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Utilization of Solubilizing Power of Safe Solids to Replace Harmful Organic Solvents to Carryout Thin Layer Chromatography

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A B S T R A C T

TLC (thin layer chromatography) is one of the most popular, cheap, and widely used separation technique. In TLC, capillary action in the finely divided stationary phase causes the mobile phase to move. In this paper, the mixed solvency concept is used to perform TLC. There are various solvents employed for TLC performance like (Benzene, 1,2-dichloroethane, carbon tetra chloride, acetonitrile, methanol, tetrahydrofuran, tetralin, toluene, sulfolane, N,N-dimethylacetamide) The mixed solvency concept is the phenomenon in which the solubility of poorly water-soluble drugs or compounds is augmented using blends of different compounds. Usually, organic solvents are used as a mobile phase in TLCs. But in this disquisition, organic solvents of class 1 and class 2 were replaced, and class 3 solvent ethanol was made more efficient and made to act like a class 1 and 2 solvent. Blends of ethanol were made with compounds like camphor, menthol, and thymol, and these blends were used as the mobile phase. The mobile phase prepared using the mixed solvency concept gave appropriate results for some drugs. In addition, more blends can be made and can be used as a mobile phase solvent. Hence, this study implies that detrimental and noxious organic solvents can be replaced by making eco-friendly solvents.

Keywords:Thin layer chromatography, Mixed solvency concept, solubility, Solid as a solvent, Organic solvents

1. Introduction

TLC is a liquid chromatography technique in which the mobile phase is a liquid and the stationary phase is a thin layer of material on top of a flat plate. The sorbent is the name given to this layer of material. The developing solvent is the mobile phase, which moves the solutes through the stationary phase. The speed with which the solute flows through the stationary phase is determined by the force of the mobile phase as it dissolves and drives the solute up the plate, as well as the resistance of the sorbent as it pulls the solute out of solution and back into the sorbent. Molecules move in a stop-and-go pattern across the plate as the solute is repeatedly absorbed and desorbed. As a result in this case, just a small portion of the solute is moving at any given time, but each area travels a mean distance. Individual changes and motions will lead the distinct zones to spread apart. Particles, as well as differences in the sorbent's homogeneity substances that are toxic. Those who are particularly attracted to the sorbent move more slowly because they spend more time there. Time in the sorbent, and those that move faster are less drawn to it. The solid layer, is more soluble in the mobile phase, and spend more time there. As a result, compounds with varied characteristics can be separated by taking the advantage of variable interactions of the solutes with the sorbent and the mobile phase.(1)

TLC can be classified in a variety of ways. It is classified according to the separation mechanism: adsorption (physical sorption of the solutes onto the sorbent particles), partition (dissolution of the solutes into a stationary liquid on the sorbent), ion exchange (attraction of ions to groups of opposite charge on the sorbent), and size exclusion or gel permission (retention or rejection based on size or shape). Because the sorbent in normal- or direct-phase TLC is polar, more polar solutes move more slowly and stay closer to the origin, whereas nonpolar solutes migrate more swiftly and closer to the solvent front. Polar solutes can be drawn farther from the origin to improve separation by increasing the polarity of the mobile phase. In the case of reverse-phase TLC, the opposite is true (RP-TLC). A nonpolar sorbent will bind nonpolar solutes better and allow them to migrate

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slowly along the plate, whereas polar components will move swiftly near the solvent front. The polarity of the developing solvent must be reduced to enhance the distance covered by the nonpolar zones.(2).

1.1. Retention factor:

The retention factor (Rf) is used to track compound movement across the TLC plate. Rf is calculated by dividing the overall distance traveled by the solvent by the distance traveled by each component. Its value is always in the range of zero to one.

Rf value= distance traveled by solute/distance traveled by the solvent

The slower a molecule migrates up the TLC plate, the stronger its affinity to the stationary phase adsorbent. Because TLC adsorbents are often polar, non-polar compounds move faster up the plate and have higher Rf values, whereas polar compounds move slower and have lower Rf values.(3)

1.2. Hydrotropic Solubilization

Hydrotropic solubilization refers to the improvement of a drug's aqueous solubility in the presence of a significant amount of a hydrotropic agent. Newberg (1916) coined the term "hydrotropic agent," which he defined as a metallic salt of organic acid whose relatively high concentration in water can improve the aqueous solubility of organic compounds that are just poorly soluble in water. It is believed that salts that improve solubility "salt in" the solute, whereas salts that reduce solubility "salt out" the solution.(4)

Hydrotropic solubilization has been employed to enhance the aqueous solubility of several poorly water-soluble drug (5-14)

Mixed hydrotropic solubilization has been employed to enhance the aqueous solubility of several poorly water-soluble drug.(15-27)

1.3. Mixed solvency concept

According to Maheshwari's mixed solvency concept, all substances in the universe have solubilizing properties, meaning that all liquids, gases, and solids have solubilizing power. Each substance is a solubilizer. All solubilizers, whether they are gases, liquids, or solids, have different solubilizing strengths for different solutes. The molecules of solids and gases must be in a liquid state in the case of these substances to be involved in hydrogen bonding and weak van der walls forces.

In case of gases, the molecules of gas may come in liquid state in two ways:

By liquefaction: When a gas is liquefied, its molecules enter a liquid state where they can form weak van der Waals forces and hydrogen bonds with solute molecules. At a specific temperature and pressure, carbon dioxide liquefies in supercritical fluid technology. The preparation of nanoparticles, the extraction of active ingredients from herbal powders, the purification of compounds, etc. all make use of the solvent action of carbon dioxide molecules.

By dissolution of gas in a solvent: By allowing gas to dissolve in a solvent, gas molecules can become liquid and then be converted into other forms of energy. weak van der walls forces with molecules of other solutes involved in hydrogen bonding. One such example is concentrated hydrochloric acid. After dissolving in water, hydrochloric acid gas molecules transition into a liquid state.

Nalidixic acid dissolves in concentrated hydrochloric acid at a rate of about 5% w/v. Nalidixic acid dissolves in water at a rate of about 0.021 percent w/v. Nalidixic acid was more soluble when hydrochloric acid gas molecules were dissolved in it. This demonstrates that gas molecules have the ability to dissolve other molecules.

The molecules of solid comes in liquid state by three ways:

By melting: Solid molecule can become liquid by melting Example For diclofenac sodium (M.P. 283℃), melted urea, a clear, colourless liquid, has good solubilizing power. Diclofenac sodium dissolves readily in one gramme of melted urea at 132℃. The molecules of diclofenac sodium and urea interact through hydrogen bonds and weak van der waals forces. Nalidixic acid, with a melting point of 230℃, dissolves in one gramme of clear, colourless, melted phenol at about 44℃. means that nalidixic acid is very well soluble in melted phenol.

By dissolution in a solvent: When a solid is dissolved in a solvent, its molecules can become liquid.

Ibuprofen dissolves in water at a rate of 0.028 percent. Ibuprofen is 2.390 percent soluble in 2 M sodium benzoate (28.8 percent w/v) solution. (84-fold increase in solubility). Furosemide is 1.7 percent w/v soluble in ethanol. It is 5 percent w/v soluble in ethanolic niacinamide (15% w/v) solution.

Piroxicam dissolves in propylene glycol at about 5 mg/ml. It is approximately 120 mg/ml soluble in propylene glycol containing 10% w/v sodium acetate and 10% w/v sodium caprylate.

By eutectic formation: Molecules of solid can also come in liquid state by formation of eutectic mixtures.

Example When menthol and thymol are triturated in equal parts, a clear, colourless eutectic liquid is obtained. This is a eutectic liquid. Metronidazole, atenolol, ornidazole, resorcinol, BHA, salicylic acid, and other drugs dissolve well in it. This eutectic liquid, on the other hand, is a poor solvent for aspartame, nimesulide, methyl paraben, carvedilol, and other chemicals. As a result, this eutectic liquid is a good solvent for some solutes but a bad solvent for others. As a result, we can call this eutectic liquid a solvent. Thymol and menthol molecules are present in liquid form and form hydrogen bonds and weak van der waals forces with solute molecules.

Because everything in the universe has solubilizing properties, various pharmaceutical additives should as well. A concentrated solution containing several solubilizers in safe concentrations can thus be used to improve a drug's solubility to the level required to formulate a pharmaceutical dosage form.

A concentrated aqueous solution (MS) composed of 5% w/v sodium caprylate, 5% w/v sodium citrate, and 5% w/v poloxamer 407. The pH of this MS was 7.0. Furosemide's solubility in MS was found to be around 35 mg/ml. Furosemide's solubility in water was found to be less than a 35-fold improvement.

Similarly, piroxicam solubility in MS was around 20 mg/ml. Piroxicam's solubility was found to be less than 1 mg/ml. As a result, there was a more than 20-fold increase in solubility.

As a result, the second parameter of the mixed solvency concept is extremely useful in developing pharmaceutical dosage forms for poorly water-soluble drugs.

1.3.1. Mixed solvency concept benefits

By carefully choosing the solubilizers, any weaker solvent (for a particular solute) can be converted into a strong solvent for that solute.

In the development of an oily injection, oily topical solution, multiple emulsion with higher drug loading in oily phase, SEDDS with higher drug loading, etc., oil soluble excipients (PVP, vanillin, BHA, BHT, propyl gallate, benzoic acid, methyl paraben, propyl paraben, etc.) may be used to increase the oil solubility of an oil insoluble drug. When these excipients (solubilizers) are combined in low concentrations, as opposed to high concentrations of a single solubilizing agent, the toxicity issue is resolved.

Similarly, by using the proper concentrations of propylene glycol soluble excipients (such as benzoic acid, niacinamide, sodium benzoate, PVP, methyl paraben, etc.), propylene glycol-based solutions of propylene glycol insoluble drugs can be produced.

Drugs that are poorly water-soluble may be solid dispersed using a combination of safe concentrations (in safe limits) of solid excipients that are water-soluble, eliminating the need for organic solvents. (Organic solvent drawbacks include high cost, pollution, and toxicity from leftover solvent.)

Mixed solvency concept has been employed for enhancement in the solubility of poorly water- soluble drugs(28-52)

2. MATERIALS AND METHOD

2.1. Materials

TLC Plates, Silica Gel GF 254, Distilled water, UV chamber, Thymol, Camphor, APIs (Paracetamol, Diclofenac sodium and Acyclovir)

2.2**. METHODS**

Preparation of different solvent systems for the mobile phase:

- **20% w/v Thymol in ethanol** – 20gm thymol was weighed and taken in a 100ml volumetric flask. To the volumetric flask, 50-60ml ethanol was added and the flask was shaken until thymol gets fully dissolved. Then, the volume was made up to the 100ml mark with ethanol.
- **15% w/v Thymol in ethanol** – 15gm thymol was weighed and taken in a 100ml volumetric flask. To the volumetric flask, 50-60ml ethanol was added and the flask was shaken until thymol gets fully dissolved. Then, the volume was made up to the 100ml mark with ethanol.
- **10% w/v Thymol in ethanol** - 10gm thymol was weighed and taken in a 100ml volumetric flask. To the volumetric flask, 50-60ml ethanol was added and the flask was shaken until thymol gets fully dissolved. Then, the volume was made up to the 100ml mark with ethanol.
- **20% w/v Camphor in ethanol** – 20gm camphor was weighed and taken in a 100ml volumetric flask. To the volumetric flask, 50-60ml ethanol was added and the flask was shaken until camphor gets fully dissolved. Then, the volume was made up to the 100ml mark with ethanol.
- **10% w/v Camphor in ethanol** – 10g camphor was weighed and taken in a 100ml volumetric flask. To the volumetric flask, 50-60ml ethanol was added and the flask was shaken until camphor gets fully dissolved. Then, the volume was made up to the 100ml mark with ethanol.
- **7% w/v Camphor in ethanol** – 7gm camphor was weighed and taken in a 100ml volumetric flask. To the volumetric flask, 50-60ml ethanol was added and the flask was shaken until camphor gets fully dissolved. Then, the volume was made up to the 100ml mark with ethanol.
- **3.5% w/v Camphor in ethanol** – 3.5gm camphor was weighed and taken in a 100ml volumetric flask. To the volumetric flask, 50-60ml ethanol was added and the flask was shaken until camphor gets fully dissolved. Then, the volume was made up to the 100ml mark with ethanol.
- **10% w/v Menthol in ethanol** – 10gm menthol was weighed and taken in a 100ml volumetric flask. To the volumetric flask, 50-60ml ethanol was added and the flask was shaken until menthol gets fully dissolved. Then, the volume was made up to the 100ml mark with ethanol.

NOTE: All mobile phases were tried for all four drugs (Paracetamol, Diclofenac sodium, Acyclovir and Diazepam). The mobile phases, which gave good spots without tailing effect were selected.

3.PREPARATION OF DRUG SOLUTIONS FOR SPOTTING:

- **Acyclovir solution**:200mg acyclovir + 10ml ethanol →20 minutes vigorous shaking →For complete dissolution.
- **Diazepam solution:**200mg Diazepam + 10ml ethanol →20 minutes vigorous shaking →For complete dissolution.
- **Paracetamol solution**:200mg Paracetamol + 10ml ethanol →20 minutes vigorous shaking →For complete dissolution.
- **Diclofenac sodium solution:**200mg Diclofenac sodium + 10ml ethanol →20 minutes vigorous shaking →For complete dissolution.

4.PROCEDURE:

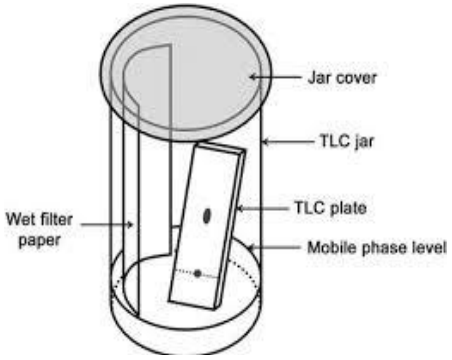

Figure 1 TLC chamber

1. ***Development of the TLC Chamber:***TLC development containers are specially built beakers with a watch glass on top. The solvent was poured into the chamber to a depth of about 0.5 cm. The filter paper was used to line the interior of the beaker to aid in the saturation of the TLC chamber with solvent vapor's. The beaker was covered with a watch glass and kept aside.

2. ***Preparation of TLC Plates:***A slurry of silica gel G254 was made. The TLC glass plates were taken and coated with silica gel G254 in such a way that an even and thin silica gel coating get formed on the plate.

3. ***Activation of TLC Plates:***The prepared TLC plates were kept in a hot air oven at 100 °C for 1hour for the activation of TLC plates.

4. ***Spots on TLC Plates:***The microcapillary was dipped into the drug solution. Then, gently spotting was done at the proper location on the TLC plate at a distance of 1cm from the bottom, and then the plate was dried at 100 °C for 20 minutes.

5. ***Development of TLC plate:*** The prepared TLC plate was placed in the beaker and covered with the watch glass. Then it was left undisturbedThe solvent was allowed to rise up the TLC plate by capillary action. It was made sure that the solvent level did not cover the spot. The plate was allowed to develop until the solvent was about half a centimetre below the top of the plate. Then the plate was removed from the beaker and the solvent front was immediately marked with a pencil. Then the plate was allowed to dry at 50 °C for 20 minutes.

6. ***Spot identification and observation in the UV Chamber:***The developed TLC plates after drying were observed in the UV chamber and spots were identified. The distance travelled by the spots were noted.

5.RESULTS:

Mobilephase	Names of drug	Rfvalue	Observation
3.5% w/v Camphor in ethanol	Acyclovir	0.77	Clearspot
7% w/v Camphor in ethanol	Diclofenac sodium	0.80	Clearspot
10% w/v Camphor in ethanol	Diclofenacsodium	0.85	Clearspot
	Paracetamol	0.71	Clearspot
	Acyclovir	0.52	Clearspot
15% w/v Thymol in ethanol	Diclofenacsodium	0.75	Clearspot
15% w/v Thymol in ethanol	Acyclovir	0.69	Clearspot

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