

Solutions

Always laugh when you can .. ♡
 it is cheap medicine 😊 ♡..
 - Lord Byron ..

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Introduction:

In physicochemical terms

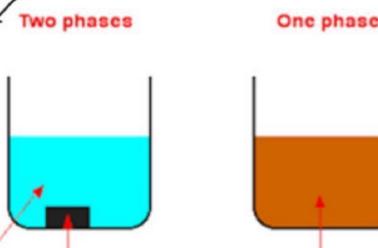
- “Solution is a one-phase system consisting of two or more components that form a homogenous molecular dispersion”

حماؤها ثابتة لا تتغير
 Density. كثافة

In pharmaceutical terms:

- solutions are “liquid preparations that contain one or more chemical substances dissolved in a suitable solvent or mixture of mutually miscible solvents”

حليما متجانسا.



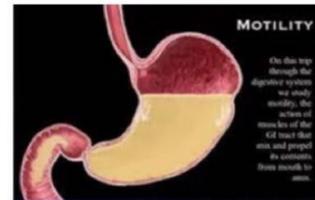
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Introduction

Advantages of solutions dosage forms:

* مزاي أشكال (Solution dosage).
التي يتحللني امضهم.

- A. Liquids are easier to swallow than solids and therefore are more acceptable for pediatric (child) and geriatric (old) use.
- B. Drug administered in the form of solution is immediately available for absorption.
- C. The drug is uniformly distributed since the solution is a homogenous system.
- D. Suitable for administration of some drugs that may irritate the stomach if localized in one area as often occurs after ingestion of a solid dosage form.



لما يكون امتصاصه يتوزع بالوحدة بشكل أسرع وبالتالي يقال التذبح ..

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على شكل سائل : مناسب للأطفال وكبار السن (سهل البلع)

الرواد الذي يدار على شكل محلول فالحق للأهتباري على الفور. لبعضها يصير مباشر (Effect أسرع)

لأنها ليطا عبارة عن محلول فالتجانس ، يتم توزيع الدواء بشكل موحد.

Introduction:

- Drug absorption from the gastrointestinal tract into the systemic circulation may be expected to occur more rapidly from solution than from suspension or solid dosage forms of the same medicinal agent.

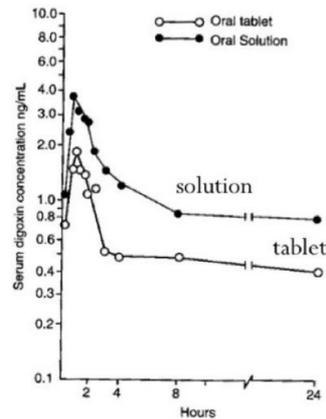


FIGURE 13.2 Serum digoxin concentrations following administration of digoxin 0.5 mg by oral tablet and elixir-like oral solution (Adapted from Huffman DH, Azarnoff DL. Absorption of orally given digoxin preparations. JAMA 1972;222:957).

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لما يكون Solution يتكون بسرعة امتصاصه أسرع من suspension حوال Solid

* حتى لو كان Same Medical agent

Disadvantages of solutions dosage forms

سليبات ال Solution dosage ←

- ✓1. Liquids are **bulky** and therefore inconvenient to transport and store.
- ✓2. The **stability** of drug in solution is often less than in solid dosage form (tablets, capsules, ..).
- ✓3. Solutions often provide suitable media for growth of microorganisms.
- ④ Dosage is usually not accurate (syringe?)
- ✓5. The **taste** of drug is usually more pronounced when in solution than when in a solid form



بناخذ حجم بالاهمة هو مثل ال Tablett + صعب نقلها وتخزينها.

رژن فيقاهما ، بزيده حركه ، لارتفاعلات .. خلا تا ابله More stability ← Solid

نماز وسما خلاش لغو البكتريا.

لان ال دوز غير بياخذ بوجه من الامثلة لو يكون في نفس الوقت حصة حقا مثل ال Tablett.

با (← (Tablett) ما بشر بياخذ ال دوا المر بياخذ ال Solution يستخدم فيه ال test Makany

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Classification

A. based on a particular pharmaceutical solution's use: oral, otic, ophthalmic, or topical solution

B. Based on their composition:

① Aqueous solutions:

- A. Syrups ← فيه Sugar . شراب
- B. Aromatic waters

② Hydroalcoholic solutions:

1. Elixirs
2. Spirits
3. Tinctures
4. Fluid Extracts
5. Collodions
6. Liniments

③ Non-aqueous solutions (e.g oily):

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Main compound water.

ماء + محلول.

No water Such Oil

Introduction

- Excipients (inactives) are frequently included to provide color, flavor, sweetness, or stability
1. Sweeteners → * مُحلّيات ..
 2. Colorants → * موادّ ملوّنة
 3. Isotonicity adjustment agents → * مثال : NaCl
 4. Viscosity enhancing agents → * آزيد اللزوجة
 5. Suspending agents → * يجتري على موادّ معلقة
 6. Antioxidants → * لأنّ في موادّ بتعمل Oxidation. → * بزيد Stability
 7. Chelating agents → * More Stability.
 8. Emulsifying agents
 9. others

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Introduction:

- the pharmacist must use information on the solubility and stability of each solute with regard to the solvent or solvent system.
- Combinations of medicinal or pharmaceutical agents that will result in chemical and/or physical interactions affecting the therapeutic quality or pharmaceutical stability of the product **must be avoided**.
- Each chemical agent has its own solubility in a given solvent.
- For many agents, their solubility's in the usual solvents are stated in the *United States Pharmacopeia— National Formulary (USP–NF)* as well as in other reference books.

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للزم آتجنب العوامل اللي

بتعمل تفاعلات غير ياريد

أو كيميائية.

بتأثر على ال Activity للدواء.

بتأثر على جودة أو
الاستقرار ..

← بلين مكتوب فيه عن ال Solubility

و ال Solubility لكل مادة في Solvent

Drugs as Solutes

- Classified as non-electrolytes and electrolytes
- Non-electrolytes** (as dextrose, sucrose, glycerin, ethanol, urea) will **not** dissociate (ionize) in solvents and the solution will not conduct electricity
- Electrolytes** will dissociate or ionize when dissolved in a solvent and these solutions will **conduct electricity**:
 - Strong electrolytes**: almost completely dissociate in a solvent (e.g. sodium hydroxide, sodium chloride, potassium chloride, sulfuric acid)
 - Weak electrolytes**: dissociate in solvents to a lesser extent (e.g. acetic acid, ammonia, and majority of drugs)

← لا يتأين ← لا يولد تيار كهربائي

← يتأين ← يولد تيار كهربائي



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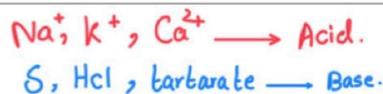
Drugs as Solutes

- Weak electrolytes subdivided into **weak acids** and **weak bases**
- A way to determine if a compound is weak acid or base is to examine the different salts the chemical has
- If the salt form is a sodium, potassium, or calcium ion, the chemical is an **acid** (e.g. sodium phenytoin, calcium carbonate, sodium phenobarbital)
- If the salt form a compound e.g. a sulfate, hydrochloride, or tartarate, the chemical is a **base** (e.g. morphine sulfate, tetracaine hydrochloride, metoprolol tartarate)

← كين برقي أكرف صفا ولا ناسه؟
* نبحص الاصلح والي بتتملكها
امانة الكيميائية.
important..

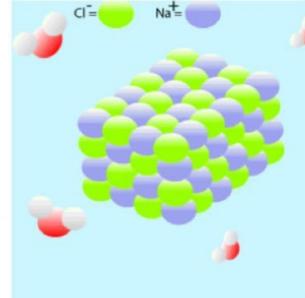


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Solubility

- When a solute dissolves → **breaking** the solute–solute forces and the solvent–solvent forces to achieve the solute–solvent attraction.
- The **solubility** of an agent in a particular solvent indicates the maximum concentration to which a solution may be prepared with that agent and that solvent.
- When a solvent at a **given temperature** has dissolved all of the solute possible, it is said to be **saturated**.
- The solubility is expressed as grams of solute dissolving in milliliters of solvent; for example, “1 g of sodium chloride dissolves in 2.8 mL of water..... at 25°C



* بونما اترعاب
 ال cm ذنفا عابا بتبرهن
 ال Solubility .. ال اجالات تدرق ..



الروابط بين ال
 $\text{H}_2\text{O} - \text{H}_2\text{O}$

بذئلك Cl^- , OH^- , Na^+ , H^+

والروابط بين ال
 ال Solvent بتزبط



شرط ان ال Solvent
 يكون قادر على كسر الروابط بين
 ال Solute

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When the exact solubility has not been determined, general expressions of relative solubility may be used. These terms are defined in the USP

حفظ

Descriptive term	PARTS OF SOLVENT REQUIRED FOR 1 PART OF SOLUTE
very soluble	less than 1
freely soluble	from 1 to 10
soluble	from 10 to 30
sparingly soluble	from 30 to 100
slightly soluble	from 100 to 1000
very slightly soluble	from 1000 to 10 000
practically insoluble	more than 10 000

للزاد ال Solvent
 ال temperature +

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Solubility

- The maximum possible concentration to which a pharmacist may prepare a solution varies greatly and depends on:

- Chemical constitution of the solute
- Chemical constitution of solvent
 - Type of solvent (hydrophilic, hydrophobic)
 - pH → ionization
 - Presence of cosolvents or solubilizing agents
- Temperature

Strong etc, weak etc
Base, Acid

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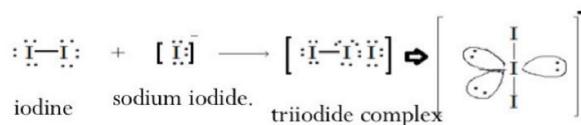
* الـهـنـق الـيـ بـقـدـر تـرـفـع فـيـهـا مـن ← Solubility →

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible:

* غـيـرت الـسـولـنـت
من Water و KI

Example 1 (Complexation): in Soluble Solute → بناتـه مـن → Soluble Substance → Soluble Complex.

- iodine granules are soluble in water only to the extent of 1 g in about 3,000 mL. Using only these two agents, the maximum concentration possible would be approximately 0.03% of iodine.
- However, through the use of an aqueous solution of potassium iodide or sodium iodide as the solvent, much larger amounts of iodine may be dissolved as the result of the formation of a water-soluble complex with the iodide salt.
- This reaction is taken advantage of, for example, in Iodine Topical Solution, USP, prepared to contain about 2% iodine and 2.4% sodium iodide.



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A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible:

- Example 1 (cont'd):

- Complexation formation: occurs when an insoluble solute reacts with a soluble substance to form a soluble complex

(e.g. the complexation of the soluble potassium iodide (KI) to the insoluble iodine molecules (I_2) to form a soluble triiodide complex (KI_3)).

inSoluble Solute (I_2)
 Soluble Substance (KI)
 Soluble complex (KI_3)
 فاعل ال
 مع
 عشان يدبلي

8mL REF 6064 NDC 59365-6064-0

EACH mL CONTAINS:
 Iodine 0.05gm,
 Potassium iodide 0.105gm.

DOSE: SINGLE USE
 DO NOT REUSE. DISCARD AFTER USE. KEEP TIGHTLY CLOSED. PROTECT FROM LIGHT. DO NOT USE IF SEAL HAS BEEN BROKEN. STORE AT CONTROLLED ROOM TEMPERATURE 15°-30°C (59°-86°F).

Manufactured for CooperSurgical
 Trumbull, CT 06611 Rev. 02/2002 CAUTION: Federal law prohibits dispensing without prescription.

LUGOL'S
 (STRONG IODINE SOLUTION USP)

CooperSurgical

LOT NO. EXP. DATE

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Concentration.

TheHealthyHomeEconomist.com

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A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Example 2: → *depend on pH.*

- Many of the important **organic medicinal agents** are either weak acids or weak bases, and their solubility depends to a large measure on the pH of the solvent.
- For instance, **the weak bases**, including many of the alkaloids (atropine, codeine, and morphine), antihistamine (diphenhydramine and promethazine), local anesthetics (cocaine, procaine, and tetracaine), and other important drugs, are not very water soluble, but they are soluble in dilute solutions of **acids**

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* *Weak Acid* بتذوب أكثر في الوسط القاعدي ،
* *Weak base* بتذوب أكثر في الوسط الحمضي .

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Example 2 (cont'd)

- Organic medicinal that are **weak acids** include the barbiturate drugs (e.g., phenobarbital) and the sulfonamides (e.g., sulfadiazine and sulfacetamide) form water-soluble salts in **basic solution**
- The free acid may precipitate from solution by a lowering of the pH
- Acid in Base -> Salt (soluble)
- Acid in acid-> Acid (insoluble)
- Base in acid -> Salt (soluble)
- Base in base -> Base (insoluble)

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Weak Acid in Basic Solution → Salt + water

↓
بملاء ترسيب عن طريق جعل تخفيف لـ pH ← جاد الملح يكون أعلى ذائبية من Weak Acid + Base.

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Example 3 (two factors; type of solvent and form of drug):

- Pharmaceutical manufacturers have prepared many acid salts of organic bases to enable the preparation of aqueous solutions.
- **Salts** of organic compounds are more soluble in **water** than are the corresponding organic bases.
- Conversely, the **organic** bases are more soluble in **organic** solvents, including alcohol, than are the corresponding salt forms.

like dissolve like

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* أزيد الذوبانية ← أسمه Salt
* الأملح يذوب أكثر في الماء.
* Organic bases تذوب
More Solubility
في الـ Organic Solvent
* like Alcohol ..

Example 3 (cont'd)

TABLE 13.2 WATER AND ALCOHOL SOLUBILITIES OF SOME WEAK ACIDS, WEAK BASES, AND THEIR SALTS

DRUG	MILLILITERS OF SOLVENT TO DISSOLVE 1 _g OF DRUG	
	WATER	ALCOHOL
Atropine	455.0	2
Atropine sulfate	0.5	5
Codeine	120.0	2
Codeine sulfate	30.0	1280
Codeine phosphate	2.5	325
Morphine	5000.0	210
Morphine sulfate	16.0	565
Phenobarbital	1000.0	8
Phenobarbital sodium	1.0	10
Procaine	200.0	Soluble
Procaine hydrochloride	1.0	15
Sulfadiazine	13000.0	Sparingly soluble
Sodium sulfadiazine	2.0	Slightly soluble

للفرقم فقط ..

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A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

- Example 4 (co-solvent usage)

- **Co-Solvent Systems**

- Solvent blending or co-solvency: by mixing miscible solvents of different polarities to form a solvent system of optimum polarity to dissolve the solute

- **Diazepam** Injection use a co-solvent mixture that contains 40% propylene glycol, 10% ethanol, and 50% Water for Injection

- **Dielectric constant (an index of solvent polarity)** is used as a guide to determine a co-solvent system

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مثل ما حكمينا اننا لما نحدد Solubility لازم درجته الحرارة تكون محددة وثابتة ، بصطيب ؟
بله بعض المواد ال Solubility لها بتتأثر مع تغير درجات الحرارة سواء كانت زيادة أو نقصان .

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Example 4

- **Temperature:**

- many compounds have greater solubility at elevated temperatures (**stability**???)

- Selecting the correct temperature will cause the solution to hold the required **amount** of drug in solution

- ①
- ② - Also will help the pharmacist know the correct formulation storage conditions

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Co-Solvent : مادة مساعدة

على الزيادة ، بتعطينها كميات قليلة
عشان تزيد Solubility للسـ (Solute)

Solvent and Cosolvent
Must be miscible with
each other..

عن طريق الـ polarity

بتتبع اعداد الـ Cosolvent
المتناسب مع الـ Solvent ..

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Temperature (cont'd):

- However, elevated temperatures cannot be maintained for pharmaceuticals, and the **net effect of heat** is simply an **increase in the rate of solution** rather than an increase in solubility.
- Pharmacists should be careful not to exceed the minimally required temperature, so as to avoid drug **deterioration**

* • **solution** Rate: amount/time

* انتبه إنه درجة الحرارة
ماتزير إلى حد التلف !!

* • Solubility: amount/volume

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في بعض المواد بتقل ذائبيتها مع زيادة درجة الحرارة (العكس) ..
تزيد الذائبة لما أخفقت درجة الحرارة!
← Calcium hydroxide

A pharmacist can, in certain instances, dissolve greater quantities of a solute than would otherwise be possible

Temperature (cont'd):

- Some chemical agents, particularly calcium salts, undergo **exothermic** reactions as they **dissolve** and **give off heat**.
- For such materials, the use of **heat would actually discourage** the formation of a solution.
- The best pharmaceutical example of this type of chemical is **calcium hydroxide (Ca(OH)₂)**, which is used in the preparation of Calcium Hydroxide Topical Solution, USP.
- Calcium hydroxide is soluble in water to the extent of
 - 140 mg per 100 mL of solution at 25°C
 - 170 mg per 100 mL of solution at 15°C.

يذوب + يهيج
heat

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زادت الكمية الذائبة لما قلت درجة الحرارة.