RECENT LITERATURE REVIEW ON PHYSICAL AND CHEMICAL METHODS FOR IMPROVING THE SOLUBILITY AND BIOAVAILABILITY OF POORLY SOLUBLE DRUGS

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Abstract

The phenomenon of a solid dissolving into a liquid phase to create a homogeneous system is known as solubility. One crucial factor in achieving the optimal drug concentration in the systemic circulation for pharmacological response is solubility, which is also known as bioavailability. The bioavailability and solubility of a medicine's drug moiety are the two main factors that determine a drug's therapeutic efficacy. The majority of newly discovered chemical substances are lipophilic and poorly soluble in water. More than 40% of drugs have low water solubility; therefore, new chemical entities generated in the pharmaceutical business are lipophillic and don't make it to market because of this. Numerous methods are now available to improve the solubility and rate of dissolution of poorly soluble medicines. The preferred solvent for liquid medicinal compositions is water. Most medications have limited water solubility and weak acidic and basic properties. In order to increase the solubility of medications that are weakly water-soluble, a variety of procedures are applied, such as micronization, chemical modification, pH adjustment, solid dispersion, complexation, co-solvency, micellar solubilization, and hydrotropy. In this review, we focused on developing innovative techniques to increase the solubility and bioavailability of medications that aren't very water soluble.

Keywords*: Solubility, Hydrotropy, Mixed hydrotropy , micronization, , co-solvency, micellar solubilization,*

Introduction:

The greatest quantity of solute that may dissolve in a certain amount of solvent is referred to as "solubility." Both a quantitative and a qualitative definition are possible. It is described quantitatively as the solute concentration in a saturated solution at a certain temperature. The spontaneous interaction of two or more substances to create a homogeneous molecular dispersion is a qualitative definition of solubility. When the solute and solvent are in balance, a solution is said to be saturated. A drug's solubility is expressed using several concentration units, including parts, percentages, molarity, molality, volume fraction, and mole fraction.

Need of Solubility

Numerous variables, including the drug's low water solubility and poor membrane permeability, might impede the absorption of drugs from the GI tract. An oral active drug must first dissolve in the stomach and/or intestines before it can pass through the GIT membranes and enter the bloodstream. Therefore, increasing solubility and increasing the rate of dissolution of medications that are not well soluble in water are two areas of pharmaceutical research that concentrate on optimizing the oral bioavailability of active substances. A medicinal substance is categorized using the BCS according to its water solubility and intestinal permeability.

Bioavailability

Bioavailability (BA) is absorption and is the administered dose of unchanged a subcategory of

fraction of an drug that reaches

Techniques for Solubility Enhancement

Formulation methods are necessary early on in the drug discovery process when the solubility of compounds in aqueous media is limited, and they continue to be crucial for the choice of lead molecules and the development of commercial medicinal products. Poorly water soluble medications have been subjected to a variety of approaches in an effort to increase solubility and dissolution rates, including the following:

a) Particle Size Reduction
b) Nanonization
c) Cosolvency
d) Hydrotropy
e) pH Adjustment
f) Sonocrystallization
g) Solid Dispersion
h) Inclusion Complexation
i) Self-Emulsifying Or Self-Micro Emulsifying Systems
j) Liquisolid Methods

The bioavailability of a medicine, on the other hand, often declines or may differ from patient to patient when it is delivered by alternative routes. One of the most important tools in pharmacokinetics is bioavailability since it must be taken into account when determining doses for non-intravenous modes of administration. Bioavailability typically refers to the amount or percentage of the ingested dosage that is absorbed for herbs, nutritional supplements, and other nutrients when the mode of delivery is almost exclusively oral.

In these methods, the carrier is key to enhancing solubility, dissolution rate, and bioavailability.

(a) Particle Size Reduction

Drug particle size is often inherently correlated with drug solubility; as a particle becomes smaller, the surface area to volume ratio rises. Greater contact with the solvent is made possible by the bigger surface area, increasing solubility. The active ingredient is disaggregated by mechanical stress in conventional particle size reduction techniques including comminution and spray drying. Thus, solubility augmentation is now possible via an effective, repeatable, and affordable method thanks to particle size reduction. However, the physical stress that is often applied to the therapeutic product during comminution processes like milling and grinding might lead to deterioration. When processing thermosensitive or unstable active chemicals, the thermal stress that may occur during comminution and spray drying is also a problem. Traditional methods may not be able to increase the solubility of virtually insoluble pharmaceuticals to the necessary degree.

(b) Nanonization

It is a method where medication particles are transformed into nano crystals with sizes between 200 and 600 nm. The bioavailability and solubility rates of several medications that are poorly soluble in water have recently been improved by the use of different nanonization techniques. The term "nanonization" generally refers to the study and use of substances and structures that are 100 nm or less in size. Drug solubility and pharmacokinetics may be enhanced as a consequence of nanonization, which may help lessen systemic adverse effects. Because micronized products have a propensity to aggregate, reducing the effective surface area for dissolving, oral bioavailability increase via micronization is insufficient for many novel chemical entities with very poor solubility; nanonization is the next step. Various

methods, such as wet milling, homogenization, emulsification-solvent evaporation process, pear milling, spray drying, etc., are employed to nanonize drugs.

(c) Cosolvency

A water miscible solvent that the medicine is easily soluble in may be added to water to boost the solubility of pharmaceuticals that are poorly soluble in water. The combination of the two solvents is referred to as a cosolvent, and the process is known as cosolvency. By lowering the interfacial tension between the aqueous solution and hydrophobic solute, cosolvent systems function. It is furthermore sometimes called solvent blending. By adding an organic co-solvent to the water, the solubility of pharmaceuticals is dramatically altered.

(d) Hydrotropy

A solubilization process known as hydrotropy occurs when a second solute is added in significant quantities, increasing the first solute's water solubility. Sodium benzoate, sodium salicylate, urea, nicotinamide, sodium citrate, and sodium acetate concentrated aqueous hydrotropic solutions have been shown to increase the aqueous solubilities of numerous medications that aren't very water-soluble.

(e) pH Adjustment

A pH shift might possibly cause a poorly water soluble medicine to dissolve in water. The buffer capacity and tolerability of the chosen pH are crucial factors to take into account in order to access the solubility of this technique. Weekly acidic medications are more soluble when excipients are soluble and raise the pH of the environment within the dosage form to a range higher than their pKa. Similarly, excipients that function as alkalizing agents may make weekly basic pharmaceuticals more soluble.

(f) Sonocrystallisation

Reducing particle size has also been accomplished by the effective use of liquid solvents and antisolvents during the recrystallization of poorly soluble materials. Sonocrystallization is a revolutionary method for reducing particle size based on crystallization utilizing ultrasound. Sonocrystallization uses ultrasonic energy with a 20–100 kHz frequency range to cause crystallization. It not only speeds up nucleation but also reduces the size of the active medicinal components and regulates their size distribution. Ultrasound is often used between 20 kHz and 5 MHz.

(g) Solid Dispersion

Sekiguchi and Obi, who studied the production and efficacy of eutectic melts of a sulfonamide medication and a water-soluble carrier in the early 1960s, were the ones who first put up the idea of solid dispersions. Solid dispersions are an effective pharmaceutical approach for boosting the drug dosage forms' ability to dissolve, absorb, and provide therapeutic benefit. A collection of solid goods with at least two separate components, often a hydrophilic matrix and a hydrophobic medication, are referred to as solid dispersion. For solid dispersions, polyvinylpyrrolidone (Povidone, PVP), polyethylene glycols (PEGs), and plasdone-S630 are the most often utilized hydrophilic carriers. The formulation of solid dispersion includes surfactants like Tween-80, sodium docusate, Myrj-52, Pluronic-F68, and sodium lauryl sulphate (SLS). Celecoxib with povidone (PVP) and ritonavir with gelucire are two acceptable hydrophilic carriers that may be used in solid dispersion to increase the solubility of celecoxib, halofantrine, and

ritonavir.

Here is a list of many methods to manufacture the solid dispersion of hydrophobic pharmaceuticals in an effort to increase their water solubility:

i) Fusion Process

In the fusion technique of preparation, the drug is absorbed into the matrix after the carrier is heated to a temperature slightly over its melting point. As it cools, the mixture is continuously stirred to evenly distribute the medication throughout the matrix. Several processes could be at work during the dispersion process. If the medication is highly soluble in the carrier, it may continue to be "dissolved" in the solid form, giving rise to what is referred to as a solid solution. Under these circumstances, particle size reduction continues all the way to the point when the medication is molecularly dispersed in the carrier matrix. Comparing these systems to control samples reveals extremely high drug dissolution rates. On the other hand, if the drug's solubility in the solid state is not as great, its crystallites will distribute throughout the matrix. Only slight increases in dissolution rates are seen in these systems. The transformation of a drug into an amorphous form in the presence of the matrix is a third mechanism, which once again exhibits varied solubility and dissolving rates. Enhanced wetting or reduced surface hydrophobicity, complexation, and crystallization of the drug in a metastable polymorphic form with changed thermodynamic characteristics are other mechanisms that might be at play. The exposure of pharmaceuticals to high temperatures is a significant drawback of the fusion technique of production, especially if the carrier is a solid with a high melting point and the drug is heat-sensitive.

ii) Solvent Method

The carrier and the active component are dissolved in an appropriate organic solvent during the solvent technique of production. This solvent evaporates either in a vacuum or at a high temperature. Super saturation happens when the solvent is being withdrawn, and the contents precipitate at the same time, leaving behind a solid residue. To remove any solvent that may have been loosely clinging to the particle surface, the coprecipitate is subsequently dried under vacuum. However, there is a chance that a solvate will develop inside the crystal lattice. Since the majority of the used solvents are poisonous and non-aqueous, this poses a barrier for pharmaceutical acceptability. Thus, it is assumed that even minute quantities of the solvent must be removed. Complete solvent removal may be shown using very sensitive methods like differential scanning calorimetry, differential thermal analysis, thermogravimetric analysis, and less sensitive techniques like gravimetry and spectroscopy.

iii) Fusion-Solvent Method

In the fusion procedures, the drug(s) is/are integrated in the form of a solution after the carrier(s) is/are melted. The necessity for solvent removal is removed if the carrier can contain a certain volume of liquid while preserving its solid qualities and provided the liquid is safe. Otherwise, this approach is criticized for the same solvent retention issue as was previously discussed. Drugs with high melting points or those that are thermolabile benefit the most from this technique. For the dispersions of spironolactone and griseofulvin in polyethylene glycol 6000, the method's viability has been shown.

iv) Spray Drying

The carrier and the active component are dissolved or suspended in a suitable solvent in this kind of preparation. By drying it and applying a stream of warm air to remove the solvent, this solvent is evaporated. The solvent quickly evaporates due to the droplets' huge surface area, and a solid dispersion forms soon..

v) Lyophilization (Spray Freeze Drying Method)

Spray freeze drying (SFD) has been successfully created to manufacture solid dispersions at ambient temperature, which was made a substantial advancement by the study effort of William III. This approach is utilized to prevent the heating during the manufacturing of thermosensitive pharmaceuticals. With SFD technology, a feed liquid comprising excipients and APIs that are either weakly or completely insoluble in water is atomized into a cryogenic liquid at room temperature, creating a frozen micronized powder that is then dried. This method has a number of benefits over conventional solid dispersion technology, including amorphous structure and large surface area.

vi) Hot-melt Extrusion

It is a technique that the polymer industry uses rather often. The first people to apply this technique for pharmacological purposes, however, were Speiser and Huttenrach. These are the sections of a melt extrusion: a feed port for raw materials, a heated barrel with extruder screws to move and mix the ingredients, and an exit port with an optional die to shape the mass while it is being extruded. The heated extruder barrel is continuously loaded with the active chemicals and the carrier. The combination of active component and carrier is changed into its "fluid like state" when it is forced through heated screws. By means of the strong shear of the extruder screws, this condition enables close-knit and uniform mixing. The melt is shaped into the desired form, such as granules, pellets, films, or powder, by an optional die in an exit port. The fact that the drug/carrier mixture only experiences a high temperature for roughly one minute during the hot melt extrusion procedure allows for the processing of drugs that are somewhat thermolabile.

h) Inclusion Complexation

The inclusion complex creation approach has been used more accurately than any other solubility enhancement method to increase the aqueous solubility, dissolving rate, and bioavailability of medicines that are not very water soluble. The nonpolar molecule or nonpolar area of one molecule (referred to as the guest) is inserted into the cavity of another molecule or set of molecules (referred to as the host) to produce inclusion complexes. The main structural need for inclusion complexation is that the guest must fit tightly within the host molecule's cavity. In order to decrease the overall contact between water and the nonpolar portions of the host and the guest, the cavity of the host must be both big enough to hold the guest and tiny enough to drain away water.

Here are several methods that may be used to get medications that are poorly soluble into inclusion complexes in order to increase their solubility in water:

i) Kneading

The process includes forming a cyclodextrin paste containing guest molecules by kneading a little amount of either water or ethanol. The mixture after kneading may be dried at 45 °C and ground.

ii) Melting

Excessive amounts of guests are melted, combined with powdered cyclodextrin, and then washed with a mild solvent that forms a complex to remove them. The technique is only suitable for sublimable guests like menthol.

iii) Solution-enhanced dispersion by the Supercritical fluids

SEDS is a brand-new, one-step technique that can create stable drug-cyclodextrin complexes. To obtain the best complexation efficiency and to compare with drugcyclodextrin complexation procedures already published in the literature (such as kneading, freeze drying, spray drying, etc.), the processing parameters must be optimized.

Advantages over other methods are

a) Preparation of solid-cyclodextrin complexes in single step process,

b) Achievement of high complexation efficiency (avoidance of excess cyclodextrin in powder).

c) Possibility to minimize the contact of drug with cyclodextrin during the process.

d) Achievement of enhanced dissolution rate of the drug (which is comparable to the dissolution behavior of micronized drug-cyclodextrin complex).

iv) Co-evaporation/Solvent evaporation method

The aqueous solution of the host is added to the alcoholic solution of the guest, agitated for a short while, and evaporated at room temperature till dry mass was formed. This mass was then ground and sieved, and the fraction was collected.

v) Microwave Irradiation

This technique was created for quick organic synthesis and reactions that call for a higher end product and a quicker reaction time.

vi) Freeze Drying/Lyophilisation technique

The cyclodextrin aqueous solution was added to with the necessary stoichiometric amounts of the host and guest, and this suspension was agitated magnetically for 24 hours. The mixture was then freeze dried at 60 °C for 24 hours.

vii) Spray drying/Atomization

In this approach, the host solution is typically made with a 50/50 ethanol and water ratio. This visitor is then added, the resultant mixture is agitated for 24 hours at room temperature, and the solution is spray dried while keeping track of the following parameters: air flow rate, atomizing air pressure, intake temperature, output temperature, flow rate of solution, etc. produced after being filtered via a 63–160 micron granulometric sieve.

i) Self-Emulsifying or Self-Micro Emulsifying Systems

The idea of in situ emulsion creation in the digestive tract is used by self-emulsifying or self-micro emulsifying devices. In the absence of an external phase (water), the mixture of oil, surfactant, co-surfactant, one or more hydrophilic solvents, and co-solvent forms a transparent isotropic solution known as the self-emulsifying drug delivery system (SEDDS), and upon dilution by the aqueous phase in the emulsifying formulations, forms fine o/w emulsions or micro-emulsions spontaneously.

j) Liquisolid Methods

Both absorption and adsorption occur when the drug in the liquid vehicle is incorporated into a carrier material like cellulose that has a porous surface and tightly matted fibers inside of it. Specifically, the liquid is initially absorbed in the interior of the particles and is captured by their internal structure, and after this process has reached saturation,

adsorption of the liquid onto the internal and external surfaces of the porous carrier particles occurs. The coating material with strong adsorptive capabilities and a large specific surface area then imparts the desired flow characteristics to the liquisolid system. Liquisolid solid system is a powdered version of liquid pharmaceuticals that flows well and may be compressed. Liquid medications with poor water solubility that have been dissolved in acceptable non-volatile solvents are transformed into free-flowing, radially compressible powders by simple mixing with chosen powdered excipients known as carrier and coating materials under the idea of liquisolid systems. Silica and cellulose powders, both crystalline and amorphous, may be employed as coating materials.

(a) Use of Co-Solvents

Increasing the solubility of a non-polar medication by adding a water-miscible or partly miscible organic solvent is a popular and efficient method. The mixture of solvents used to make pharmaceuticals more soluble is referred to as cosolvency, and the solvents themselves are referred to as cosolvents. The cosolvent system operates by lowering the interfacial tension between the hydrophobic solute and the mostly aqueous solution. Blending solvent is another name for it that is often used. cosolvents such polyoxyethylene glycols, sorbitol, glycerin, propylene glycol, and ethanol, among others.

(b) Hydrotropy Method

By adding significant quantities of a second solute (hydrotropic agents), one solute may be made more soluble in water. This process is known as hydrotropy. Alkali metal salts of different organic acids make up the solute. Ionic organic salts are hydrotropic agents. The solute is said to be "salted in" by additives or salts that improve solubility in a particular solvent, and "salted out" by additives or salts that reduce solubility. The phenomenon known as "Hydrotropism" is caused by the "salting in" of non-electrolytes termed "hydrotropic salts" by a number of salts with big anions or cations that are also extremely soluble in water. Utilizing hydrotropes like urea and nicotinamide improved rofecoxib's solubility [30,31].

(c) Micronization

Due to the huge surface that is produced, the particle size reduction approach improves the solubility and rate of dissolution of medications that are weakly water soluble. By using air attrition techniques such fluid energy mills, jet mills, rotor stator colloid mills, etc., the process requires shrinking the size of the solid drug particle to 1 to 10 microns, which is often accomplished by spray drying or other means. It is also known as "Micromilling" throughout the procedure. Because micronization does not alter the drug's saturation solubility, it is not appropriate for medications with large dosage numbers. Because of the propensity of micronized products to agglomerate and reduce the effective surface area for dissolving, micronization of drugs is not recommended.

(d) Change in Dielectric Constant of Solvent

By lowering the solvent's dielectric constant, the addition of a cosolvent may make hydrophobic molecules more soluble. Water has a high dielectric constant and is an excellent solvent for polar compounds because of hydrogen bonding. The energy required to separate two charged objects that are at odds with one another is measured by a substance's

dielectric constant. The dielectric constant of the medium has an inverse relationship with the energy needed to separate two charged substances that are at odds with one another.

(e) Amorphous forms

Amorphous structures have greater thermodynamic energies than equivalent crystalline forms due to the random placement of atoms or molecules. In general, solubility and dissolution rates are higher.

(f) Chemical modification of drug

By boosting hydrogen bonding and the interaction with water, polar groups like carboxylic acids, ketones, and amines promote solubility.

(g) Use of Surfactants

Surfactants are amphiphilic substances with a circular head that is polar and a tail that is non-polar in nature. Micelles will develop when a surfactant, such tween-80 sodium lauryl sulphate, is added to water. A non-polar medication will partition into the micelle's hydrophobic core, and the polar tail will cause the complex to dissolve. The solubilization and wetting effects of bile salts on the solubility of steroids have served as examples of this.

(h) Inclusion complex/clathrates

The usage of cyclodextrins has significantly improved the drug's solubility and dissolution. ß-cyclodextrin (ß-CD) and HP-ß-CD may be used to make these complexes; the necessary amount of ß-CD is weighed, and water is then added to create a tough consistency. A measured amount of the medicine is introduced to the bulk. The mixture is thoroughly dried in a hot air oven at 60 0C for two hours after being kneaded in a glass mortar for an hour. The dry substance is passed through mesh number 12014 for sieving.

(i) Alteration of pH of solvents

When the pH of the solvent is lowered, solubility is improved. Additionally synergistic in nature is the combined impact of pH and complexation on solubilization. By changing the pH, it was hoped to improve gliclazide solubility.

(j) Use of Hydrates or Solvates

A crystalline substance may include inclusions, which are solvent molecules trapped within the crystal lattice, or non-stoichiometric adducts. A stoichiometric adduct, also known as "Solvate," is a chemical complex that contains molecules of the solvent that is crystallizing at certain locations within the crystal lattice. The compound is referred to as "Hydrate" when water serves as the included solvent. "Anhydrous" refers to a substance whose crystal structure doesn't include any water. Anhydrous forms have greater aqueous solubilities than hydrate forms.

(k) Use of Soluble Prodrugs

Bio-reversible chemical modification enhances the medications' physicochemical characteristics. Incorporating a polar or ionizable component into the parent chemical to increase water solubility is the most used prodrug approach. The pro-drug strategy has been utilized effectively to increase the water solubility of benzodiazepines, vitamins, and corticosteroids. By creating a prodrug, the rate of allopurinol dissolution was effectively increased.

(l) Application of Ultrasonic Waves

Solubility can be increased by the use of ultrasonic vibrators. An oscillator of high frequency (100-500 KHz) is used and the device is known as "Pohlman whistle".

(m) Functional Polymer Technology

By avoiding the lattice energy of the drug crystal, which is the principal obstacle to fast dissolution in aqueous environments, functional polymers increase the rate of

dissolution of poorly soluble medicines. These polymers are ion exchange materials because they include basic or acidic groups that interact with the surrounding medium's ionizable molecules and exchange mobile ions of equal charge in a reversible, stoichiometric manner. The finished product, known as "Resinate," may be made as a tablet, dry powder, or solution. The medicine is released from the resinate when exposed to the bodily fluids since the resins are insoluble and cannot be absorbed by the body.

(n) Controlled Precipitation Technology

This method involves dissolving the medicine in an organic water-miscible solvent before dissolving it in a water-based media that contains stabilizers (HPMC, cellulose ethers, and gelatin). The medication crystallizes into microparticles as a result of the solvent dissolving in water. Due to the stabilizers' extensive hydrophilized surface area from adsorption, they regulate particle development and speed up the dissolving of drugs with low solubility. For instance, Soliqs' proprietary nanomorph technology for the controlled crystallization of pharmaceuticals.

(o) Evaporative Precipitation in Aqueous Solution

Rapid phase separation is used in the EPAS method to nucleate and produce lipophilic drug nano- and microparticles. The medication is first dissolved in an organic solvent with a low boiling point. This solution is pumped through a tube, heated there under pressure to a temperature over the boiling point of the solvent, and then sprayed into a heated aqueous solution via a fine atomizing nozzle. To enhance particle formation and solubilization, surfactants are added to the organic solution and aqueous solution. By using this method, the solubility of danazol was increased.

(p) Use of Precipitation Inhibitors

Super-saturation, which may result in drug precipitation or crystallization, is caused by a substantial rise in free drug concentration above equilibrium solubility. Utilizing inert polymers like HPMC, PVP, PVA, PEG, etc. that work via one or more of the following methods will help avoid this. Reduce the pace at which pharmaceuticals crystallize by increasing the viscosity of the crystallization media. Drug molecules are protected by a stearic barrier, and crystallization is prevented by particular intermolecular interactions on developing crystal surfaces. Adsorb onto host crystal surfaces, slowing host crystal development and resulting in smaller crystals.

(q) Solvent Deposition

This process involves dissolving the weakly water soluble medicines in an organic solvent like alcohol, depositing the solution over an inert, hydrophilic solid matrix like starch or microcrystalline cellulose, and then letting the solvent evaporate. An example of this technique is the use of liquisolid compacts to speed up piroxicam's dissolving rate. Using liquisolid compacts, the weakly soluble medication indomethacin's dissolving rate was accelerated.

(r) Precipitation

In this process, the medication that is not very soluble in water is first dissolved in an appropriate organic solvent, then it is quickly mixed with a non-solvent to precipitate the drug in nanosize particles. "Hydrosol" is another name for the prepared product. Hydrosols are colloidal aqueous solutions used for intravenous delivery that include drug nanoparticles of

poorly water-soluble medicines. They are made using a precipitation process in which a sizable amount of water (96–98% after mixing) and stabilizing chemicals such poloxamer and modified gelatins, which serve as "short term stabilizers," are added to the drug solution.

(s) Microremulsion Technology

Microemulsions are dispersions of two immiscible liquids that are thermodynamically stable, isotropically transparent, and stabilized by interfacial coatings of surface-active molecules. Simple agitation of oil, water, surfactant, and co-surfactant produces the microemulsions. The co-surfactant and surfactant work together to significantly lower the interfacial tension, sometimes even to temporary negative levels.

(t) Self Dispersing Lipid Formulation

The Self Dispersing Lipid Formulation contain oil and a surfactant mixture into which the drug is incorporated. They emulsify when mixed with aqueous environment.

(u) Micellar Technologies

Above a certain critical concentration, amphiphilic, ionic, anionic, or ampholytic molecules that may reduce a solvent's surface tension tend to group together to form micelles. Only solute concentrations above the critical micellar concentration and solution temperatures above the critical micellar temperature will result in the production of micelles.

6. Conclusions

This article has led us to the conclusion that a drug's solubility is its most crucial physical property for oral bioavailability, formulation, the creation of various dosage forms, therapeutic effectiveness, and quantitative analysis. The secret to achieving the objectives of a good formulation, such as excellent oral bioavailability, decreased frequency of dose, and improved patient compliance, along with a cheap manufacturing cost, is proper process selection for solubility improvement. The various methods mentioned above may be employed alone or in combination to improve the drug's solubility. Numerous methods including fold increases in solubility may improve solubility. The bioavailability of many medications is impacted by their solubility issues, necessitating the need for solubility improvement. With the aid of the numerous procedures outlined above, it is now feasible to improve the solubility of medications that are not very soluble.

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