IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A REVIEW ON SOLUBILITY ENHANCEMENT TECHNIQUE

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ABSTRACT-

. Solubility is the process of soluble solids in a liquid phase to give the same system. Solubility is one of the most important parameters for achieving the desired concentration of a drug in the distribution system to reflect the drug response. Water-soluble drugs usually require high doses to achieve plasma concentration after treatment orally. Low-melting aqueous melting is a major problem encountered with the construction of new chemical enterprises. Any medicine to be absorbed should be present in the form of an aqueous solution in the place of absorption. Water is the solvent of choice in the manufacture of pharmaceutical liquids. Most drugs have a weak acid and a poor foundation

water melting. Therefore various methods are used to improve the solubility of soluble drugs including micronization, chemical modification, preparation, solid dispersion, compaction, mixing, micellar solubilization, hydrotropy etc. The purpose of this review article is to explain solubilizaton techniques for effective absorption and improved bioavailability

Keyword-Particle size, cosolvents**,** Temperature,Pressure Molecule size.

INTRODUCTION-

An important and also often discussed but not yet fully resolved issue, the process of improving melting or dissolving remains a major challenge for researchers in design and process development. Melting and dissolving this is a key concept of any natural and chemical science that includes biopharmaceutical and pharmacokinetic considerations in the treatment of any drug [1]. non-biopharmaceutical. These properties such as level and absorption rate, distribution rate etc. [2].

Thus, according to IUPAC, melting can be defined as, the forming of a complete solution that is expressed as part of a solute set in a fixed solvent for the dissolution of that mixture. It is expressed as concentration, molality, mole part, mole measure etc. [3].

Table No -1 Solubility Expression-

Descriptive terms	Approximate volume of solvent in ml/gm 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
Insoluble	More than 10,000

.. Melting water solubility is a challenge that is often encountered in the testing of New Chemical Entities (NCE) and in the design and development. There are many ways that can be developed to improve its bioavailability properties. After oral administration, they are completely absorbed but show good melting in the gastric medium and good bioavailability. But this discovery of bioavailability depends on a few factors mentioned as drug ingestion of the lipophilic membrane. So in the melting of low concentration it is difficult to measure by analysis. Therefore in order to ensure the rapid formation and efficiency of the melting phase in order to select the appropriate formulation system for the most effective compounds with good penetration is introduced. [4,5]

It was August 2000, the U.S. FDA issued an Industrial Guide that included the Biopharmaceutical Classification System (BCS). BCS is the scientific framework for classifying a substance into a substance based on its fluid solubility and intestinal penetration. When combined with the in vitro elimination characteristics of a drug product, BCS considers three major factors: melting, rate of dispersion and intestinal penetration. These three factors control the level and intensity of oral drug absorption to produce strong oral dose forms. The BCS classifies four categories of drug substances on the basis of their solubility and susceptibility factors. [6]

Table 2: The Biopharmaceutical Classification system for drugs.

	H High solubility	**Low solubility**
High permeability	Cl Class I	Cl Class II
Low permeability	Cl Class III	Cl Class IV

PROCESS OF SOLUBILIZATION-

. It involves the breakdown of intermolecular or interionic bond in the solute, the separation of the solvent molecule to provide space for the solute solvent, the interaction between the solvent and the solute or ion molecule. [7] This solubilization process takes three steps-

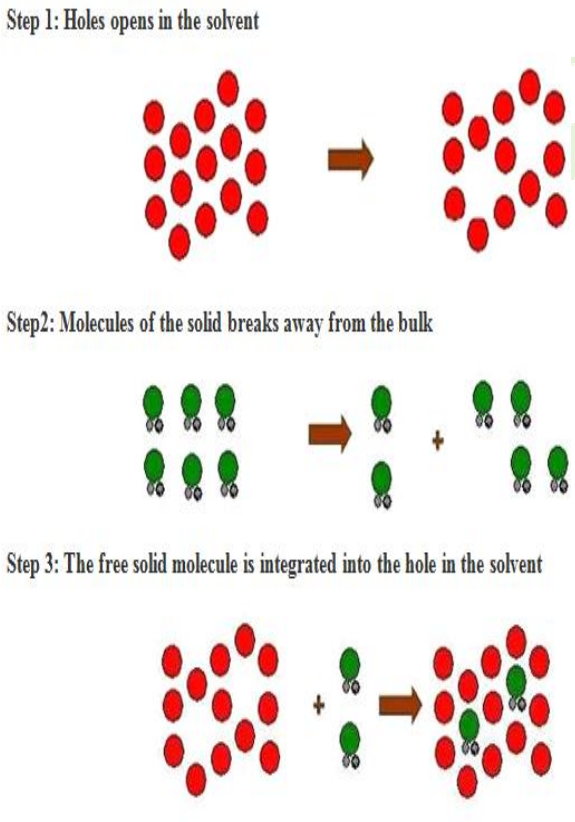

Fig.1 Process of solubilization

MPORTANCE OF SOLUBILITY-

1. The effectiveness of a drug depends on the availability of bioavailability and on the eventual melting of the drug cell.

2. Melting is one of the most important parameters for achieving the desired concentration of a drug in the circulation system in order to reflect the drug response.

3. Currently only 8% of new drug candidates are soluble and accessible.

4. About 40% of the available chemicals do not dissolve well in water.

5. Any medicine to be absorbed should be present in the form of an aqueous solution in the place of absorption.

FACTORS AFFECTING SOLUBILIZATION-

. Melting depends on the environment and the composition of the soluble, the apparent type of solidity and the temperature and pressure of the system.

. 1) Particle size:

Particle size affects melting. As the size of the article decreases, the surface area and volume increase. As the surface area of the particles grows it causes greater contact with the solvent.

The effect of particle size on melting can be described as

$$\frac{S}{S_0} = \text{Log} \frac{2yV}{2.303\ R\ T\ r}$$

Where,

S is the solubility of infinitely large particle

S_0 is the solubility of fine particle

V is the molar volume

y is the surface tension of solid

r is the radius of the fine particle

T absolute temperature

R universal gas constant

1) Temperature :

The temperature will affect the melting. When the solution process absorbs energy the temperature rises as the melting point will increase. If the solution process releases energy then the melting will decrease with increasing temperature. Generally, an increase in the temperature of the solution increases the solubility of the solid solute. A few strong solvents do not melt slightly in warm solutions. In all gases, the solubility decreases as the temperature of the solution increases

2)Pressure :

In soluble solvents, expansion of pressure creates solvency and reduced pressure reduces melting. In solids and solvents in liquids, pressure changes do not have all the purposes and objectives have no effect on solvency.

2) Molecule size:

When particles are large or the weight of a small atom makes an object insoluble. Larger particles are harder to combine with soluble atoms in order to dissolve an object. Due to the increase in nature the rate of carbon dioxide will expand dissolving as further scattering will reduce the size (or volume) of particles and make it easier to dissolve atoms by dissolving them.

2) Polarity:

The size of the solute atom and the soluble atom will influence the solvency. For the most part non-environmental solute atoms will decompose into non-polar solvents and polar solute particles will disperse into polar solvents.Polar solute atoms have both positive and negative atoms. In the event that the molten particles re-polar, then good parts of the bargains will pull in the negative parts of the bargains. This is a type of intermolecular force known as a dipole-dipole connection. All particles additionally have a form of intermolecular energy that is much weaker than a different force called the London Dispersion force where the positive cores of the solute atomic particles will absorb the negative iota electrons of the soluble particles. This allows the non-polar dissolvable to dissolve solute particles.

2) Solute & solvent environment:

Although only one gram of lead chloride (II) can be separated by 100 grams of water at room temperature, 200 grams of zinc chloride can disperse. The dramatic differences in the melting

of these two elements are a result of the diversity of their personalities.

2) Polymorphs:

Polymorphs can vary in the melting point. As a solid melting point is related to melting. The polymorph will therefore have different solubility. usually the width of the melting difference between the different polymorph is only 2-3 folded due to the small difference in free energy.

•

3)Rate of solution :

The rate of substance is measures how fast substances dissolve in solvent. A various factors affecting rate of solution like-

- **Particle size:**

Breaking the solute into smaller pieces increases its area, where the total area of solute particles increases; the solute dissolves very quickly because the action occurs only on each particle and thus increases its solubility.

- **Temperature:**

In solids and solvents, increasing the temperature not only increases the amount of solute dissolved but also increases the rate at which the solvent will dissolve..

- **Amount of solute already dissolved:**

If a small solute has already been resolved, dissolution occurs very quickly. As the solution approaches the area where no solute can be dissolved, dissolution occurs gradually.

• Motivating:

With liquid solids and solids, the stirring brings new solvent components into contact with the solute and leads to an increase in the solubility.]

WAYS TO IMPROVE SERVICE

There are various ways to improve the solubility of solvents. Some of the latest and most innovative methods techniques to improve the solubility are –

I) Chemical Modification

1) The formation of salt
2) Co-crystalization
3) Co-solvency
4) Hydrotrophy
5) Use of novel solubilizers
6) Nanotechnology

II) Physical Modification:

1. Reduce particle size

a) Normal method

b) Doing small things

c) Nanosuspension

2. Modification of crystal pattern

a) polymorphs

b) psuedopolymorphs

3. Complexity

a) body composition

b) mixing method

c) the corresponding rain method

4. Strategies Based on Complex Integration

a) Lyophilization

b) Microwave irradiation method

5. Solubilization by surfactants

a) Microemulsion

b) A microemulsifying drug delivery system

6. Distribution of drugs to carriers

a) Solid solution

b) Solid dispersion

i) The merging process

ii) Melting method

iii) Drying

iv) Lyophilization

v) Hot melt extrusion

vi) Disposal method

III) pH adjustment

IV) Supercritical fluid process

V) Liquisolid technique

VI) Polymeric alteration

Chemical Modification:

1. The formation of salt-

Salt formation is a common and effective way to increase the rate of solubility and solubility of acidic and basic drugs. Salts of acidic and base drugs, in general, have a higher solubility than their corresponding acid or base forms. In solid dosage forms, the solubility rates of the salts of a few compounds with a weak acid under the pH conditions of the stomach (GI) were much higher than those of their free acid species. Alkaline iron salts of acidic drugs such as penicillin and solid acid salts of basic drugs such as atropine are more soluble in water than parent drug [9].

. 1. Co-crystalization-

Co-crystallization alters cell interactions and is considered another promising way to improve drug properties. A more pure co-crystal definition could be “a multicomponent crystal formed between two solid compounds under ambient conditions, in which at least one component is an ion or acceptable molecule. Co-crystallization overcomes various physical, chemical or physiological APIs. The Mechanism of co solvency favors the elimination of non-polar solute by reducing facial tension. The most suitable co-crystal can be selected using analytical techniques and logical physicochemical studies that include melting and stabilization investigations Pharmaceutical Co-crystal crystals basically consist of two components namely API and pre-co-crystal [10].

• Different methods of co-crystallization:

1) Solvent solvent

2) Grinding

3) Slurry Co - Crystallization

4) Grinding Solvent drop (Grinding Modification)

5) Hot melt extrusion

6) Sonocrystallization Method**.**

. • Character Frames:

1) Melting

2) High wavelength

3) Stability

4) Internal termination

5) Bioavailability

6) Melting Point

7) Melt (hot stage microscope)

8) XRD

9) Calorimetry Scanning (DSC)

3. Consolidation of Co-solvency / Solvent:

It improves the solubility of a soluble water soluble by incorporating a soluble water solution where the drug is soluble by reducing the surface tension between the aqueous solution and the hydrophobic solute. The form of medicine is always liquid. High-dissolved lipophilic or crystalline composites with high solubility in solvent mixtures may be suitable for the melting process. It has found its main use in parental doses due to the low toxicity of many soluble solvents, as well as its high potential compared to solvents to dissolve non-earth-based drugs [11].

• Most widely used cosolvents-

Glycerol, propylene glycol, PEG 400, Dimethyl Sulfoxide, Dimethyl Acetamide, Ethanol, n-Octanol cosolvents are widely used.

• Benefits of integrating co-solvency / solvent Blending-

1. It has a high concentration of soluble drugs, is easy and quick to develop, produce and test.

2. It can be combined with other solubilization techniques and pH adjustments to improve the melting of non-soluble compounds.

• Disadvantages of co-solvency / solvent Blending-

1. Toxicity and tolerance associated with controlled solvent level should be considered

. Hydrotrophy -

It is a solubilization process in which the addition of a large amount of second solute results in an increase in the dissolution of the existing solute. How it improves solubility is closely related to complexity involving weak interactions between hydrotropic agents such as sodium benzoate, sodium acetate, sodium alginate, urea and insoluble drugs. Hydrotropic agents are ionic organic salts. Hydrotropic solutions do not show colloidal properties and include weak interactions between the hydrotropic agent and the solute. [12]

• .The beauty of hydrotrophy-

1. Hydrotropy is suggested to be higher than other solvents, such as solvent, micellar solubilization, co solvency and salting in, because the solvent

component is independent of pH, has high selectivity and does not require emulsification.

2. The solvent is independent of pH, hydrotrophy has high selectivity and does not require emulsification.

5) Use of the novel solubilizer:

The solubility of a soluble plant can be enhanced with a variety of solvents. Ex. Conventional solubilizerPolysorbates, PEG 400 Sepitrap, Soluplus, Povacoat, dendrimers, improve melting hydrophobic API. [14]

• Sepitrap as a Novel Solubilizer- In less than 5 minutes, 80% of solvents are extracted from the SepitrapTM (Microencapsulated solubilizer for strong dosage use) and are therefore available to solubilize the drug. The dosage of sepitrap and drug (2: 1) is good for improving the rate of elimination and at the same time does not affect the properties of the pills and can be used without any inventive barriers [15].

• Dendrimers- act as solubilizing agents to capture both hydrophilic and hydrophobic drugs and are known for their three-dimensional, monodispersed, large branch, and macromolecular and nano scopic architecture with a number of end-to-end functional groups found respectively. repetitive reactions. Dendrimers are considered to be unimolecular vertical micelles and their micellar structure remains stable at high concentrations even solvent.

1. . 6) Nanotechnology

2. Specify in the research and application of materials and structures at the nanoscale level of approximately 100 nanometers (nm) or less. In many new chemical companies for very low melting, the oral enhancement of bioavailability by micronization is not enough because the micronized product has a very low dispersion area and the next step was nanonization. Preparatory methods such as digestion, high pressure homogenization, vacuum deposition, and high temperature evaporation can be used

• Benefits of nanotechnology-

3. 1. It results in the production of nano or circular particles of small size with smooth surfaces and distribution of particle size and high precision areas, resulting in increased melting and melting.

II) Physical Transformation-

1. Reduce part size

-a) Normal method

b) Doing small things

c) Nanosuspension

Solubility of a tree is often closely related to the size of the particle. As the particle size decreases, the surface area and volume increase. The larger surface area allows the interaction of the grater with the solvent resulting in an increase in melting. The bioavailability of soluble drugs is

usually related to the particle size of the drug. Increased surface area by reducing particle size improves dispersion structures and allows for a wider range of design methods and delivery technologies.

• Benefits of reducing particle size -

1. Efficient, renewable, economic means of improving melting

2. Increase the solution level in the case of chemical substances, because reducing the particle size increases the surface area of the solvent action.

3. Allows rapid penetration of solvent.

• Disadvantages of reducing particle size-

1. Due to the high charge of different small particles, there is a strong tendency for particle agglomeration.

2. Physical, mechanical stress may cause the breakdown of the active ingredient.

3. Heat stress that occurs during operation may indicate problems in processing hot agents.

a) A common way to reduce particle size-

The different methods involved in the common method of reducing particle size are cutting, compression, impact, extraction**,** joint impact and reduction. Common methods of reducing particle size, such as starting and drying the spray, rely on mechanical compression to separate the active component. Reduction in particle size therefore allows for economical, repetitive, and efficient ways to improve melting. However, mechanical forcing, such as digestion and digestion, often bring significant amounts of physical stress to a drug product that may cause degeneration. Potential thermal stress during production and drying of the spray is also considered when considering sensitive or unstable active agents. Only through traditional methods of improving solubility is it possible to increase the solubility of soluble drugs**.** upto desirable level.

b) Micronization-

It is a good idea to reduce the particle size that can convert coarse particles into particles less than 5 μ in diameter. Micronization results in the uniform distribution of particles of small particles in order to develop a uniform scale method. As micronization process occurs the surface area increases with the reduction of particle size and the solubility increases. Micronized wood material properties such as particle size, size distribution, composition, surface properties, and agglomeration behavior and powder flow are influenced by the type of micro-materials used. Mechanical contact, spray drying and supercritical fluid (SCF) technology are the most commonly used methods for producing very small chemical particles. According to Noyes - Whitney postulations, micron-based drug administration is an important way to improve the bioavailability of water-soluble drug substances.

• Micronization Strategies-

a) Jet grinding machine / liquid milling machine or micronizer

b) Stator columns of Mill rotor

c) Microprecipitation & microcrystallization

d) Controlled gloss

e) Supercritical fluid technology

f) Sprinkle the liquid into a liquid

• Benefits of micronization–

1. It provides uniform particles by increasing the area and dispersing the particle size.

• Disadvantages of micronization–

1. . The high energy process, which causes the crystal lattice of the tree and this, may result in the formation of abnormal or amorphous regions in the final product.

2. Amorphous regions are not thermodynamically stable and are vulnerable to crystal regeneration when stored mainly in hot and humid conditions.

c.) Nanosuspension:

This technology is used in medicines that are insoluble in water and oil. Medical nanosuspension biphasic systems consisting of nano-sized drug particles in a liquid vehicle formed by surfactants for oral or topical administration or parenteral administration and lungs. Distribution of solid particle size in nanosuspensions is usually less than one micron with an average particle size between 200 and 600 nm. Nanosuspension is produced by low technology and high technology. Advanced technology includes a variety of technologies such as nanoeedege, nanojet technology, milling tech (Nanocrystals).

• Benefits of nanosuspension -

1. In nanosuspension the particle size of the drug is reduced which increases the surface area which also increases the solubility, melting point, and ultimately the presence of bioavailability.

2. Nanosuspension suspension leads to improved accessibility.

3. Nanosuspension results in increased bioadhesion and longer duration of action.

2. Modification of crystal structure- a) Polymorphs

b) Pseudopolymorps

Polymorphism is the ability of an element or a compound to glow in more than one crystal form. The different polymorphs of the drug are chemically similar, but exhibit different physicochemical properties including melting, melting point, density, texture, stability. Similarly the amorphous type of tree is always more suitable than the crystalline form due to the higher potency associated with local expansion. Order of dispersion of different solid types of drug Amorphous> Metastable polymorph> Stable polymorph**.**

3**. Difficulty-**

Is the relationship between two or more molecules to form a non-binding business with well-defined stoichiometry [19].

There are two types of complex: -

1. Stacking complexes:

It is driven by the association of a non-drug environment with a compound agent this leads to the removal of a non-tropical environment in contact with water. Stacking can be the same or mixed, but it results in a clear solution.

2.Inclusion complexes:

It is formed by inserting a non-polar molecule, a circuit of one molecule in the hole of another molecule or group of molecules. Cyclodextrine and its derivatives are commonly used in combination.

a) Body composition-

In this case the CDs or polymer suitable and the drug are mixed well with trituration in the mud and passed through a suitable filter to determine the required particle size in the final product. It is an easy method of trituration.

b) How to mix-

This method is based on immersing CDs or polymer suitable with a small amount of water or hydro alcoholic solutions to be converted into pastes. The drug is then added to the top dough and mixed for a while. The strained mixture will be dried and passed through a sieve.

c) Co-precipitate method-

The required amount of the drug is added to the CD solution or a suitable polymer. The complex is kept under magnetic resonance by controlled process parameters. The complex is protected from light. The resulting precipitate is separated by vacuum filtration and dried at room temperature to avoid building fluid loss from the inclusion complex. This method works in the industry.

4.Inclusion Complex Formulation Based Techniques-

a) Lyophilization: How to Freeze:

In this process, the solvent process from the solution is eliminated by primary freezing and subsequent drying of the solution containing both drugs and CDs or polymer suitable for reduced pressure. Lyophilization is highly dependent on the unique properties of water and its role such as solvent, gas, diluent, plasticizer, stabilizer. It is an alternative to melting and involves the mixing of drug and carrier molecules into a normal solvent. **[20]**

• Advantages of lyophilization / frize-drying technique -

1. Lyophilization / ice drying method is considered suitable for powdered, amorphous powder with a high degree of interaction between the drug and a suitable polymer.

2.Thermolabile materials can be successfully made into a complex form in this way.

• Disadvantages of lyophilization / frize-drying technique-

1. Use of special equipment

2. A process that is time consuming, and produces poor quality flour product.

. b) Microwave Irradiation Method:

It involves the reaction of microwave radiation between a drug and a complex agent using a microwave oven. The drug and the CD at a specific molar rate dissolve in a mixture of water and organic solvent in a specified portion into a circular bottom flask. The mixture reacts for a short time about one to two minutes at 60 ºc in the microwave oven. After completing the reaction, a sufficient amount of solvent mixture was added to the reaction solution above to remove residue, free drug and CD. The rain is separated by a whatman filter paper, then dried in a 40 ºc vacuum oven for 48 hours.

5) Solubilization by surfactant-

Molecule surfactants have cool, non-white surfaces. Many surfactants comprise a portion of the hydrocarbon connected to the polar group. The polar group can be anionic, cationic, zwitterionic or nonionic. When small polar molecules are added they can accumulate in the hydrophobic core of micelles. This process of solubilization is very important in industrial and environmental processes. The addition of surfactants reduces local tension and increases drug solubility by increasing the dissolution of lipophilic drugs in a wet environment.

a) Microemulsions-

. The micro emulsion is an optically precise, isotropic, thermo dynamically stable precision, translucent system, consisting of a mixture of oils, hydrophilic surfactant and hydrophilic solvent soluble in water soluble. Conditions for surfactant selection are HLB and non-toxic. When in contact with water, the formulation self emulsifies and forms a clear emulsion of small and uniform oil droplets that contain soluble soluble solvents. Microemulsions have been used to increase the solubility of many soluble drugs in water, as well as the incorporation of oral, parenteral protein. Oil-in-water (o / w) microemulsion is a highly efficient solvent, which is expected to increase the solubility by dissolving low-soluble compounds into an oil phase. They can also improve oral bioavailability by reducing droplet size (<100 nm), and thus increase absorption rate due to changes in surfactant-permeability **[14]**

. • Benefits of microemulsions–

a)Ease of preparation, clarity, filtration ability and integration of many different solubility drugs.

b) Drug delivery programs:

It uses the in situ concept of emulsion formation in the intestinal tract. A mixture of oil, surfactant, co-surfactant, one or more hydrophilic solvent and co-solvent form a clear isotropic solution known as a self-emulsifying drug delivery system (SEDDS). Self-emulsifying drug delivery systems (SEDDS) and self microemulsifying drug delivery systems (SMEDDS) are isotropic

solutions for oil and surfactant that cause oil-based microemulsions in small volumes where there is water. These colloidal formulations appear in oral administration and act as microemulsions for oil in water.

. 6) Distribution of drugs to carriers-

a) Solid solution-

A solid solution is a combination of two solid crystals that exist as a new solid crystal. A mixed crystal is formed because the two parts shine together in a single-phase system. Therefore, it is expected to produce significantly higher dissipation rates than simple eutectic systems.

Amorphous precipitation- Amorphous rainfall occurs when a tree degrades like an amorphous carrier. The high potency of a tree in this system usually produces much higher melting values than the corresponding crystalline forms of the tree [

Ways to prepare solid dispersions -

i) The Fusion Process:

The carrier is heated to a temperature just above its melting point and the tree is placed in a matrix. The mixture is cooled by stirring constantly to dissolve the drug evenly throughout the matrix. Other possible contributing factors include the solving effect given by the carrier itself, enhanced hydration or reduction of local hydrophobicity, mixing, and drug coating in a modified polymorphic structure of modified thermodynamic structures [23]

ii) Melting method:

The carrier and the active ingredient are dissolved in a suitable living solvent. This solvent evaporates at high temperatures or under vacuum. As the solvent is released, high saturation of super saturation occurs followed by simultaneous rainfall of nutrients leading to solid residue. The co precipitate and then dried under a vacuum to remove any solvent that adheres freely to the particles. Removal of equal amounts of solvent is suggested. Highly sensitive techniques such as differential temperature analysis (DTA), different scanning calorimetry (DSC), thermogravimetric analysis (TGA), and less sensitive processes such as spectroscopy, gravimetry can also be used to demonstrate complete solvent removal [24].

iii) Fusion-Solvent Method:

The network company is melting and the drugs are / are being integrated into a solution. If the carrier is able to hold a portion of the liquid but retains its solid properties, and if the liquid is innocent, the need for solvent removal is eliminated. The method is useful for drugs with high soluble points or with thermolabile

iv) Spray Dry:

The carrier and the active ingredient are melted, suspended in a suitable solvent. This solvent evaporates by drying the hot air to remove the solvent. Due to the large droplet area, the solvent evaporates rapidly and solid dispersion is carried out quickly.

v**) Lyophilization**:

This method has been successfully developed to prepare strong dispersions of atambient temperatures and to avoid overheating during the preparation of thermosensitive drugs; spray dryer (SFD). SFD technologies include the atomization of feed feeds containing water-soluble or insoluble APIs and auxiliary substances into cryogenic fluid at ambient temperature to produce frozen freeze powder that will be dried later. This process offers various advantages compared to traditional solid dispersion techniques, which include amorphous structure and surface area**.**

. vi) Hot-melt Extrusion:

The active ingredients and the carrier are placed in a hot extruder barrel at a constant rate. When a mixture of the active ingredient and the handle are passed through hot screws, it is converted into a "liquid-like state". This condition allows for close and even mixing with high shear extruder screws. The exit hole, which contains voluntary death, prepares to melt in the required manner such as granules, pellets, films, or powder. An important advantage of the hot melt extrusion method is that the drug / network mixture is at a low temperature for about one minute, making the othermolabile drug somehow processed.

vii) Disposal Method:

The solid dispersion of the dissolved drug mixture is inserted into the pipes and lowered to the plate, where it solidifies into circular particles. The size, the shape of the particles can be influenced by factors such as melt viscosity and pipette size. Since viscosity is highly dependent on temperature, it is very important to adjust the temperature so that when the melting is lowered to the plate it hardens to a circle.

III) PH-

A bad soluble substance can be dissolved in water by changing the pH. In order to achieve melting in this way, buffer volume and tolerance of the selected pH are important to consider. Dissolved solvents that increase the natural pH within the dosage form to a higher extent than pKa of weekly acidic drugs increase the solubility of the drug, those auxiliary agents acting as alkalizing agents may increase the solubility of basic weekly drugs. [11**]**

• Benefits of pH adjustment-

1. Easy to edit and analyze.

2. Uses low composite values, consistent with high performance testing.

• Disadvantages of pH adjustment-

1. The danger of rain when diluted with water pH with a pH when the mixture does not melt slightly. Intravenous infusion can cause embolism, or oral contraceptives.

2. Toxicity tolerance in both the environment and the system associated with the use of unnatural pH and extreme pH should be considered.

3. As with all soluble and soluble systems, soluble wood in a wet environment is generally less chemically stable compared to solid crystalline formulations. Selected pH may

accelerate hydrolysis or cause other degradation processes.

IV) Supercritical fluid process-

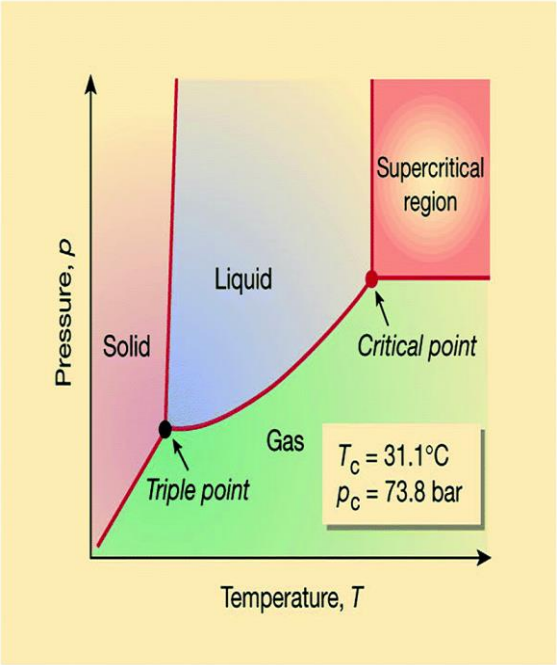

Figure 2 – Phase diagram of super critical fluid

. The most sensitive liquid is a liquid that is present as a single liquid in addition to its critical temperature and pressure. SCF reflects your characteristics in both liquid and gas in addition to its critical nature. It is safe, environmentally friendly, and economical. Low operating conditions (temperature and pressure) make SCFs attractive in medical research. At near-critical temperatures, SCFs are highly compressed, allowing moderate pressure changes to drastically change the density and transport characteristics of the liquid that determines its melting potential. Once the drug particles have melted within the SCF, they can be re-crystallized in a very reduced size.

V) Liquisolid Method-

In liquisolid form the liquid can be transferred to a free flowing, easily compressed and apparently into a dry powder by easily mixing with the selected carrier and coating materials. A portion of a liquid which can be a liquid medicine, suspension drug or drug solution in a suitable fixed fluid can be converted into an acceptable flow and pressure powder by mixing with selected powder equipment. The most acceptable and effective powder form for liquid medicine is liquisolid compact. Liquisolid is a new and promising method due to its simple production process, low production capacity, and is effective in the industry due to the good flow and integrated properties of the liquisolid structure. When a drug dissolved in a liquid car is placed in a carrier with a porous area and adjacent filaments such as cellulose, both absorption and advertising occur; that is, the liquid initially absorbed within the particles is trapped by its internal structure, and after the completion of this process, the insertion of the liquid into the inner and outer part of the porous carrier particles takes place. Then, coating materials with high attractive properties and a large surface area provide the liquisolid system with the desired flow characteristics [25].

Table no -3 Components of liquisolid system-

Component	Examples
Non volatile	Polyethylene Glycol 200, Poly Ethylene Glycol 300
Liquids	Glycerine , Propylene Glycol, Fixed oils
Disintegrants	Sodium starch Glycolate (Explotab, Primogel) ,Pregelatized Starch

Benefits of the liquisolid method:

1. The method improves the solubility and bioavailability of oral water controlled by soluble or insoluble drugs.

2. The method works in the industry.

3. It is useful for making oily / liquid drugs.

• Disadvantages of solid liquid method:

1.The high solubility of the drug in stable liquid drugs to improve the degree of dissolution and the presence of bioavailability.

2. It needs recipients of high-rise buildings and a certain high point

CONCLUSION-

With this article we conclude that, drug degradation is the most important factor in controlling the formation of a drug and the therapeutic efficacy of a drug, which is why it is a very important factor in the development of the drug. Drug eradication determining the action of oral absorption of soluble drugs and soluble is a basic requirement for the development and development of different dosage forms for different drugs. The different techniques described above alone or combined can be used to improve the solubility of a tree. Melting can be improved by many techniques and the amount of coagulation increases in melting. Due to the melting problem of many drugs their bioavailability is affected and that is why solubility enhancement is needed. It is now possible to increase the solubility of soluble drugs with the help of various techniques as mentioned in this article.

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