INTERNATIONAL COLLEGE OF PHARMACEUTICAL INNOVATION

国际创新药学院

From Drug to Tablet

Course BSc (Pharm) or BSc (ATT)

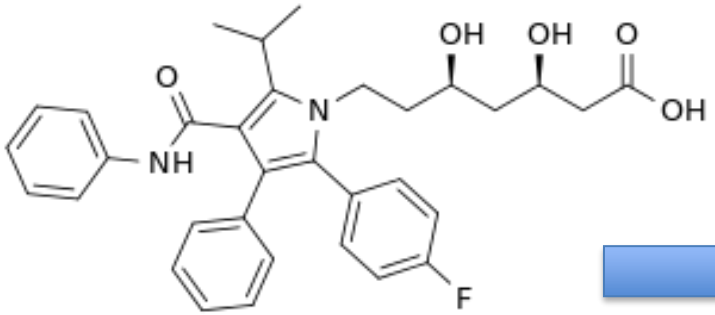
Year 2024-2025 II

Module Medicines: Pharmaceutics 1 (MP1)

Lecturer Dr. Shi Du

Learning Outcomes

1. Describe the common types of oral solid dosage forms used in pharmacy
2. Outline the advantages and disadvantages of using oral solid dosage forms
3. Describe the stages of dosage form design and how these stages relate to oral solid dosage forms
4. List the preformulation characterisation steps that are important for oral solid dosage forms
5. List the major processes involved in the manufacture of oral solid dosage forms



Atorvastatin

RCSI

Oral Solid Dosage Forms: What types are available?

- Tablets
  - A solid dosage form containing active pharmaceutical ingredient(s) (API(s)) with suitable excipients
  - Obtained by compressing uniform volumes of particles
  - Immediate release (IR)
  - Modified release (MR)

- Capsules
  - A solid oral dosage form consisting of a shell and a filling
  - Shell-> Composed of a single sealed enclosure or two halves that fit together and sometimes sealed with a band
  - Filled with solid, semi-solid or liquid ingredients
  - Immediate release (IR)
  - Modified release (MR)

- Powders and granules
  - Mixtures of finely divided solids containing API(s) with suitable excipients
  - Bulk and divided powders
  - Normally dissolved before oral administration
  - Powders important for tablet and capsule manufacture

RCSI

Oral Solid Dosage Forms: What types are available?

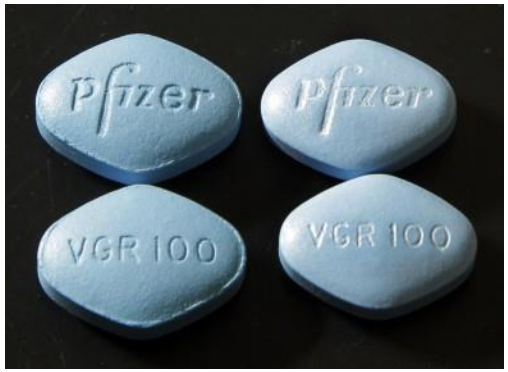
Tablets	Capsules	Powders & Granules
IR tablets	Hard capsules	Bulk powders
MR tablets	Soft capsules	Divided powders
Dispersible	MR capsules	Effervescent powders
Effervescent		Granules
Orodispersible		
Chewable		
Lozenges		

Focus of this lecture series: Tablets

RCSI

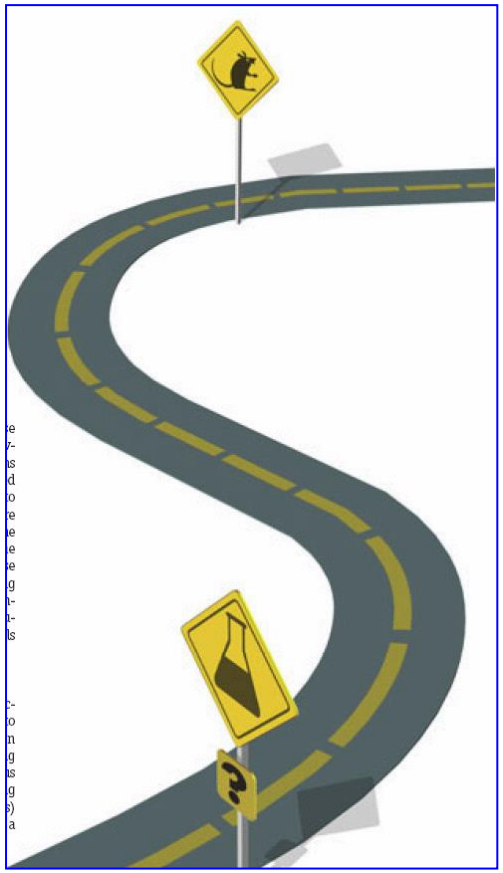
Oral Solid Dosage Forms: Advantages and Disadvantages

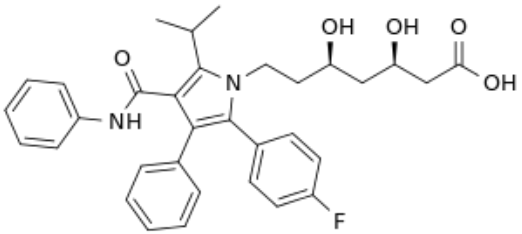
Advantages	Disadvantages
Ease of self-administration	Larger tablets difficult to swallow (>500mg)
Portable	Less flexibility in dosing
Easy to mask organoleptic drug properties	Unsuitable for certain patient groups
High accuracy of dosage	Unsuitable for certain disease states
Physical, chemical & microbiological stability	Oral route unsuitable for certain drug molecules
Potential for modified delivery	
Cheap production with high throughput	
Potential for brand image	



RCSI

Oral Solid Dosage Forms: Types of Dosage Forms





✓ Drug Compound (Discovery Phase)

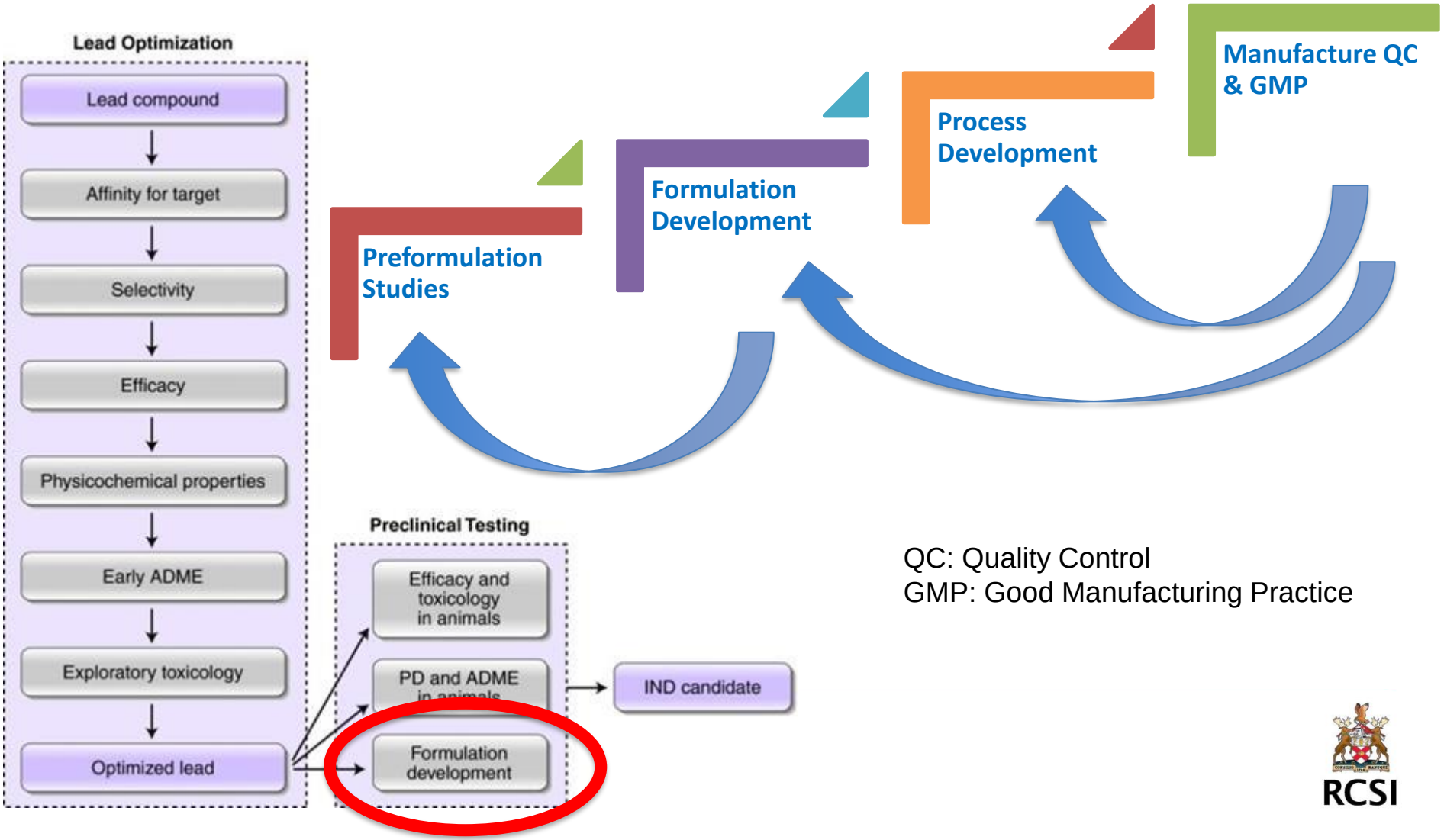
✓ Pharmaceutical Development

Medicinal product (patient-end user)

EXCIPIENTS

RCSI

From Drug to Tablet: Dosage Product Development



QC: Quality Control
GMP: Good Manufacturing Practice

RCSI

Preformulation

- Concept
  - Preformulation seeks to determine the ***fundamental*** physical and chemical properties of a drug molecule in addition to the ***derived*** properties of the drug powder
  - This information dictates the following steps for formulation and scale-up manufacture

- Importance of preformulation studies
  - Allows selection of correct dosage form of the drug for development of an optimal drug product
  - Allows rational selection of formulation ingredients
  - Scientific understanding of formulation and process parameters-> Excipient selection, processes required
  - Improve pharmaceutical manufacturing output and quality-> Avoid future formulation problems
  - Regulatory requirement

- Preformulation and the drug development process
  - Normally performed on several drug candidates
  - The final formulation can even not be fully determined when clinical trials begin

RCSI

Preformulation & Oral Solid Dosage Forms: Relevance

Table 24.2 Preformulation drug characterization

Test	Method/function/ characterization
1 Spectroscopy	Simple UV assay
2 Solubility	Phase solubility, purity
aqueous	Intrinsic solubility, pH effects
pK_a	Solubility control, salt formation
salts	Solubility, hygroscopicity, stability
solvents	Vehicles, extraction
partition coeff K_w^o	Lipophilicity, structure activity
dissolution	Biopharmaceutics
3 Melting point	DSC – polymorphism, hydrates, solvates
4 Assay development	UV, TLC, HPLC
5 Stability (in solution and solid state)	Thermal, hydrolysis, oxidation, photolysis, metal ions, pH
6 Microscopy	Morphology, particle size
7 Powder flow	Tablet and capsule formulation
bulk density	
angle of repose	
8 Compression properties	Excipient choice
9 Excipient compatibility	Excipient choice

Table 24.3 Analytical preformulation

Attribute	Test
Identity	Nuclear magnetic resonance (NMR) Infrared spectroscopy (IR) Ultraviolet spectroscopy (UV) Thin-layer chromatography (TLC) Differential scanning calorimetry (DSC) Optical rotation, where applicable
Purity	Moisture (water and solvents) Inorganic elements Heavy metals Organic impurities Differential scanning calorimetry (DSC)
Assay	Titration Ultraviolet spectroscopy (UV) High-performance liquid chromatography (HPLC)
Quality	Appearance Odour Solution colour pH of slurry (saturated solution) Melting point

N.B. Solid state properties for Solid Dosage Forms

RCSI

Formulation Development

- Concept
  - Formulation focuses on excipient selection, the recipe formulae and the method of formulation
- Same analytical techniques used from preformulation
  - Formulation-> Larger quantities of API and excipients
  - Solid dosage forms-> Increased focus on material properties and mass transfer properties
- Preformulation and formulation interplay
  - Data from preformulation guides formulation steps
  - Feedback from formulation steps can reveal new data and outcomes that can improve preformulation
  - Two stages used in determination of lead formulation and progression to process development

Table 24.16 Suggested primary candidates as excipients for tablet and capsule formulations

Excipient	Function*
Lactose monohydrate	F
Dicalcium phosphate dihydrate	F
Dicalcium phosphate anhydrous	F
Microcrystalline cellulose	F
Maize starch	D
Modified starch	D
Polyvinylpyrrolidone	B
Sodium starch glycollate	D
Sodium croscarmellose	D
Magnesium stearate	L
Colloidal silica	G

* B, binder; D, disintegrant; F, filler/diluent; G, glidant; L, lubricant.

RCSI

Process Development for Oral Solid Dosage Forms

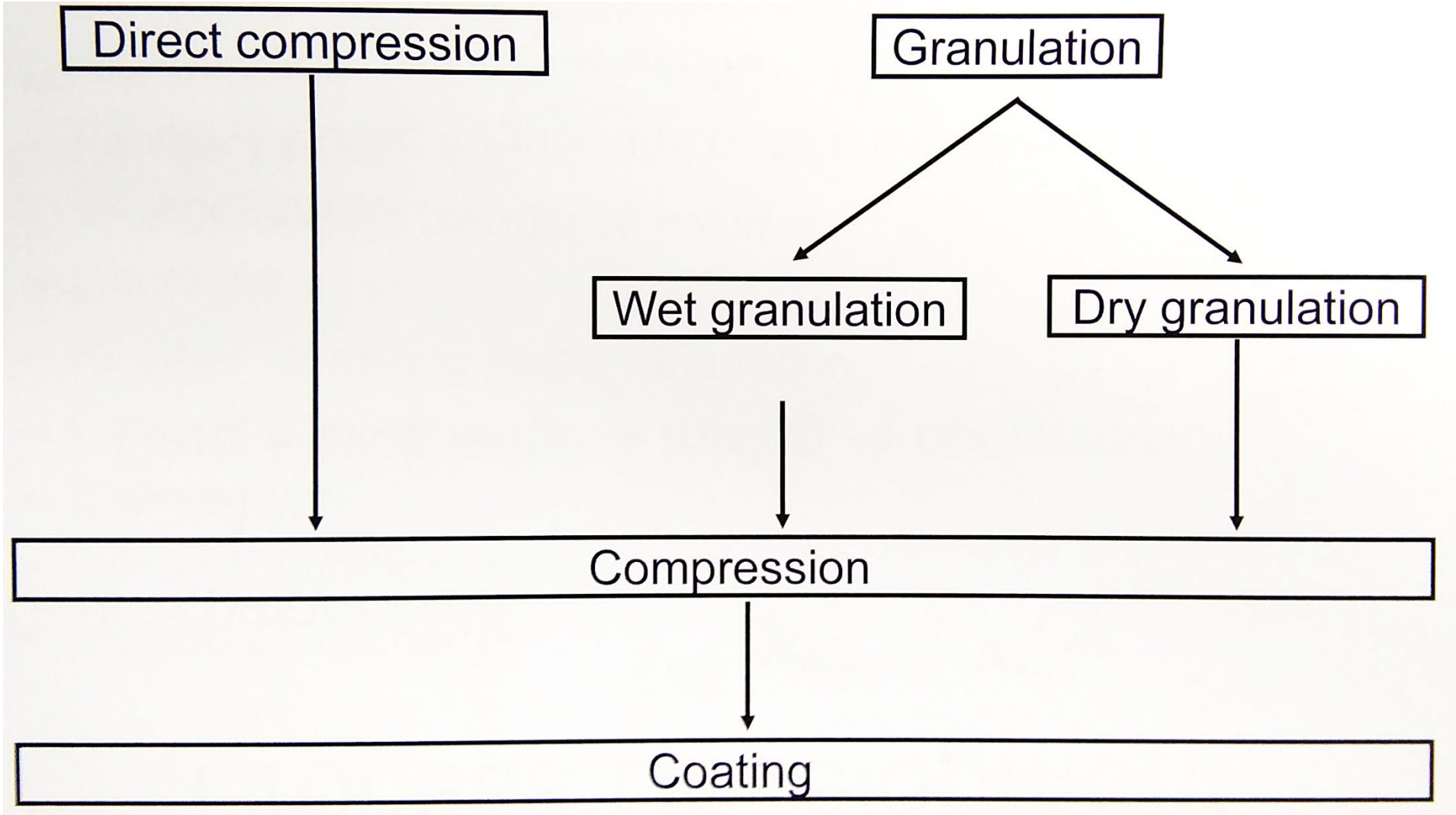
- Concept
  - The major objective at this stage is to scale up the manufacture process
  - Cost-effective-> High throughput
  - Maintenance of standards for solid dosage forms-> Quality, safety, efficacy

- Examples of manufacturing processes
  - Particle size reduction
  - Mixing
  - Granulation
  - Drying
  - Tabletting-> Compaction

- The success of this stage hinges upon good formulation!
  - The formulation is the single most important factor in determining the tabletting behaviour
  - Adequate flow properties are essential for large-scale manufacture and accurate tablet production
  - Material properties must be sufficient for compression into tablets-> Function of mechanical properties of the component powders and the interactions between them

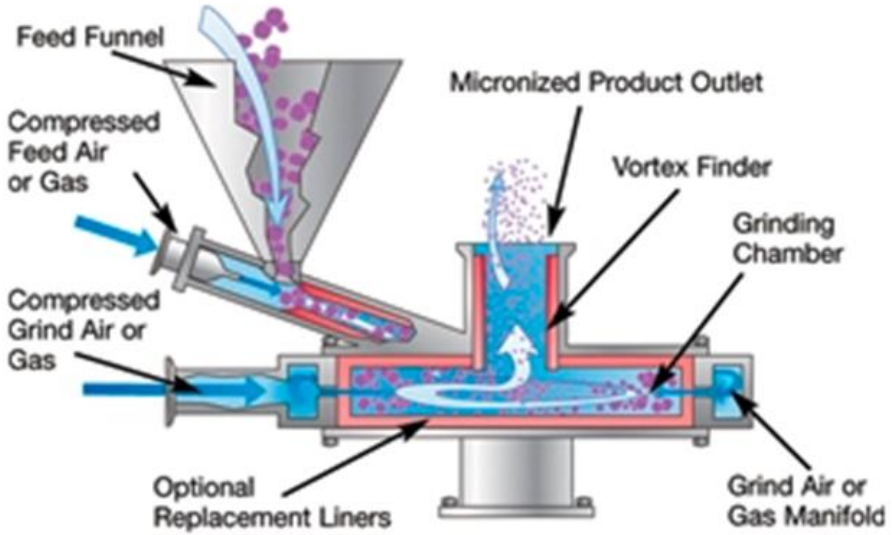
RCSI

Process Development: Tabletting



RCSI

Process Development



Particle Size Reduction

Tumbling Mixer

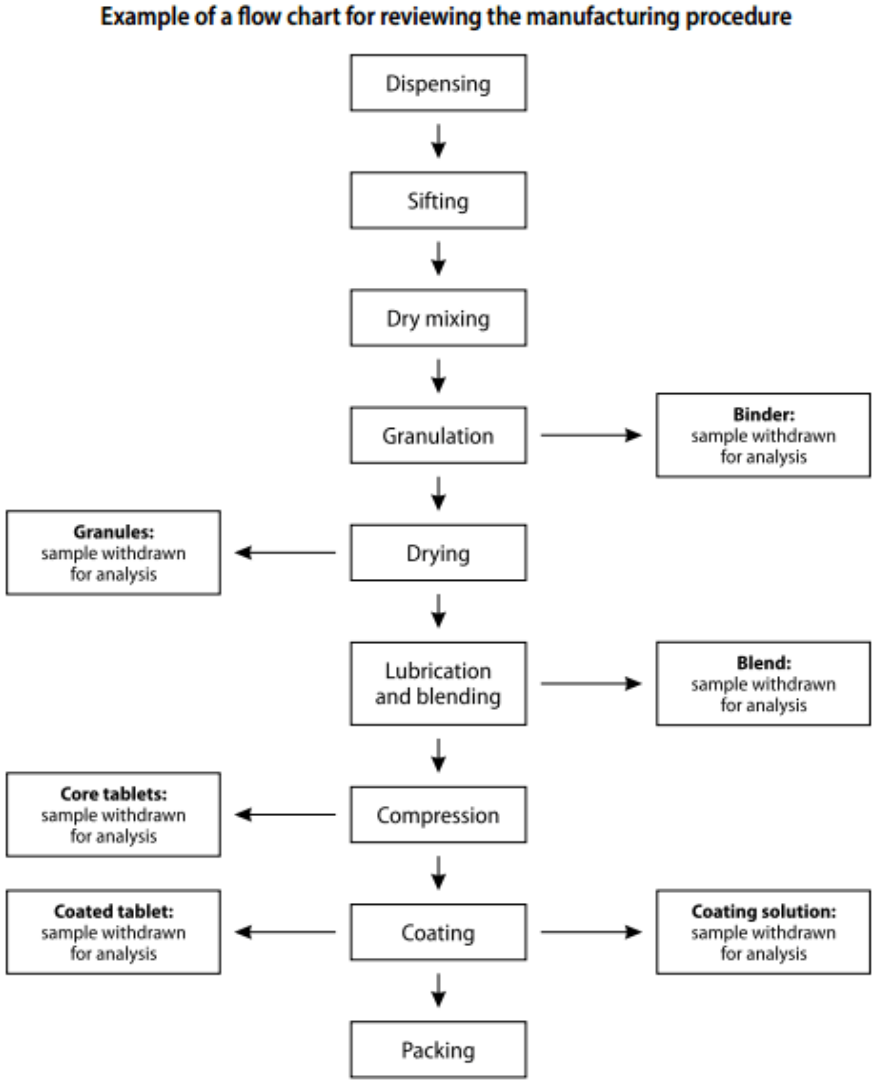
Fluidised Bed Dryer

Rotary Tablet Press

RCSI

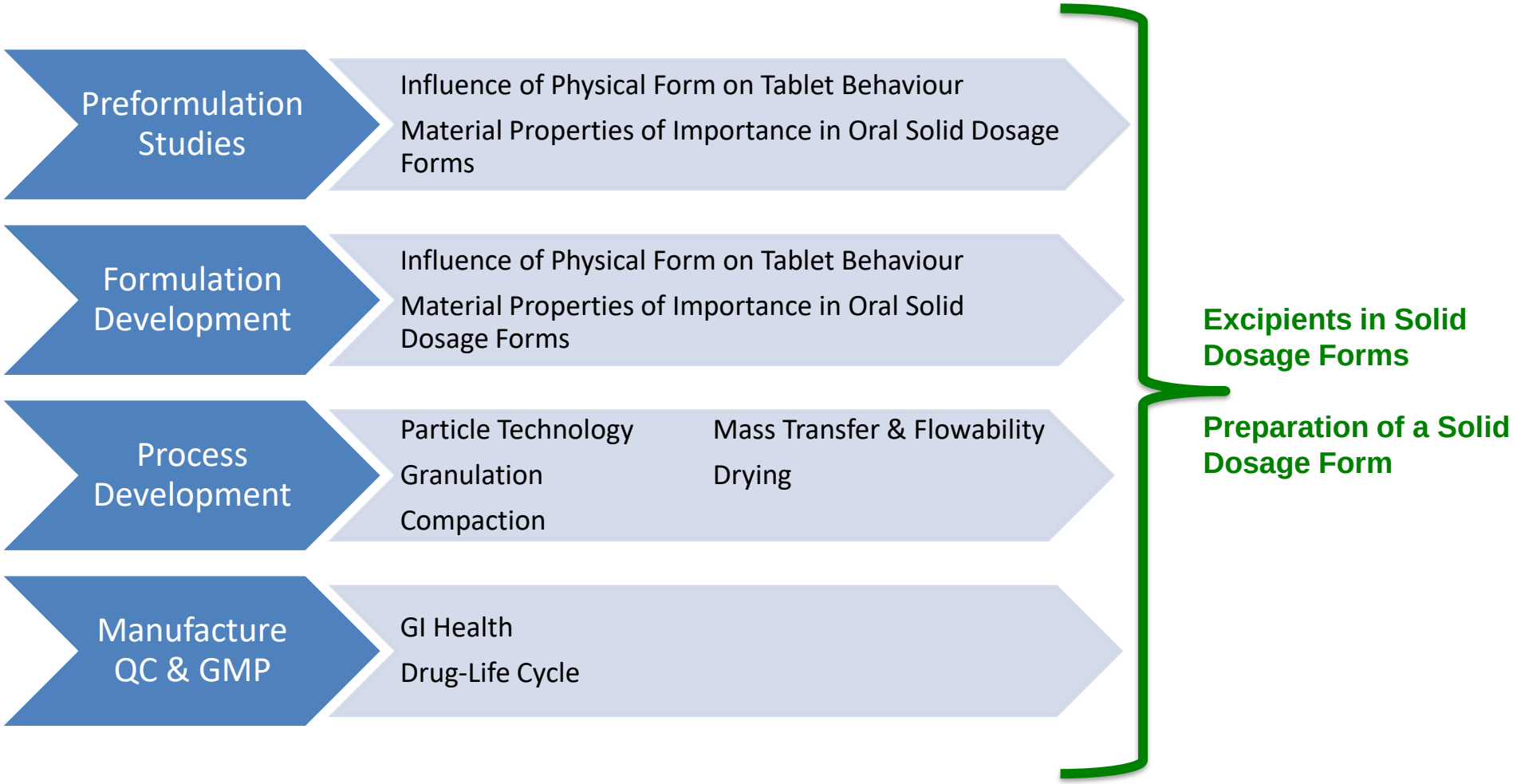
Manufacture Monitoring: Quality Control (QC)

- QC of tablets
  - Absorption-> Disintegration, dissolution
  - Uniformity-> Mass, content
  - Strength-> Friability, hardness
- In-process QC testing
  - Sampling at defined intervals in manufacture process
  - Important to build into process design (N.B. Scale-up)
- Process analytical technology (PAT)
  - A system for designing, analysing and controlling manufacture processes
  - Measurement of critical process parameters which affect critical quality attributes
  - Continuous “real-time” quality assurance
  - Integrate QC into the design of the process rather than solely batch testing the final products at the end of manufacture (“quality by design”)
  - “Analytical”-> Includes chemical, physical, microbiological, mathematical and risk analyses



RCSI

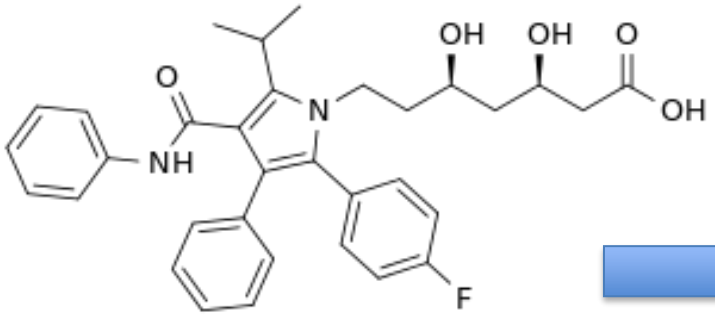
From Drug to Tablet: Blueprint for PCP2 Lecture Series



RCSI

Learning Outcomes

1. Describe the common types of oral solid dosage forms used in pharmacy
2. Outline the advantages and disadvantages of using oral solid dosage forms
3. Describe the stages of dosage form design and how these stages relate to oral solid dosage forms
4. List the preformulation characterisation steps that are important for oral solid dosage forms
5. List the major processes involved in the manufacture of oral solid dosage forms



Atorvastatin

RCSI

Reading Reference

- Oral solid dosage form overview
  - Pharmaceutical Codex: Oral Solids
  - Ansel's Pharmaceutical Dosage Forms: Powders and Granules

- Preformulation
  - Aulton's Pharmaceutics: Pharmaceutical Preformulation

RCSI

CONTACT INFORMATION

Shi Du

Associate Professor

International College of Pharmaceutical Innovation

Soochow University

Room 707, International Innovation Center

Jiuyong East Rd #1, Wujiang District, Suzhou, China

T: +86-15952400997

E: dushi@suda.edu.cn

RCSI