REVIEW ARTICLE

Self-emulsifying Drug Delivery System for Improvement of Solubility of Drug

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Abstract

In this review, we examine the solubility properties of compounds and the different ways to improve solubility for more efficient action. We also address the common variables that affect solubilities, such as polarity, polymorphs, molecular size, temperature, pressure, wildlife of the solute and flush, and particle scope. To overcome these solubility problems, various approaches have been taken to increase solubility. These include physical modification, chemical modification, and miscellaneous methods. One of the most efficient techniques we discuss is the Self-Emulsifying Medicine Transfer Scheme (self-emulsifying drug delivery system), which is suitable for emulsions with droplet sizes around 100 nm to 300 nm. We also discuss the further modification of SEDDS, which is the self-micro blending medication transfer system (self-microemulsifying drug-delivery system). SMEDDS is useful for droplet sizes around or near 50 nm, and we compare its advantages and disadvantages with those of emulsions. We also cover the criteria for selecting excipients such as oil, surfactant, and solvents for the groundwork of SEDDS and SMEDDS. In addition, we discuss the methods of preparation of emulsions and their characterization. Finally, we examine the different techniques for solidifying liquid/semisolid emulsions into solid preparations along with their advantages and disadvantages. We conclude with a list of dosage forms for oral administration. This review provides a comprehensive analysis of the solubility properties of compounds, focusing on the different approaches to enhance solubility for more efficient action. We also delve into the common variables that affect solubilities, including polarity, polymorphs, molecular size, temperature, pressure, countryside of the solute and solvent, and particle magnitude. To overcome these solubility problems, various approaches have been taken to increase solubility. These include physical modification, chemical modification, and miscellaneous methods. Among these, the Self-Emulsifying Treatment Delivery Scheme (SEDDS) stands out as an efficient technique that is suitable for emulsions with droplet sizes around 100 nm to 300 nm. Furthermore, we discuss the Self-Micro Emulsifying Preparation Transfer Organization (SMEDDS), which is a further modification of SEDDS and offers advantages over emulsions. We also provide an in-depth analysis of the criteria for selecting excipients such as oil, surfactant, and solvents for the training of SEDDS and SMEDDS. In addition, we explore the methods of preparation of emulsions and their characterization. Finally, we examine the different techniques for solidifying liquid/semisolid emulsions into solid preparations, highlighting their advantages and disadvantages. We conclude with a list of dosage forms for oral administration. This review aims to provide a comprehensive guide for researchers and professionals to overcome solubility issues and enhance solubility for more efficient drug delivery.

Key words: Self-emulsification, self-micro combining medicine delivery arrangement, solubility problem

INTRODUCTION

Solubility of a chemical compound refers to its ability to melt in a hard, liquid, or vaporous flush, creating a uniform key.[1] This is measured by the saturation concentration of the solvent, which means that adding more of the solute will not have any effect on the amount that can be dissolved. To determine solubility, the maximum dosage of an instant-release product is used. A volume of 250 mL is calculated based on conventional bioequivalence testing procedures, which involves administering medical material to three human test subjects along with a glass of water.

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Orally administered medications can only be fully absorbed if they are well soluble in gastrointestinal fluids and have high bioavailability. Two factors that affect bioavailability are drug water solubility and permeability through lipophilic membranes.

Drug molecules that are solubilized can be taken up by cellular membranes and transported to the site of pharmacological action. Since permeability and solubility are the key determinants of drug absorption *in vivo*, they cannister remain changed before improved through using improvement methods. For example, ill-solvable biopharmaceutical organization scheme (BCS) class II mixes pose numerous formulation challenges *in vitro*, including limited delivery options with little to no correlation to *in vivo* absorption, which makes dissolution testing increasingly difficult.

Medicinal businesses consume remained talented toward overcome tests with medications that are actual poorly solvable. However, persons that are a smaller amount soluble in water (fewer than 0.1 mg/mL) current approximately sole difficulties.

SOLUBILITY PARAMETERS

Hildebrand solubility boundary

TThe Hildebrand solubility limit ((δ) is particularly useful for non-polar materials such as many polymers. It delivers an arithmetical assessment of the level of communication amid resources and is a reliable indicator of solubility.[2] Materials with comparable values are likely to be miscible. The solubility parameter unified vigor thickness is a numerical value that describes the behavior of a certain thinner's relative solvency. It is derived from vaporization heat. The Hildebrand solubility limit is the four-sided cause of the unified vigor breadth and reproduces the total van der Waals force.

$$\delta = \sqrt{\Delta H\upsilon - RT/Vm} \quad (1)$$

Hansen solubility parameter

Charles M. Hansen, the founder of Hansen Solubility Limits, developed a set of parameters in his 1967 Ph.D. thesis that are used to predict whether two substances will form a solution. The limits are founded on the principle that "similar melts similar," meaning two molecules are considered "like" if they have similar types of bonds. Apiece particle consumes 3 Hansen limits, which are typically measured in MPa.

δ_d = Molecular forces that result in the dispersion of energy

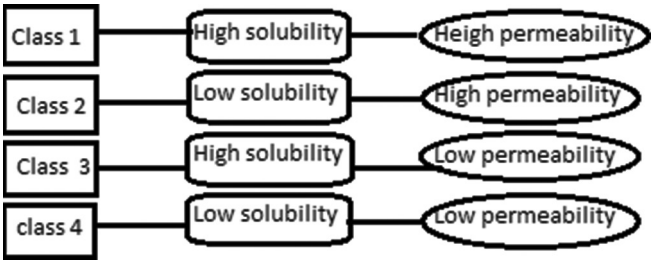
δ_p = Energy of the dipolar intermolecular strength amid bits

δ_h = Hydrogen liveliness creates connections amid particles.

BCS

The biopharmaceutical categorization scheme is founded on the gastrointestinal penetrability and aquatic solubility of solid instantaneous oral dosage forms. This system helps categorize pharmacological compounds and calculate the contributions of the three main parameters: Intestinal permeability, solubility, and quick-release solid oral dosage forms that dissolve and affect oral medication absorption. The use of this categorization system is important in the early stages of medication development and throughout its life cycle to control product change. It is a scientifically sound technique that has garnered interest in the pharmaceutical industry.[3]

BCS classification



FACTORS AFFECTING SOLUBILITY

Atom scope

The solubility of a particle is determined by its size, as the superficial share-to-capacity relation surges as the atom gets smaller.[4] The greater superficial part lets more of the solvent to interact with the particle. We can describe how solubility changes with particle size (2).

$$logS/S0 = \gamma V/2.303\ RTr \quad (2)$$

Temperature

The solubility of a substance generally decreases as the temperature rises, as the solution process absorbs energy in this process. Conversely, the solubility of a substance decreases due to the energy that is released when the solution process occurs. For example, when liquids are heated, some solid solutes become less soluble. In addition, as the fever of the answer increases, gases in the solution become less soluble.[5]

Pressure

In the case of vaporous solutes, an upsurge in heaviness promotes solubility while a diminution in weight reduces it.

The impact of pressure changes on a substance's solubility in a liquid and a solid is practically negligible.

Molecular size

When a substance has a high molecular weight or contains larger molecules, it becomes less soluble. This is because the larger molecules require more solvent molecules to surround them before they can dissolve. However, if the molecule has greater branching, it will result in smaller molecules, making it easier for the solvent to surround and dissolve the molecules. Therefore, organic molecules with greater branching tend to be more soluble.

Polarity

The expression "similar melts similar" income that solutes with alike divergence to the flush determination melt in it.[6] Polar solutes have positive and negative ends. Uncertainty the flush is too glacial, the negative end of the solute particles determination entice the positive end of the solvent molecules. In addition, London dispersion forces attract electrons from negative atoms in the solvent molecule toward positive atoms in the solute molecule. This allows the solute molecules to dissolve in a non-polar solvent.

Polymorphs

Polymorphs can have different solubilities and melting points.[7]

Rate of solution

How quickly things dissolve in solvents is gauged by the rate of solution. Several elements that impact the pace of solution, such as;

Scope of the atoms

Contravention of a solute particle into small pieces surges the state surface part, which, in turn, increases the degree of closure. This happens because the shallow part is the only place where the solute dissolves, so by breaking it down, there are more surfaces available for dissolution to occur. As a result, the solute dissolves faster, leading to a faster rate of solution.[8]

Temperature

Both the volume of the soluble solute and the pace at which it will dissolve will rise with temperature for both liquid and solid solutes. The opposite is true for gases.

Amount of solute already dissolved

If the solution previously contains only a small amount of solute, dissolution happens rather quickly. Dissolution happens more slowly when the solution gets closer until no more solutes can be dissolved.

Stirring

Stirring increases the liquid and solid solutes are both soluble by bringing new solvent into contact with the solute.[9]

TECHNIQUES FOR SOLUBILITY ENHANCEMENT

Solubility augmentation strategies can be used to increase the solubility of medicine by changing its physical or chemical makeup or using other methods.

Physical modification

Drug dispersion in eutectic mixtures, solid solutions, solid dispersions, and cryogenic methods[10] – alteration of quartz morphology, including polymorphs, formless forms, and manifestation; atom scope decrease techniques including micronization and nanosuspensions.

Chemical modification

Salt production, derivatization, complexation, usage of buffers, and pH change.

Miscellaneous methods

Employment of adjuvants such as surfactants, solubilizers, solvency, and hydrotropes throughout the supercritical fluid process.

Self-emulsifying medication distribution scheme

The spoken way of management is the most usually used technique of medication delivery due to its potential benefits. This results in poor and irregular oral bioavailability, as solubility regulates the rate at which these medications are absorbed from the gastrointestinal tract (GIT).[11] Therefore, suitable formulations must be developed to improve their bioavailability. However, self-emulsifying drug delivery system (SEDDS) and microemulsions have been reported to be effective in overcoming these issues.

SEDDS has gained attention for the situation aptitude to increase the bioavailability of medicines with poor marine solubility. They stand for isotropous blends of hydrophilic

solvents and cosolvents, oils, and surfactants. They are typically used in formulations to recover the spoken pre-occupation of lipotropic medications. SEDDS can be administered orally in the form of soft or hard gelatine capsules, which, when diluted with water, produce fine and relatively stable oil-in-water emulsions. They rapidly spread in the GIT, and the procedure of self-emulsification is facilitated by the motility of the stomach and intestine. These systems are beneficial because the medication is present in a melted state with a small drop scope, creating a large superficial part for medication pre-occupation.[12]

REWARDS OF SELF-MICROEMULSIFYING DRUG-DELIVERY SYSTEM (SMEDDS)

Development in oral bioavailability

Numerous medications that are ill-solvable in water have limited bioavailability due to poor absorption, which is directly related to the dissolution rate. However, SMEDDS can improve bioavailability by delivering the medication to the gastrointestinal area in a solubilized and micro-emulsified format with drop sizes amid 1–100 nm. This increases the specific external part of the drug, resulting in much higher bioavailability than the tablet format. For instance, halofantrine's bioavailability was found to have increased by 6–8 times.[13]

Scale-up and production efficiency

SMEDDS has a significant advantage ended additional medication delivery methods similar to hard dispersals, liposomes, and nanoparticles – it increases bioavailability and is easy to fabricate and scale up.[14] SMEDDS can be manufactured on a large scale using rudimentary and reasonable equipment such as a modest churn with a campaigner and volumetric runny substantial equipment, which clarifies why businesses are absorbed in this method.

Reduced intra- and inter-subject variability, and the impact of diet

There is a lot of variation in how well medications are absorbed in our bodies, both between individuals and within a person over time. This can make the medications less effective and increase the likelihood that patients will not take them as directed. One factor that can affect how well a medication works is whether it is taken with food. However, SMEDDS (self-microemulsifying medication distribution organizations) can help improve the absorption of certain medications. Research has shown that SMEDDS can be effective regardless of whether they are taken with food, and can also provide consistent results in terms of how the medication is distributed in the bloodstream.[15]

No impact on the procedure of fat ingestion

SMEDDS is a type of drug delivery system that is not affected by pancreatic lipase action, varied micelle manufacture, bitterness salty emulsification, or lipolysis, which are factors that can impact the performance of additional lipid-based medication transfer systems. SMEDDS brings medicine in a micro-emulsified method that container simply penetrate the mucin and water unstirred layer. As a result, the drug can be absorbed without the need to be digested first.[16]

Increased capability for loading drugs

Likened to traditional fat answers, SMEDDS has the advantage of taking a greater drug loading volume due to the higher solubility of amphiphilic surfactants, co-surfactants, and co-solvents, which is particularly useful for medicines with moderate partition coefficients (2log P>4) but poor water solubility.

Advantages of SMEDDS over emulsion

It is worth noting that SMEDDS (Self-Micro-Emulsifying Medicine Distribution Scheme) offers the same benefits as emulsion when it comes to promoting the solubility of hydrophobic medicines. However, unlike emulsions, SMEDDS does not suffer from creaming over time. It is a member of a thermodynamically stable system, which makes it easy to store.

The microemulsion created by SMEDDS is highly stable and transparent. The size of its droplets distinguishes it from conventional emulsions. While ordinary emulsions have droplets ranging from 0.2 to 10 m, SMEDDS droplets typically range from 2 to 100 nm, which are called nanoparticles. Due to their small size, these nanoparticles have a larger surface area for absorption and dispersion, making it easier for them to be absorbed and enter the gastrointestinal system. This enhances the drug's bioavailability compared to solid dosage forms.

SMEDDS offers various delivery options such as hard gelatin capsules and softgels.

Unlike emulsions, which are limited to being administered as oral solutions, gelatin capsules or tablets can be produced.[17]

Disadvantages of SMEDDS

i. Interaction of fill with the capsule shell in case of L-SNEDDS
ii. At low temperatures, there might be precipitation of APIs and/or some excipients, which can be liquefied again when warmed to room temperature

iii. Low drug loading capacity,
iv. High concentrations of surfactants and storage temperature, etc.

SELECTION OF EXCIPIENTS FOR SELF-EMULSIFICATION IN SSEC

Oils

Oil plays a crucial role in the creation of many emulsions. It serves as a vehicle for dissolving lipophilic medication.

Classification of oils

a. Naturally-derived oils
b. Synthetic or chemically modified oils.

Naturally derived oils

Natural oils have a weak ability to dissolve a significant quantity of lipophilic medication; hence, they are not usually employed as the oil fraction in multiple emulsions.

Synthetic or chemically modified oils

For instance, many emulsions can employ hydrolyzed vegetable oils. Chemically, altered oils have greater self-emulsification capabilities since they have their own surfactant qualities.

Advantages

i. Oils serve as a vehicle for the dissolution of lipophilic medicines
ii. Oils may self-emulsify more easily than other substances.

Disadvantages

i. Since vegetable oils have a low ability to dissolve lipophilic medicines, they are not employed in the preparation.
ii. Instability.

Surfactants

Amphiphilic compounds called surfactants have both hydrophilic and lipophilic components. Surfactants can be employed to speed up the multiple emulsions' capacity to self-emulsify, which helps to enhance or raise the bioavailability of medications with low absorption rates. Diffusion and stranding are two terms used to explain the intricate dynamics at play.[18]

Classification of surfactants

According to their hydrophilic-lipophilic balance (HLB) values, surfactants are categorized.

1. Hydrophilic surfactants: These are those having higher HLB, that is, 8–18
2. Lipophilic surfactants: These are those having lower HLB, that is, 4–6.

Factors will influence the selection criteria for the type of surfactant to be employed in the creation of multiple emulsions.

a. The efficiency of its emulsification
b. The stability and safety of the emulsion that is created when an aqueous medium is contacted
c. The quantity of surfactants to be employed is crucial since using too much might irritate the digestive tract
d. It was recommended that the concentration of surfactants employed be in the range for stable multiple emulsions.

Advantages

1. Surfactants can be employed to speed up the self-emulsification of multiple emulsions, increasing the bioavailability of medications that are difficult to absorb
2. Surfactants have good spreading characteristics and hasten cloud formation, allowing for quick emulsification.

Disadvantages

The high concentration of surfactant may irritate the digestive tract.

Table 1 lists examples of surfactants along with their kinds.

Solvents/co-solvents

To improve the solvent ability of the formulations, particularly those that include a high concentration of hydrophilic surfactants, solvents, and co-solvents are added to multiple emulsions. Multiple emulsions need high solvent capacities to dissolve a lot of lipophilic medicines or hydrophilic surfactants. Organic solvents such as alcohols and other volatile solvents would not be the best choice since they will migrate into the gelatine capsules' hard and soft shells, precipitating the lipophilic medicines [Figure 1].[16]

Advantages

1. The formulation's solvent capacity is enhanced
2. Solvents can dissolve a significant amount of lipophilic medication.

Table 1: Types of surfactants

Surfactant	Examples
Amphoteric Surfactants	Soya phosphatidylcholine, Egg Phosphatidylcholine, and Egg Lecithin
Non-Ionic Surfactants	Poloxamer 188, Span 85, and Tween 80.
Ionic Surfactant	Sodium cholate, Sodium taurocholate, Sodium coco ampho acetate, and Sodium dodecyl Sulfate

Disadvantages

The large amounts of organic solvents are harmful to humans.

MECHANISM OF SELF-EMULSIFICATION

Emulsion creation is a process known as self-emulsification. In this process, the increase in entropy that favors dispersion is countered by the energy required to expand the surface area of the dispersion, resulting in emulsification. Equation 3 represents the change in free energy (G) related to the emulsification process, excluding the free energy of mixing.

$$G = \Sigma Ni4\pi ri2\ \sigma \quad (3)$$

Self-emulsification can only occur naturally in situations where there is little interfacial energy. However, the resulting emulsions are generally not thermodynamically stable, as the oil and water phases tend to separate over time, decreasing the system's interfacial area and free energy. Emulsifiers create a barrier around the oil droplets, thereby lowering interfacial tensions and the system's free energy. In the case of self-emulsifying systems (SES), the aqueous phase is first introduced into the oil phase with moderate agitation. Unless the interface between the two phases is disturbed, the aqueous phase will permeate into the oil phase. Emulsification takes place when oil droplets form. The ease of water penetration on the surface of the droplets determines how easily an emulsion forms. The process of self-emulsification can be affected by several variables, including the oil/surfactant combination, the amount of surfactant used, and other factors.

The properties of the emulsion will vary depending on the presence of the therapeutic compound.[19]

Phase diagram

A phase diagram is a graphical representation that shows the physical state of a substance at different pressures and temperatures. These diagrams provide a clear picture of the various phases that exist in a system under equilibrium conditions. They are helpful in analyzing the impact of stage variables on a system. Equilibrium diagrams, phase diagrams, and constitutional diagrams are all names given to these diagrams. A single-component phase diagram can be represented by a simple one- or two-dimensional graph that shows the phase change in a material as temperature and/or pressure varies.

Phase rule

The phase rule connects the number of components in a system and its circumstances to the physical state of a mixture. The rule may be expressed as follows when temperature and pressure are the state variables:

$$f = c - p + 2 \quad (2)$$

Show the differences in the states of matter of different elements or compounds in relation to pressure and temperature. The following are the spots on the phase diagram Figure 2:

Triple point

Refers to the location where the three states of matter – gas, liquid, and solid – coexist.

Critical point

Is the location when a material cannot be told apart from its liquid and gaseous forms.

Fusion (melting) (or freezing) curve

Is the curve that shows the transition from a liquid state to a solid state.

Vaporization (or condensation) curve

Is the curve that shows the change from the gaseous to the liquid state.

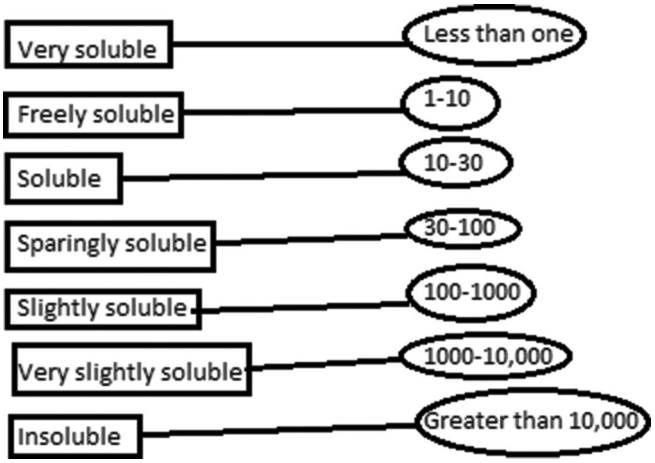


Figure 1: Classification of solubility in terms of quantification as per United States Pharmacopeia and BP

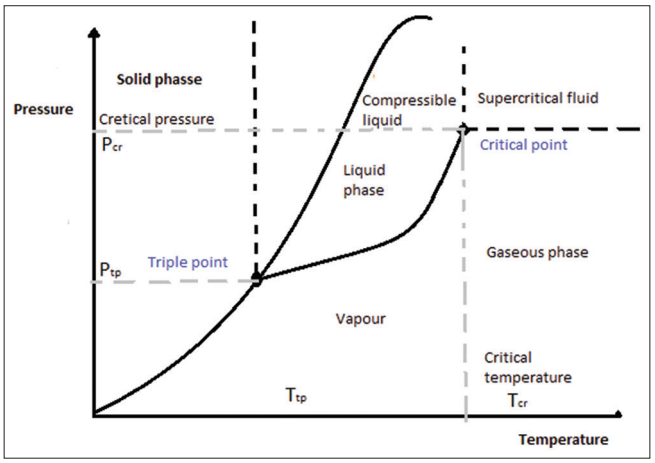


Figure 2: The phase diagrams

Sublimation (or deposition) curve

Is the phase transition curve on a phase diagram a representation of the change from a gaseous to solid state.

METHOD FOR PREPARATION OF EMULSIONS

High-pressure valve homogenizers and traditional rotor-stator homogenizers are commonly utilized during the emulsification process to create multiple emulsions. Another method of producing multiple emulsions is by pushing the primary emulsion through a small porous membrane or channel arrays into a continuous phase liquid. The subsequent techniques are used to create the various emulsions:

1. Two steps emulsification (double emulsification)
2. Phase inversion technique (one step technique)
3. Membrane emulsification technique
4. Microchannel emulsification.

Characterization

As the system is complex and the particles are colloidal, it is crucial to accurately characterize the multiple emulsions. This is necessary to ensure the quality, stability, and kinetics of the product's release which are regulated. Therefore, it is important to use sensitive and precise characterization techniques.

The following are the characterization techniques:

1. Particle size
2. Zeta potential (ZP)
3. Shape and morphology
4. Crystallinity and polymorphism

Particle size

Particle size is a crucial factor when it comes to gastrointestinal absorption and the ability of the reticulon endothelial system to remove particles. The particle size range of emulsions is typically between 100 nm and 1000 nm. The most commonly used and effective techniques for measuring the particle size of different emulsions are laser diffraction and photon correlation spectroscopy (PCS). PCS is also known as light scattering in motion. This method involves measuring the variation in scattered light intensity caused by particle movement. The PCS approach is highly sensitive and accurate.[2]

Importance

1. To measure medication release and absorption, as well as their rate and extent
2. According to emulsion droplets that are smaller may result in improved bioavailability.

Polydispersity index (PDI)

Different emulsions are naturally polydisperse, meaning that the PDI can be calculated to determine their monodispersity. A lower PDI value indicates a higher level of monodispersity in the emulsion. An ideal PDI value, as per most academic sources, is <0.3. PCS is commonly used to calculate the PDI. A PDI of <0.1 indicates a highly homogeneous particle population, while high PDI values suggest a wider size variation.

Importance

1. To ascertain the particle size distribution's breadth
2. The PDI is crucial for figuring out how big the emulsion droplets are.

ZP

The stability of a nano-dispersion during storage is determined by its ZP, which represents the electrical charge on the droplet surface. The ZP values, whether positive or negative, are widely recognized as indicators of the dispersion's long-term stability. The ZP value was found to be unaffected after 3 months of storage. The ZP determines the amount of repulsion between similarly charged particles in the dispersion. Repulsion prevents particles from aggregating, and a high ZP value (either negative or positive) electrically stabilizes the dispersion of nanoparticles. In contrast, a low ZP value indicates that attraction outweighs dispersion, leading to flocculation or congealing. A ZP value of −30 mV is sufficient for the effective stability of nanodispersion. PCS can be used to measure the ZP of a nanodispersion.[20]

Importance

1. To anticipate and regulate the stability of colloidal suspensions or emulsions
2. Key for understanding the dispersion and aggregation processes
3. For determination of stable formulation.

Crystallinity and polymorphism

Two commonly used techniques for assessing the crystallinity and polymorphic behavior of the self-emulsified pellet's constituents are the differential scanning calorimeter (DSC) and X-ray diffractometry (XRD). DSC provides information on the melting points and crystallization patterns of both solid and liquid components of the particles, while XRD is used to determine the crystal structure of certain crystalline compounds. DSC uses the fact that different lipid modifications have different melting points and melting enthalpies to analyze the materials. On the other hand, XRD measures the diffraction pattern and intensity of each

form of crystalline material to determine the lipid and drug molecules' structure and how lipid molecules will be arranged and behave in phase.

Solidification transforming liquid/semisolid emulsions into solid preparation techniques

The stability of emulsions can be maintained by transferring the liquids or semisolid emulsions into the solid formulation.

Filling capsules with liquid and semisolid self-emulsifying mixtures

The straightforward and widely used process for encasing liquid or semisolid multiple emulsions formulations for oral administration is capsule filling. Processing processes for semisolid formulations are as follows:

Heating the semisolid excipient to a temperature that is at least 20°C higher than its melting point;
1. Including the active ingredients (while stirring)
2. Using the liquid mixture to fill the capsules
3. Room-temperature cooling.

It includes a two-step method for liquid formulations:
1. The body and cap of the capsules are then sealed by banding or micro-spraying once the formulation has been added
2. To manage the distribution of peptides or insoluble medicinal compounds, liquid-Oros technology has been developed along with advancements in capsule technology.

Advantages

1. Production simplicity
2. The possibility for large drug loading (up to 50% [w/w]) and low-dose, very powerful drug suitability.

Disadvantages

Higher amount of drug cannot be loaded.

Spray drying

To prepare a formulation for spray drying, lipids, surfactants, medicine, and solid carriers are combined and solubilized. Once the formulation is solubilized, it is atomized to create droplets. These droplets are then received in a drying chamber and exposed to regulated temperature and airflow conditions. This process causes the volatile phase, such as water in an emulsion, to evaporate, resulting in the formation of dry particles. The choice of atomizer, temperature, drying chamber design, and optimal airflow arrangement is based on the product's drying capacity and the powder's specifications. For example, amlodipine 1.1% can be used as a medicine in this process.

It undergoes into three-step process:
1. Mixing of drug with lipid, surfactant, and solid carriers
2. Spray the dryer with a solubilized liquid composition
3. Collection of products.

Advantages

Fully dried form product.

Disadvantages

1. Degradation of drugs is possible during manufacturing
2. Less amount of product is formed.

Adsorption to solid carriers

Solid carriers can be used to convert liquid multiple emulsion formulations into free-flowing powders through adsorption. As part of the adsorption process, the liquid formulation is applied to the carriers using a blender. The resulting powder can be directly added to capsules or combined with appropriate excipients before being compressed into tablets, such as indomethacin.

Advantage

1. Simple
2. High amounts of several emulsions (maximum 70% [w/w]) can be absorbed upon appropriate carriers.

Disadvantage

Less amount of drug may be entrapped.

Melt granulation

Melt granulation is a technique that uses a binding substance which melts or softens at extremely low temperatures to achieve powder agglomeration. It offers several benefits over traditional wet granulation as it is a "one-step" process that eliminates the liquid addition and subsequent drying stages. The primary variables that affect the granulation process are mixing time, binder particle size, impeller speed, and binder viscosity. Meltable lipids are commonly used as binders in solid and semisolid forms. The melt granulation technique is often utilized to adsorb surfactants, lipids, and medicines onto stable neutral carriers, such as silica and magnesium aluminometa silicate.

Advantages

1. Melt granulation is one step operation
2. Drying phase is avoided in the melt granulation technique.

Disadvantages

This only applies when a SES is adsorbing onto a solid carrier.

Melt extrusion/extrusion spheronization

Extrusion is a process that involves pushing a raw material with plastic-like properties through a die at a controlled temperature, pressure, and product flow. This process transforms the material into a finished product with uniform shape and density. The size of the spheroids produced depends on the aperture size of the extruder. The pharmaceutical industry commonly uses the extrusion-spheronization technique to produce uniform-sized spheroids (pellets).

The extrusion-spheronization is processed in the following ways:

1. Dry blending of excipients and active components to produce a uniform powder
2. Extrusion into a wet mass that resembles spaghetti after wet massing with a binder
3. The extrudate is spheronized into spheroids of the same size
4. Drying
5. To get the required coating and size distribution, sift (optional).

The proportions of the SES, water, lactose, and microcrystalline cellulose in the wet masses had a significant effect on the pellets' surface roughness, disintegration time, size spread, and extrusion force. The water level rises as the disintegration time increases. Diazepam and progesterone self-emulsifying pellets as well as pellets that are bi-layered cohesive and self-emulsifying have been created for extrusion-spheronization.

Advantages

1. The method of solvent is not used in melt extrusion
2. For homogeneous composition and high drug loading (60%)

Disadvantages

For the extrusion process, a large number of excipients are required.

ROUTE OF ADMINISTRATION FOR SELF-NANO EMULSIFIED PELLETS

Preparing an aqueous dispersion for oral administration is possible, but it can also be turned into traditional dose forms such as pills, pellets, capsules, or sachet powders. For oral delivery, multiple emulsion and/or multiple emulsion formulations containing both hydrophobic and hydrophilic medicines are used. The main goal of this method is to increase gastrointestinal absorption or bypass first-pass metabolism, resulting in increased oral bioavailability. However, the w/o/w emulsion system is administered through the depot route, which can be costly and inconvenient for patients.

DOSAGE FORMS FOR ORAL DELIVERY

Because self-emulsifying preparations are by their very nature, they changed into self-emulsifying tablets, capsules, solid dispersions, and pellets.

The dosage forms created by a solid, self-dual emulsifying drug delivery device include.

Dry emulsions

Oil/water emulsions (O/W) with a solid carrier such as lactose or maltodextrin in the aqueous phase are commonly used to produce dry emulsion formulations through spray drying, rotary evaporation, or freeze-drying. To eliminate the aqueous component of the O/W emulsion, it can be formulated and then spray-dried. During the process, the spraying rate, temperature, atomizer, drying chamber design, and an appropriate airflow pattern should be considered based on the product's drying properties.

Advantages

1. Dry emulsions can be beneficial for further tablet and capsule manufacturing
2. Dry emulsions may be used for the peptide and protein medication delivery orally
3. For the creation of enteric-coated formulations, dry emulsions can be helpful.

Disadvantages

Unstable after a short time period.

Self-emulsifying capsules

Micro-emulsion droplets are formed in the GIT after taking capsules containing traditional self-emulsifying liquid formulations. These droplets then disperse to reach the absorption sites. This technique enables the use of solid carriers to create a solid or semi-solid state while using liquid self-emulsifying components such as adsorbents and polymers for filling capsules. One option for this purpose is to select a solid matrix. a.k.a. Gentamycin. The processing factors having to be considered during the process are the amount of liquid to be filled, and time can affect the preparation.

Advantages

1. It has a smaller concentration of a surfactant, which lessens GI side effects
2. Patient compliance.

Disadvantages

It could only be administered as an injection or topically applied dose form.

Self-emulsifying sustained/controlled-release pellets

Pellets are a type of medication that comes in a multiple-unit dosage form. They can be made without using solvents and have a consistent drug content, with up to 60% of the pellet being made up of the drug itself. In the manufacturing process, a material with plastic-like properties is heated to a controlled temperature and forced through a die. This process, called extrusion, results in a finished product that has a uniform shape and density. The pharmaceutical industry often uses a technique called extrusion-spheronization to create spheroids of uniform size, which are also known as pellets. During the manufacturing process, factors such as the speed of the impeller, the duration of mixing, the viscosity of the binder, and the particle size of the binder must all be taken into account.

Advantages

1. Reducing the variability of plasma profiles within and across subjects
2. Reducing GI discomfort while maintaining medication absorption, such as with diazepam.

Disadvantages

1. Requires capsule filling, which may raise prices
2. From formulation to formulation, particle sizes differ.

Self-emulsifying sustained/controlled-release tablets

Tablets can be created by adding a solid carrier, such as lactose, to emulsions. Maltodextrin can improve the penetration effectiveness of the emulsion through the GI mucosal membranes. The self-emulsion osmotic pump tablet is the latest advancement in the development of self-emulsion tablets. This tablet uses an elementary osmotic pump system as the self-emulsification system carrier, offering stable plasma concentrations and a controlled medication release rate, for example, carvedilol. During the process, excipient concentration, punching time, and speed are the processing factors that need to be considered.

Advantages

1. Gastrointestinal bleeding can be minimized by increasing its penetration efficacy
2. To cover up the unpleasant taste of medicines.

Disadvantage

The bioavailability of the preparation may be decreased.

Self-emulsifying solid dispersions

Solid dispersions made from emulsions can increase the bioavailability of weakly water-soluble drugs.[21] Such medicines can be absorbed more easily when taken with excipients used in the formulation of the dispersion. The final product can be poured into firm gelatin capsules that have been melted. During the procedure, the amount of excipient, the length of mixing time, and the amount of medicine to be filled are crucial factors that need to be considered.

Advantages

The dissolution rate may be increased by solid dispersions.

Disadvantage

1. Solid dispersions are unstable preparations
2. Cost of the preparation increases due to further processing into tablets.

CONCLUSION

The overall objective of the study is to find methods or techniques that can improve the solubility of drugs, especially those that have solubility-related problems, to enhance their action and bioavailability. Advanced drug delivery systems have been developed to overcome the various problems associated with such drugs. One such system that has proven to be effective is the SEDDS and self-microemulsifying drug delivery system. By carefully selecting the excipients and related components according to the drug to be prepared, most solubility issues can be resolved, and an efficient dosage form can be created. There are many techniques and methods available to overcome the solubility problem, and they can be applied depending on the specific drug and its properties.

AUTHORS' CONTRIBUTIONS

All authors contributed to the manuscript. The corresponding author developed the study idea, supervised, and revised the manuscript. The first author collected data and wrote the primary draft.

CONFLICTS OF INTEREST

Authors declare no conflicts of interest.

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