

General guideline for solubility:

- the most widely written guideline for the prediction of solubility is **"like dissolves like,"**.
- Thus, organic compounds are more soluble in organic solvents than in water.
- The greater the number of **polar groups present**, the greater soluble in water than in organic. Polar groups include OH, CHO, COH, CHOH, CH₂OH, COOH, NO₂, CO, NH₂, and SO₃H.
- An increase in the molecular weight of an organic compound without a change in polarity reduces solubility in water.

* أي زيادة بالوزن الجزيئي للمركب، بدون زيادة بالقطبية تقل قابلية الذوبان.

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Organic Compound
is More Soluble in
Organic Solvent, than
water, but if the compound
has polar group, the greater
soluble in water than in organic.

الذائبة سرياً يمكن تزيدها بالطرق التي سيجعلها قبل بزيد الـ amount / volume .

General guideline for solubility:

- To speed up the dissolution rate a pharmacist may employ one or several techniques such as:
 - A. Applying heat (not suitable for volatile and thermolabile substances)
 - B. Reducing the particle size (Comminution, grinding)
 - C. Utilizing a solubilizing agent ← **المضام عامل الذوبان.**
 - D. Vigorous agitation

Amount / time
Dissolution rate.



انفصال قويحة.
Movement of one or more
compound of a mixture to
improve contact.

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لما تزيد هذه الـ
Dissolution rate
رج يذوب الـ
Solubility
نهن وقت مخرجين .

TABLE 13.3 SOLUBILITIES OF SELECTED ORGANIC COMPOUNDS IN WATER AS A DEMONSTRATION OF CHEMICAL STRUCTURE-SOLUBILITY RELATIONSHIP

COMPOUND	FORMULA		MILLILITERS OF WATER REQUIRED TO DISSOLVE 1 G OF COMPOUND
Benzene	C_6H_6		1430.0
Benzoic acid	C_6H_5COOH		275.0
Benzyl alcohol	$C_6H_5CH_2OH$		25.0
Phenol	C_6H_5OH		15.0
Pyrocatechol	$C_6H_4(OH)_2$		2.3
Pyrogallol	$C_6H_3(OH)_3$		1.7
Carbon tetrachloride	CCl_4		2000.0
Chloroform	$CHCl_3$		200.0
Methylene chloride	CH_2Cl_2		50.0

Handwritten notes in Arabic:
 - Next to Benzyl alcohol: *→ less M_w, More Solubility.*
 - Next to Pyrogallol: ** كل ما زحت هنى ال OH بتزيد نسبة الذائبة.*
 - Next to Methylene chloride: ** كل ما قلته ال Cl بتزيد نسبة الذائبة. لأن ال M_w بتقل ..*

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General guidelines for solubility

- No effect* →
- Water is the most commonly used solvents for oral solutions
 - ① • The **physiological actions** of many solvents greatly **limit** their use. With few exceptions, **most organic solvents are irritating or toxic.** *يقتضون ..*
 - ② • Thus, **toxicity and irritation** limit the solvents employed to a few compounds:
 - **For internal use**, only a few solvents such as glycerin, alcohol, and propylene glycol are indicated for internal use
 - **for topical use**, acetone, isopropanol, polyethylene glycols, saturated aliphatic hydrocarbons, ether, and various oils may be used



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Some solvents for liquid preparations:

لما استخدم الحمول ←

• **ALCOHOL, USP:**



• **ETHYL ALCOHOL, ETHANOL, C₂H₅OH:**

- Next to water, alcohol is the most useful solvent in pharmacy.
- Together with water, it forms a hydroalcoholic mixture that dissolves both alcohol-soluble and water-soluble substances
- **Alcohol, USP:** is 94.9% to 96.0% C₂H₅OH by volume (i.e., v/v) when determined at 15.56°C

يمكن زيديك من ال solubility
لانته بجوي على (OH) ..

water + alcohol → hydro
Alcoholic

• **Dehydrated Alcohol, USP:** contains not less than 99.5% C₂H₅OH by volume and is used when an essentially water-free alcohol is desired. (**Absolut ethanol**)

• It is also used in liquid products as an antimicrobial preservative

مؤنق الماء ..
بجوي على درجات قليلة
و مدومة من الماء ..

* بنسبها أيتها عشان
يعمل حمايتها من نمو البكتيريا ..

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Advantages of hydroalcoholic solutions:

1. They generally can dissolve more oil soluble drugs (or the free acid or free base form) compared to aqueous solutions
2. They have some preservation capacity because of the presence of alcohol
3. They can be used to dissolve either alcohol soluble or water soluble drugs

تدرة أيضا تذوب الذيبوت ..

القدرة على الاحتفاظ ..

↓
OH

قادرة أيضا تذوب الحمول أو الماء ..

Disadvantages of hydroalcoholic solutions:

1. The used solvents are not always physiologically inert → Side effect ..
2. Elixirs are less sweet and less viscous than syrups
3. Less effective in masking taste compared to syrups

أقل قدرة على إبقاء الدواء
أقل حلابة ، أقل لزوجة
موردتها حاملة غير لوجيا ..

حامل ..

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Some solvents for liquid preparations:

- The U.S. Food and Drug Administration (FDA) restrict the use of alcohol **in over-the-counter (OTC)** oral drug products and include appropriate warnings in the labeling:
- ✓ - For **OTC oral products** intended for children **under 6 years of age**, the recommended alcohol content limit is **0.5%**;
- ✓ - **children 6 to 12 years of age**, the recommended limit is **5%**;
- ✓ - **children over 12 years of age** and for adults, the recommended limit is **10%**.

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Some solvents for liquid preparations:

- **DILUTED ALCOHOL, NF:** * كيف أعمل dilute للكحول؟
- Diluted Alcohol, NF, is prepared by mixing equal volumes of Alcohol, USP, and Purified Water, USP.
- **RUBBING ALCOHOL:**
- Rubbing alcohol contains about **70% ethyl alcohol** by volume, the remainder **consisting of water**, denaturants **with or without color additives** and perfume oils, and stabilizers.
- **To decrease alcohol abuse:**
- Each 100 mL must contain not less than **355 mg of sucrose octaacetate** or **1.4 mg of denatonium benzoate** (bitter substances that discourage accidental or abusive oral ingestion).



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Some solvents for liquid preparations:

- According to the Internal Revenue Service, U.S. Treasury Department, the denaturant employed in rubbing alcohol is formula **23-H**, which is composed of:
 1. 8 parts by volume of acetone,
 2. 1.5 parts by volume of methyl isobutyl ketone, and
 3. 100 parts by volume of ethyl alcohol.
- The use of this **denaturant mixture** makes the separation of ethyl alcohol from the denaturants virtually **impossible with ordinary distillation apparatus**. This discourages the illegal removal for use as a **beverage of the alcoholic** content of rubbing alcohol.

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Some solvents for liquid preparations:

- Rubbing alcohol is used as:
 1. Rubefacient externally → قانينار → topical preparation Skin في الجلد
 2. Soothing rub for bedridden patients
 3. Germicide for instruments ← تنظيم لأعداد البكتيريا
 4. Skin cleanser before injection
 5. Vehicle for topical preparations ← ناقلة للأدوية عن طريق الجلد



يخفف الألم الموضعي، يقيح الجلد، يزيل البكتيريا.

- A **rubefacient** is a substance for topical application that produces redness of the skin, e.g. by causing dilation of the capillaries and an increase in blood circulation.
- They have sometimes been used to relieve acute or chronic pain, but there is limited evidence as to their efficacy.

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Some solvents for liquid preparations:

GLYCERIN, USP (GLYCEROL):

- Glycerin is a clear syrupy liquid .. سائل لزج نقي ..
with a sweet taste.
- It is miscible with both water and alcohol
- Glycerin :
- has preservative qualities
- and is often used as a stabilizer
- and used as an auxiliary solvent in conjunction with water or alcohol



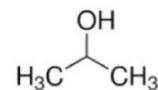
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Some solvents for liquid preparations:

ISOPROPYL RUBBING ALCOHOL:

- Isopropyl rubbing alcohol is about 70% by volume isopropyl alcohol, the remainder consisting of water with or without color additives, stabilizers, and perfume oils.

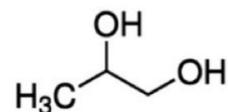
زيت الالهول



PROPYLENE GLYCOL, USP:

- Propylene glycol, a viscous liquid, is miscible with water and alcohol. It is a useful solvent with a wide range of applications
- It is sometimes substituted for glycerin in some pharmaceutical formulations.
- Although orally administered propylene glycol has a low toxicity in animals, it may exhibit a weak central nervous system depressant activity

نشاط مثبط دنييف



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ما يستخدمه
Orally
لأنه يمكن جعل آثاره
للعجز العصبي

Some solvents for liquid preparations:

Fixed oils (vegetable oils) ^{موستطير}

- These are non-volatile oils that consist mainly of fatty acid esters of glycerol.
- Sesame oil, cotton seed oil, etc
زيت القطن. زيت السمسم



Liquid paraffin

- It is often used as a solvent for the topical application of drugs
- Liquid paraffin or mineral oil is a transparent, colourless, odourless, or almost odourless, oily liquid composed of saturated hydrocarbons obtained from petroleum.



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creams, emulsion. ←

رجيحة نفوينة
topical application
على الـ skin: ←

Some solvents for liquid preparations:

PURIFIED WATER, USP, H₂O

- Naturally occurring water contains various amounts of dissolved inorganic salts, organic matter and microorganisms.
- Ordinary drinking water obtained from the tap is **not** accepted for the manufacture of aqueous pharmaceutical preparations or for the extemporaneous compounding of prescriptions
- Purified water is obtained by distillation, ion-exchange treatment, reverse osmosis or other suitable process.
- aqueous dosage forms except those intended for parenteral administration (Injections) use Purified water, USP is used
- **for parenteral (injections):** Water for Injection, USP; Bacteriostatic Water for Injection, USP; or Sterile Water for Injection, USP, is used

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← ماء اللى تستخدمها من
الصنعية، وده صوح استخدمها
في طباعة الأدوية،
لان نسبة الامواج اللى فيها بتأثر
على الـ stability للتصنيعات.

كصوح استخدمها (purified)
1- distillation.
2- ion-exchange.
3- reverse osmosis.

← بتستخدمها في كل
injection
water injection
تستخدمها
تخليها من البكتريا دولها.