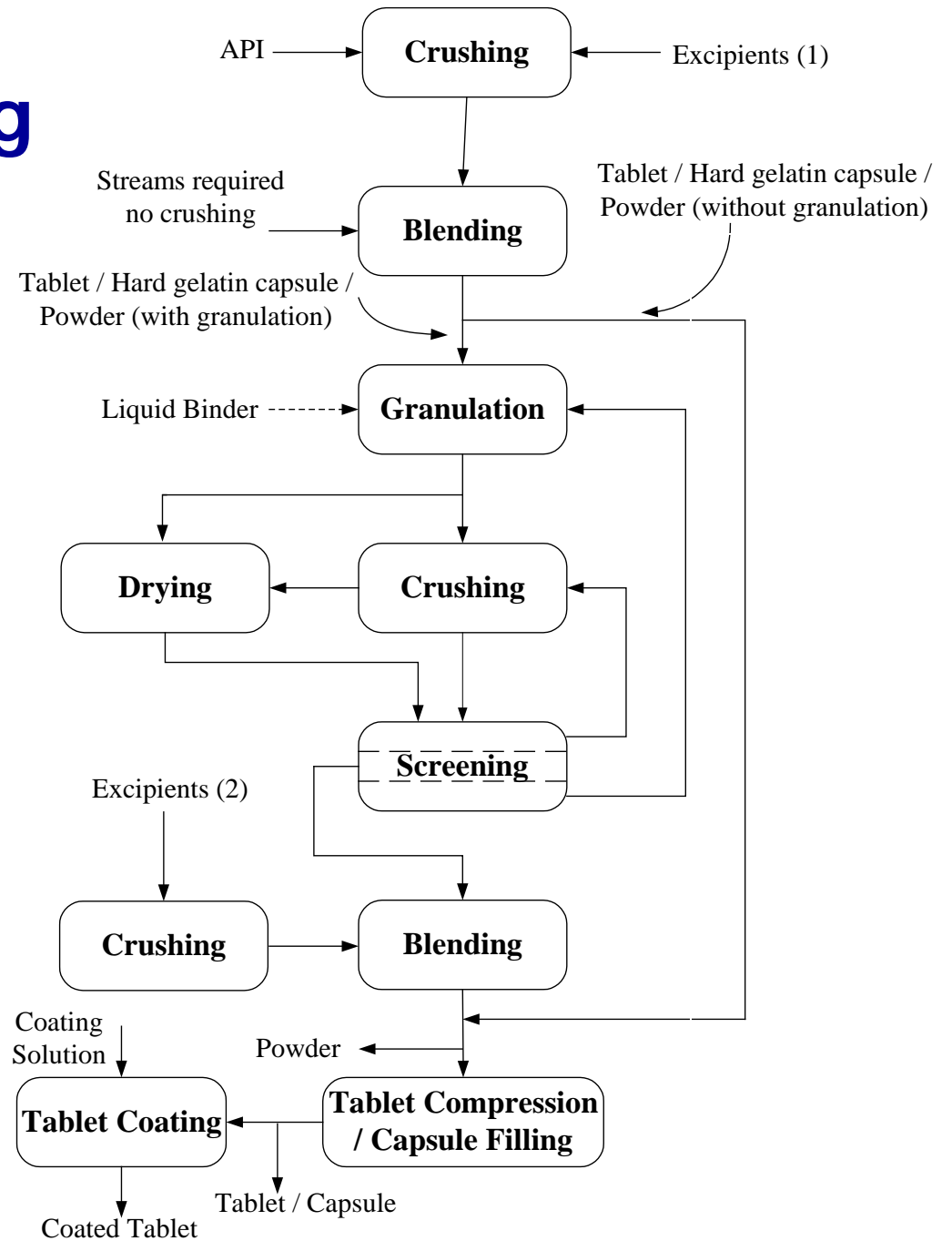
Final Dosage Form

Powder, granules, capsules, tablets

ProWare



Powder Processing



ProWare

Functions and interfaces:

1. API and other excipients input format;
2. Flowsheet generation;
3. Process flow diagram;
4. Particle size distribution calculation; and
5. Data storage

Input Information

Items shown in BLUE are the minimum required information.

Product | API | Diluents | Binder | Disintegrant | Lubricant

Dosage Form Selection

Tablet Powder
 Capsule Granule

Product Specification

Production rate: tab/hr

Tablet specifications

Mass: mg/tab

Diameter: 6 12 mm

Final Particle Size: 1 10 μm

Tensile Strength: 0.1 1 MPa

Porosity: 0.01 0.25

Disintegration time: 1 60 < mins

Dgne

Selection of API and Excipients

Input Information

Items shown in BLUE are the minimum required information.

Product	API	Diluents	Binder	Disintegrant	Lubricant
API Specification					
Active Pharmaceutical Ingredient (API):	Ascorbic Acid				
Mass per dosage:	g				
Mean particle size:	200 μm				
Standard deviation on particle size distribution:	2.1				
API Physical Properties					
Melting point:	464	K			
Water solubility:	30	g/100mL			
Crystal form:	monoclinic				
Taste:	sharp acidic taste				
Bulk density:	530	kg/m ³			
Hamaker constant:	4.5E-20	J			
Yield strength:	3	MPa			
Angle of internal friction:	40	degrees			
Angle of wall friction:	23	degrees			

Done

Flowsheet Generation – Crushers and Granulator

Flowsheet Generation

Streams that require crusher:

API Diluents Binder Disintegrant Lubricant None

Disintegrant adds to

Crusher 1 and Blender 1 Crusher 2 and Blender 2

Crusher System 1

Number of Crushers: 1

API → 1st Crusher

Diluents → 1st Crusher

Binder → 1st Crusher

Crusher System 2

Number of Crushers: 1

Lubricant → 1st Crusher

Heuristics

Done

Flowsheet Generation

Granulation required: Yes

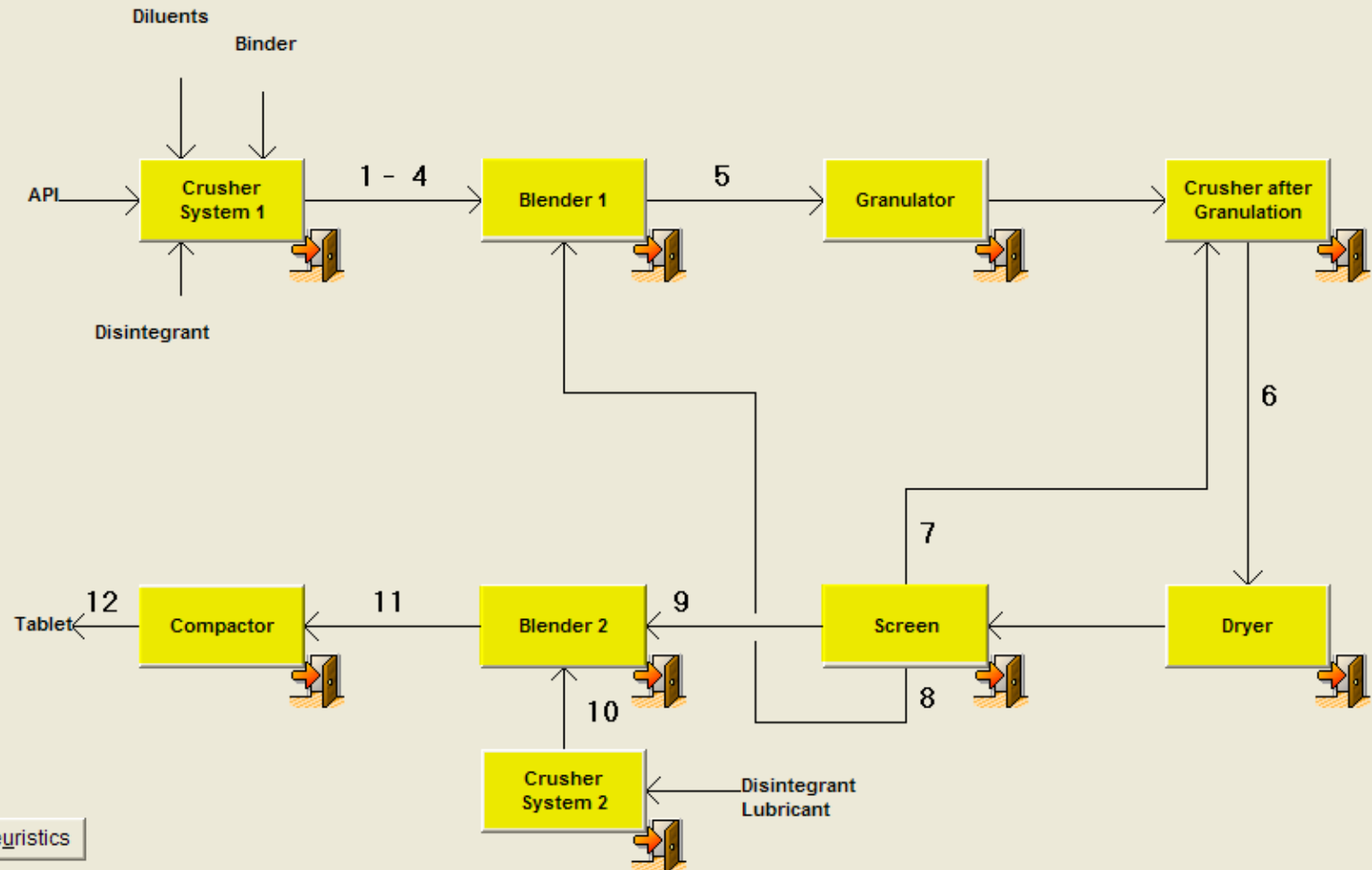
Crusher required after granulation: Yes

Granulation type: Wet granulation

Heuristics

Done

Process Flow Diagram



Heuristics

Done

Unit Operations

Crusher System 1 **Pharmaceutical Dosage Form Program - [Compactor]**

File Input Result Window Help

1st Crusher

Component

Power:

So: 0.01

q: 0.5

truch: 1

Granulator

Granulato

Breakage

Agglomer

Granulatio

Granulato

Maximum

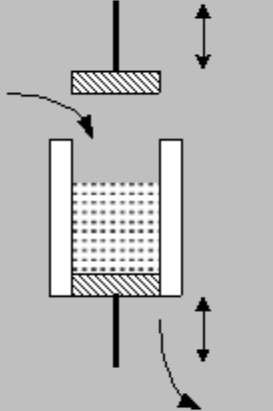
Compaaction Specification

Rotary Tablet Press

Number of stations per press:

Compression pressure: kPa

Power: kW



Done

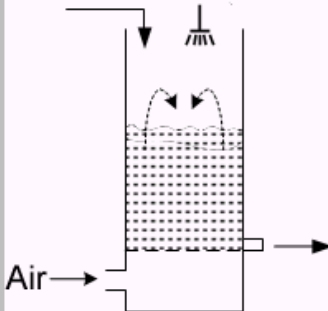
Granulator selection

Pan granulator

Fluidized-bed granulator

High shear mixer granulator

Roller compactor



Air →

Screen selection:

Vibrating screen

Rotary screen

Fixed grizzly

Air classifier

Cyclone

10 80

0.3

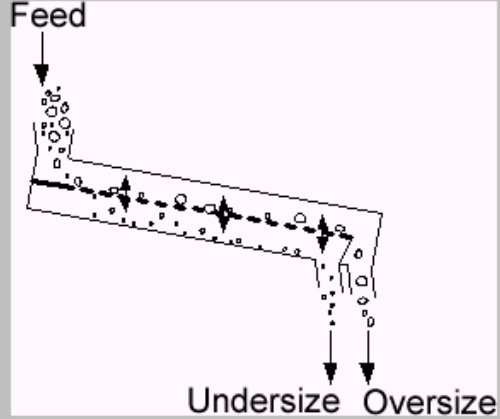
100 600 mm

100 70 mm

kW

²m

Feed



Undersize Oversize

Done

Particle Size Distribution

Pharmaceutical Dosage Form Program - [Particle Size Distributions]

File Input Result Window Help

Pharmaceutical Dosage Form Program - [Equipment Sizing]

File Input Result Window Help

Equipment Sizing

Production size kg/ hr Safety

Please click the following items to show the information you wanted.

- Crusher System 1
- Blender 1
- Granulator**
- Dryer
- Crusher after Granulation
- Oversize Crusher
- Screen
- Crusher System 2
- Blender 2
- Compactor

Granulator

Granulator Type : Fluidized-bed granulator

Granulation Time : min

Required Power : kW

Required Capacity : m³

Particle Size Disturbution Feed Input Equipment Input Suggestion Exit

5:50 AM

Further Development

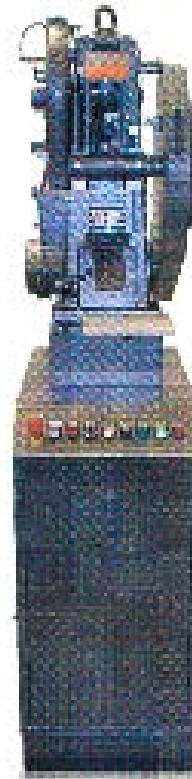
- 1. To modify the existing GUI of ProWare on bulk solids processing and dosage form design**
- 2. To be more user-friendly**
- 3. To simulate the whole pharmaceutical process by adding unit operations of reactions, separations and purifications**
e.g., reactors, crystallizers, extractors, chromatographic columns, distillation columns, etc.

Bulk Solids Processing and Dosage Forms

Obtain empirical relations between the equipment operating parameters and particle size distribution from experimental results.



Granules



Tablets



Unit Operations

Reaction/
Crystallization



Supercritical
Fluid Extraction



SFChromat

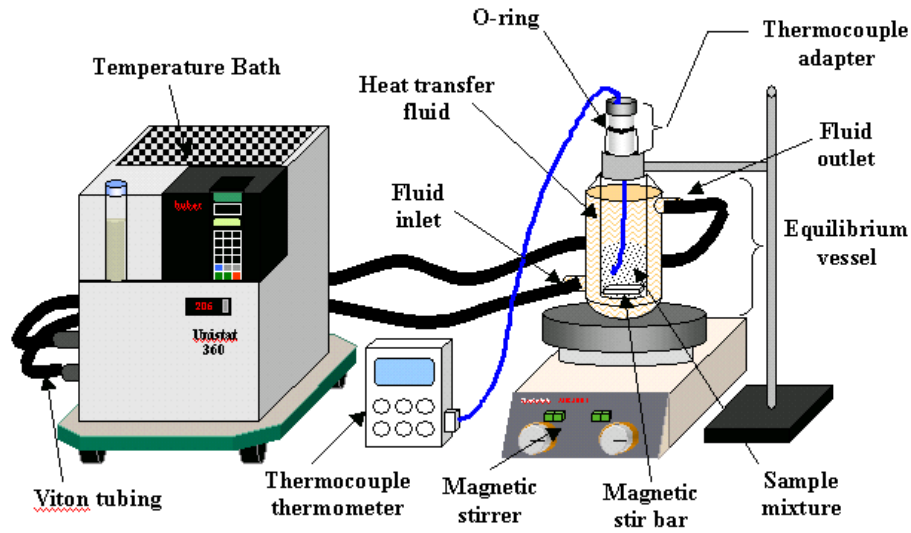


Granulation

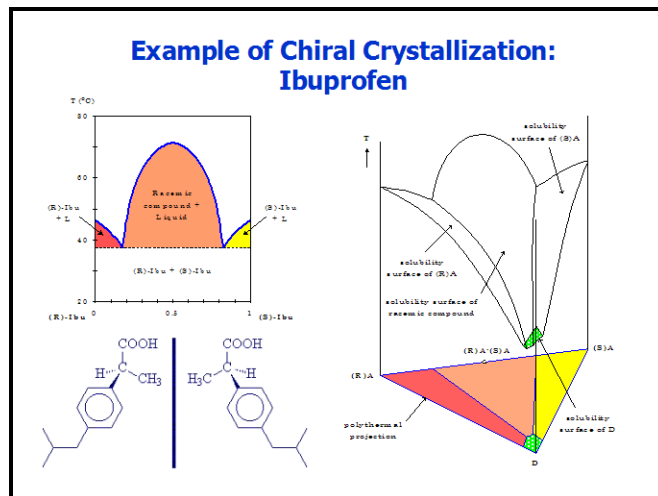


Basic Thermodynamics - Phase Diagram

Solid Liquid Equilibrium



Liquid Liquid Equilibrium



Acknowledgements

- 1. We would like to thank the CLI and UGC for supporting the further development of the software.**
- 2. We would like to thank Y. C. Cheng, H. K. Lee, K. F. Tsang, S. K. Tsang and Kelvin K. Y. Fung on the development of ProWare.**