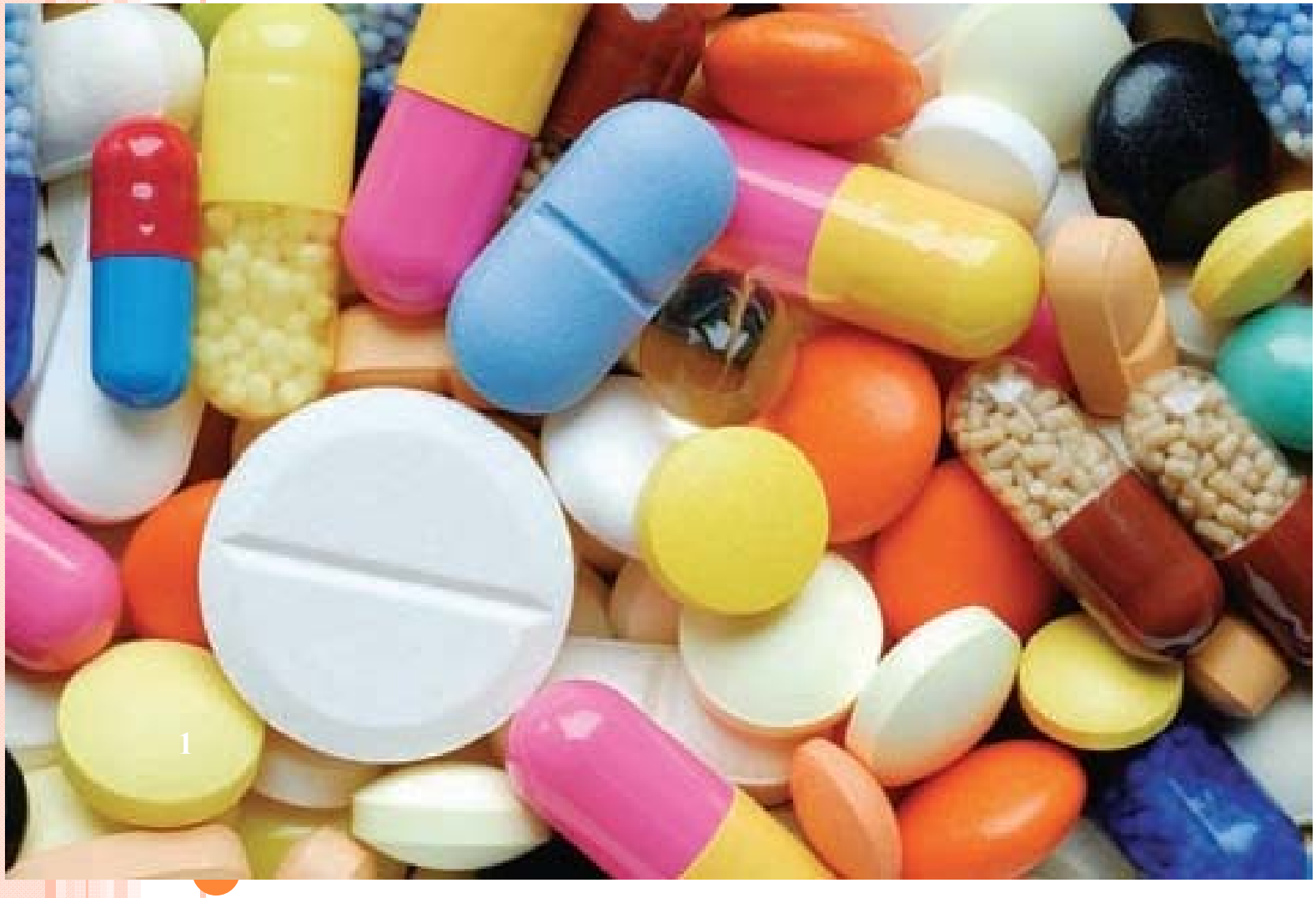
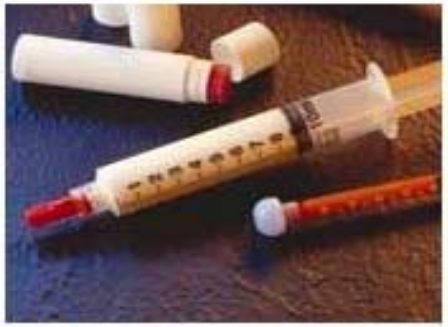
Pharmaceutics الصيدلانيات



PRINCIPLES OF DOSAGE FORMS DESIGN

بعض الأشكال الصيدلانية



Tablets

Hard capsules

Toothpastes

Coated tablets

Oral strips

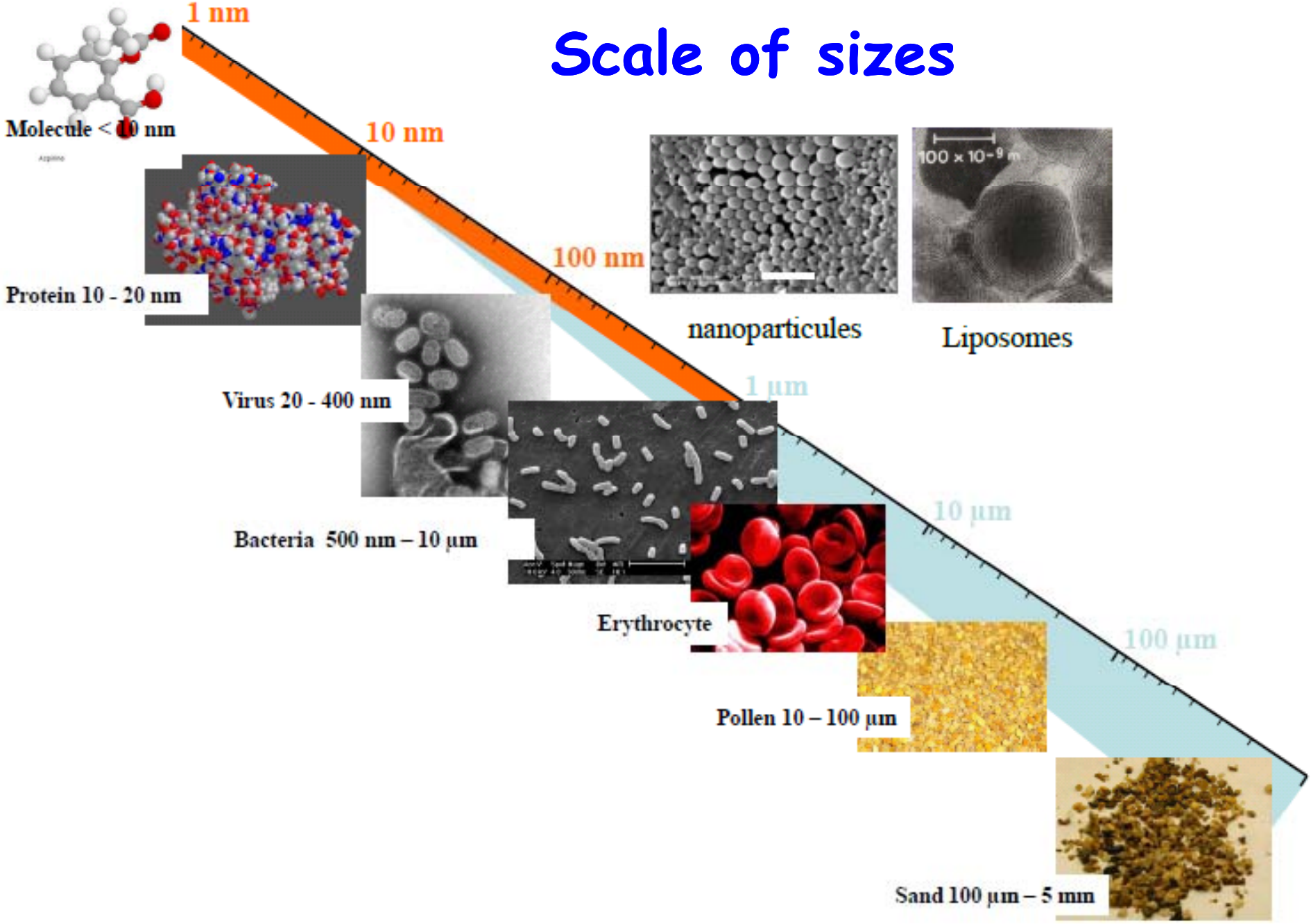
Pharmaceutical confectionery

Lyophylised tablets

Granules

Syrups

Scale of sizes



Pharmaceutics:

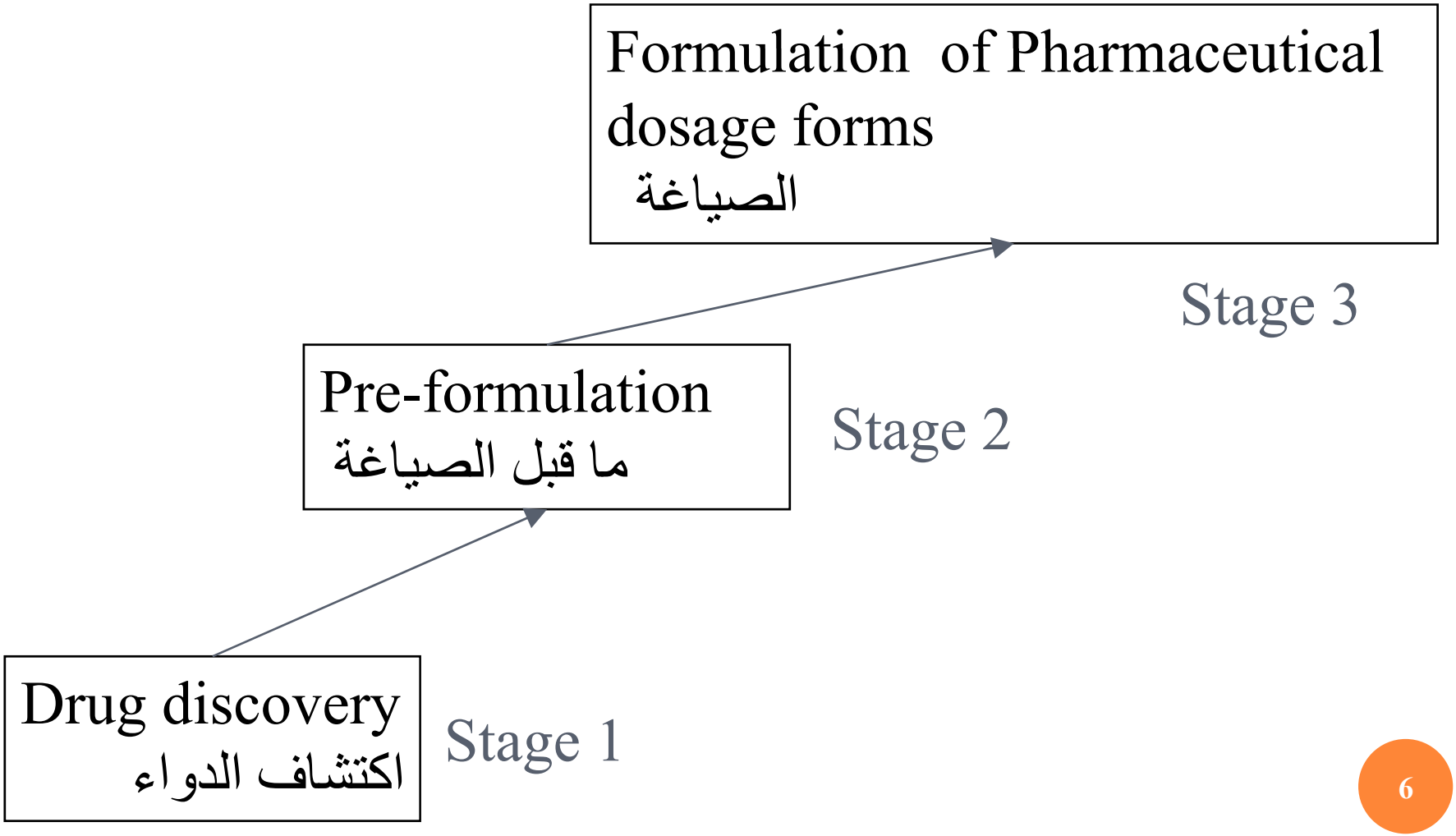
is the general area of study concerned with the formulation, manufacture, stability, and effectiveness of pharmaceutical dosage forms.

الصيدلانيات: دراسة صياغة، تصنيع، ثباتيّة و فعالية الأشكال الصيدلانية.

Drug : a natural or synthetic chemical substance intended for use in the diagnosis, treatment, or prevention of disease in man or other animals.

الدواء: مادة طبيعية أو صنعية معدّة للاستخدام في التشخيص، العلاج أو الوقاية من المرض عند ألإنسان أو بهدف استخدامها عند الحيوانات

Introduction: Pharmaceutical Dosage Form development



DRUG'S LIFE STAGES FROM DISCOVERY TO MARKET LAUNCHING

مراحل تطور الدواء من الاكتشاف حتى بدء التسويق

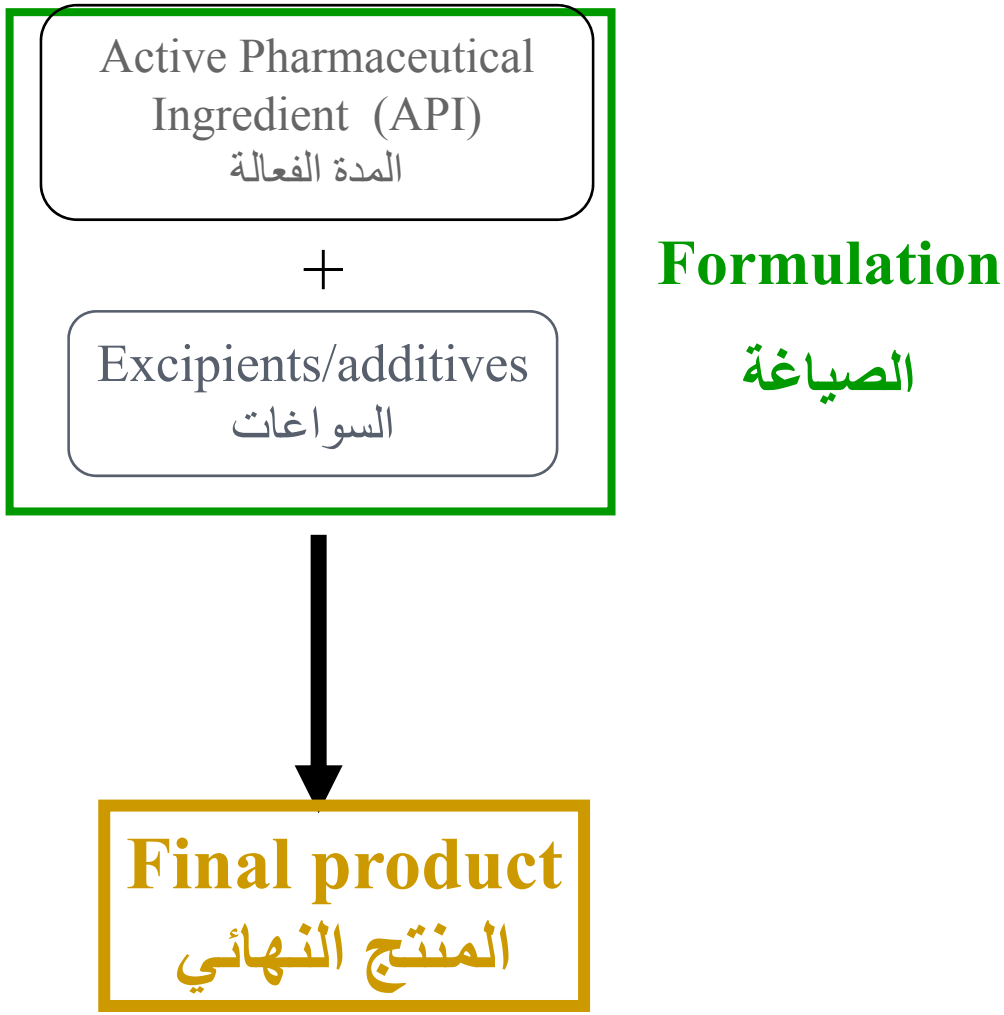
6.5 years 7 years 1.5 years

Preclinical studies دراسات قَبْلَ سَّريرِيّة	**Clinical trials** تَجْارُب سَريرِيَّة	**FDA review** مُراجَعَة	**Post-market studies**
Starts when a new chemical entity NCE is obtained from: Chemical synthesis Isolation from natural sources This stage include the study of: • Physicochemical properties (pre-formulation) • Pharmacology and toxicology studies They are carried out on animals	**Consists of three phases:** **Phase 1:** test the drug candidate in a small group of healthy human volunteers to ensure it is safe **Phase 2:** test the drug candidate in a small group of patients for evidence of efficacy and determination of dose, in parallel with longer term nonclinical safety testing in animals. **Phase 3:** define the marketable dosage form of the drug candidate or "drug product" and test the potential drug product in a large group of patients for evidence of safety and efficacy.		

- **Pharmaceutical formulation involves the rational design and manufacture of dosage forms to ensure that the required biological and physical performances of the therapeutic agent are attained. The formulation scientist is therefore expected to have knowledge of several scientific disciplines, including physical pharmaceutics, pharmaceutical chemistry and biopharmaceutics.**
- **الصياغة الصيدلانية تشتمل على تصميم وصناعة شكل صيدلاني يضمن بلوغ التأثير الحيوي و الثباتية الفيزيائية للدواء، لذا ينبغي للصيدلاني أن يمتلك معرفة في عدة علوم كالفيزياء، الصيدلانيات، الكيمياء الصيدلانية، الصيدلة الحيوية.**

Pharmaceutical Dosage Form: Drug + ?

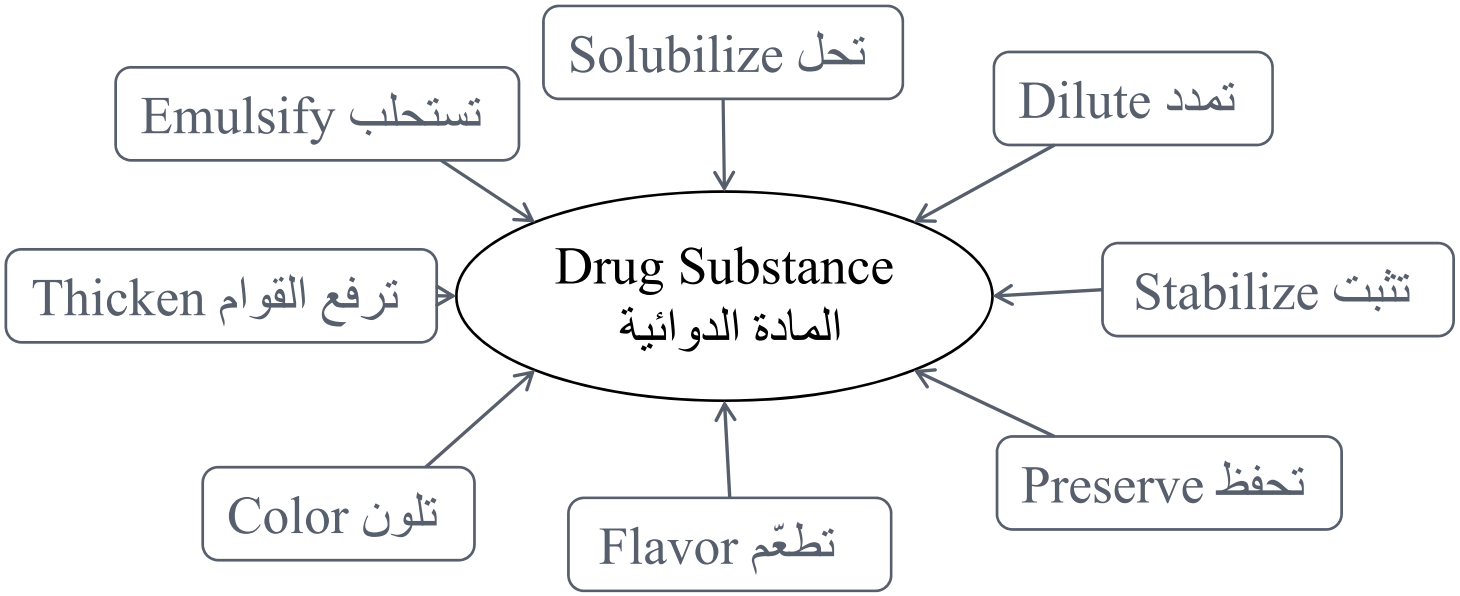
الشكل الصيدلاني: دواء + سواغات



Formulation

الصياغة

THE PHARMACEUTICAL INGREDIENTS (EXCIPEINTS) MAY:



The drug and pharmaceutical materials (excipients) must be compatible with one another to produce a drug product that is stable, efficacious, attractive, easy to administer, and safe.

الدواء و السواغات يجب أن يكونوا متوافقين مع بعضهم لإعطاء منتج دوائي ثابت، فعال، مقبول و ملائم لطريق الإعطاء، و آمن.

WHY DO WE NEED DOSAGE FORMS?
لماذا نحتاج الشكل الصيدلاني؟

1. To provide a mechanism for safe and convenient delivery of accurate dosage, especially for potent drugs (drugs with low dosage;e.g. Ethinyl estradiol)

لتقديم آلية لتحرير آمن و ملائم من أجل جرعات دقيقة و خاصة للأدوية الفعالة بجرعات صغيرة

٢ To conceal the bitter, salty, or offensive taste or odor of a drug substance (capsules, coated tablets, flavored syrups)

لإخفاء الطعم أو الرائحة للمادة الدوائية

WHY DO WE NEED DOSAGE FORMS?

٣ To protect the drug substance from the destructive influences of atmospheric oxygen or humidity (coated tablets, sealed ampules)

تحمي الدواء من تأثير العوامل المخربة المحيطة كالأكسجين و الرطوبة

٤ To protect the drug substance from the destructive influence of gastric acid after oral administration (enteric-coated tablets)

تحمي الدواء من تأثير العوامل المخربة كالحموضة المعدية بعد الإعطاء الفموي

٥ To provide for optimal drug action through inhalation therapy (inhalants and inhalation aerosols)

تقديم تأثير مثالي من خلال استخدام الضبوبات الاستنشاقية

٦ To provide liquid preparations of substances that are either insoluble or unstable in the desired vehicle (suspensions)

لتحضير مستحضرات سائلة لمواد قد تكون غير محلولة أو غير ثابتة في المحل المرغوب مثل تحضير المعلقات

٧ To provide clear liquid dosage forms of substances (syrups, solutions)

لتحضير أشكال صيدلانية كمحاليل رائقة

٨ To provide rate-controlled drug action (various controlled-release tablets, capsules, and suspensions)

لتأمين تأثير للدواء مضبوط

٩ To provide optimal drug action from topical administration sites (ointments, creams, transdermal patches, and ophthalmic, ear, and nasal preparations)

لتقديم تأثير مثالي للأدوية عند مواقع الإعطاء الموضعي.

١٠ To provide for placement of drugs directly in the bloodstream or body tissues (injections)

تطبيق الدواء مباشرة في الدوران أو أنسجة الجسم.

DOSAGE FORMS AVAILABLE FOR ROUTS OF ADMINISTRATION الأشكال الصيدلانية المتوفرة وفقاً لطرق الإعطاء

Administration route طرق الإعطاء	Dosage forms الشكل الصيدلاني
Oral فموي	Solutions, suspensions, emulsions, gels, powders, granules, capsules, tablets
Rectal مستقيمي	Suppositories, ointments, creams, powders, solutions
Topical موضعي	Ointments, creams, pastes, lotions, gels, topical aerosols
Parenteral Injections حقني	Solution, suspension, emulsions, implants
Respiratory تنفسي	Aerosols inhalations, sprays, gases
Nasal أنفي	Solutions, inhalations
Eye عيني	Solutions, ointments, creams
Ear أذني	Solutions, suspensions, ointments, creams

ROUTES OF ADMINISTRATION طرق إعطاء الأدوية

TERM	SITE
Oral فموي	Mouth
Peroral عبر الفم	Gastrointestinal tract via mouth
Sublingual تحت اللسان	Under the tongue
Parenteral حقني	Other than the gastrointestinal tract (by injection)
Intravenous حقن الوريد	Vein
Intraarterial حقن شرياني	Artery

TERM	SITE
Intracutaneous, Intradermal في الأدمة	Skin
Subcutaneous تحت الجلد	Beneath the skin
Intramuscular حقن عضلي	Muscle
Ocular عيني	Eye عين
Intrarespiratory عبر جهاز التنفس	Lung رئة
Rectal مُسْتَقيمِيّ	Rectum مستقيم
Vaginal مهبلي	Vagina مهبل

Pharmaceutical dosage forms and percentage of manufacturing

الأشكال الصيدلانية والنسبة المئوية لصناعتها

Dosage Form	%
Tablets مضغوطات	٤٦
Oral liquids محاليل فموية	١٦
Capsules محافظ	١٥
Injections أشكال حقنية	١٣
suppositories تحاميل	٣
Topical preparations مستحضرات موضعية	٣
مستحضرات عينية Ophthalmic preparations	٢
Aerosols ضبوبات	١
others	١

The International Pharmaceutical Excipients Council (IPEC) have defined a pharmaceutical excipient as:
any substance other than the active drug or prodrug which has been appropriately evaluated for safety and is included in a drug delivery system to either:
1. aid processing of the system during manufacture, or
2. protect, support or enhance stability, bioavailability or patient acceptability, or
3. assist in product identification, or
4. enhance any other attribute of the overall safety and effectiveness of the drug product during storage or use.

Sources of information for excipients and packaging materials.

Source	Information	Comments
Various pharmacopoeias, e.g., United States/National Formulary; British, European, Japanese, Pharmacopoeias; Martindale, The Extra Pharmacopoeia; The Merck Index; The British Pharmaceutical Codex	Include standards and monographs for drugs, excipients, containers/closures and medical devices	Updated regularly; many available in book format or CD-ROM; can be obtained through various publishers including Interpharm
FDA Inactive Ingredient Guide	Lists excipients used in FDA-approved drug products marketed for human use by route of administration and dosage form	Published by FDA, Division of Drug Resources (DDIR); available through FDA Web site; updated regularly
Handbook of Pharmaceutical Excipients	Excipient monographs containing data on uses, properties, safety, excipient interactions, standards; also a supplier's directory	A joint publication of the American Pharmaceutical Society and the Royal Pharmaceutical Society of Great Britain

Handbook of Pharmaceutical Additives	Excipients used in prescription and OTC products approved by the FDA or recommended by USP/NF, BP and Ph.Eur.; details manufacturers, composition, properties, function and applications, toxicology and regulatory status of additives	Compiled by M. and I. Ash; Published by Gower, Aldershot, UK, and Vermont, USA
Japanese Pharmaceutical Excipients Directory	Monographs on excipients used in pharmaceutical and cosmetic products	Edited by the Japan Pharmaceutical Excipients Council; available through Interpharm
Le Dictionnaire VIDAL	A codex of French approved medicines includes quantitative composition of many products	
ABPI Compendium of Data Sheets and Summaries of Product Characteristics	Data sheets prepared by pharmaceutical companies on prescription and OTC products, including quantitative details of formulation ingredients and packaging used	Published annually by Datapharm Publications Ltd., London
Physicians' Desk Reference	Compendium of FDA approved pharmaceutical products; details formulation, pack, administration and use; identification guide	Published by Medical Economics Co., N.J., USA, in participation with individual manufacturers; also PDRs for ophthalmology and non-prescription drugs; CD-ROM or hard copy

OTHER CONSIDERATIONS
بعض الاعتبارات

- Some other features are required to **ensure dosage form quality**, include :

بعض الميزات المطلوبة لضمان نوعية الشكل الصيدلاني

1. chemical and physical **stability** **الثباتية الفيزيائية و الكيميائية**
2. suitable **preservation** against microbial contamination حفظ مناسب ضد التلوث الميكروبي
3. **uniformity of dose** of drug تجانس جرعة الدواء
4. **acceptability** to users including both prescriber and patient القبول من كِلا الطبيب و المريض
5. suitable **packaging and labeling** تعبئة و عنونة الأدوية واللصاقات

Classification of substances according to Solubility (in Pharmacopoeias)
تصنيف المواد وفقاً لانحلاليتها في الدساتير

Description	Approximate weight solvent (g) necessary to dissolve 1 g of solute
Very soluble شديد الانحلال	< 1
Freely soluble سهل الانحلال	Between 1 and 10
Soluble منحل	Between 10 and 30
Sparingly soluble معتدل الانحلال	Between 30 and 100
Slightly soluble قليل الانحلال	Between 100 and 1000
Very slightly soluble قليل الانحلال جداً	Between 1000 and 10 000
Practically insoluble غير منحل	> 10 000

Table 1 Properties of Nonparenteral Routes of Administration with Respect to Systemic Delivery als

Route	Surface area and accessibility[a]	Physical barrier properties[a]	Enzymatic barrier properties[a]
Oral	>200 m^2 fairly accessible, site-specific location difficult	Thick mucus layer, columnar epithelial monolayer (10 μm), pH variations	+++++ (and hepatic first pass metabolism)
Oromucosal	~0.02 m^2 easily accessible	Mucus, stratified, partly keratinized epithelium (500–600 μm), hydrated	+++
Nasal	~0.015 m^2 fairly accessible	Mucus, ciliated, columnar pseudostratified epithelium (10 μm)	+++
Pulmonary	~80–140 m^2 not easily accessible	Bronchi and bronchioles: mucus, ciliated columnar pseudostratified epithelium (10–60 μm) Alveoli: squamous epithelial monolayer (<1μm)	++
Cutaneous	~1.8 m^2 easily accessible	Keratinized stratified epithelium (100–200 μm)	+

[a]Relative properties ranged at a level of + to +++++.
Source: Merged from Refs. 5–7.

التصنيف الأطفال وفقاً للعمر

Table 1 Classification by Age of the Pediatric Population

Age group	FDA classification	ICH classification
Intrauterine	Conception to birth	
Preterm newborn infants		<37 wk of gestational age
Neonate or term newborn infant	Birth to 1 mo	0–27 day
Infant and toddlers	1 mo–2 yr	28 day–23 mo
Children	2 yr to onset of puberty	2–11 yr
Adolescent	Onset of puberty to adult	12–16 or 18 yr (depending on regions)

ICH: International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use

أهم الوحدات الدولية للقياس

Table 1.4 Basic units in the SI system of measurement

Base quantity	Unit	Symbol
Length	metre	m
Mass	kilogram	kg
Time	second	s
Electric current	ampere	A
Thermodynamic temperature	kelvin	K
Luminous intensity	candela	cd
Amount of substance	mole	mol

الطب المثلي

- الطب المثلي: القانون الأساسي للطب المثلي هو قانون المتماثلات . نبات الكينا المعروف علمياً باسم Cinchona officinalisوهو النبات الذي كان يستعمل لعلاج الملاريا استخدمه احد العلماء Dr. Samuel Hahnemannو جربه على نفسه، حيث بدأ يتناول جرعات يومية من منقوع هذا النبات. ولاحظ أن جسمه ظهرت عليه أعراض مشابهة لأعراض الملاريا. وفقاً لقانون المتماثلات الذي ينص على أنه من أجل أن يشفى الجسم من مرض، فمن الضروري إعطائه مادة من شأنها أن تتسبب في حدوث نفس أعراض هذا المرض لو أعطيت لجسم سليم.
- **Homeopathy** مُعالَجَةٌ مِثْلِيَّةis a form of alternative medicine in which practitioners treat patients using highly diluted preparations that are believed to cause healthy people to exhibit symptoms that are similar to those exhibited by the patient.

معالَجَةٌ إِخْلافِيَّة (إحداث حالة لدى العليل تُضادُّ المرض

- **Allopathy** معالَجَةٌ إِخْلافِيَّة**:** The system of medical practice which treats disease by the use of remedies which produce effects different from those produced by the disease under treatment.

نظام المعالجة الطبية التي تعالج الأمراض باستخدام أدوية تعطي تأثيرات مختلفة عن تلك الناتجة عن المرض قيد المعالجة.

- **Allopathic medicine** refers to the practice of conventional medicine that uses pharmacologically active agents or physical interventions to treat or suppress symptoms or pathophysiologic processes of diseases or conditions.
- و هو ممارسة الطب التقليدي الذي يستخدم العوامل الفعالة دوائياً أو تداخلات فيزيائية لمعالجة أو كبت الأعراض أو العمليات الفيزيولوجية المرضية للمرض أو الحالة