A Concise review on application of solid lipids and various techniques in the formulation development

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Abstract

Lipids have wide range of applications in food and pharmaceuticals. The pharmaceuticals application of lipid is to improve solubility of drug also helps to improve the bioavailability. The dissolution/dissolving phase, which is probably the rate-limiting component for oral absorption of poorly water-soluble drugs, is eliminated by pre-dissolving pharmaceuticals in lipids, surfactants, or combinations of lipid excipients and surfactants. The most widely used co-solvents, together with lipid excipients, are propylene glycol, glycerol, and polyethylene glycol 400, poloxamer etc. Various technologies are used such as melt extrusion, melt granulation for preparation of lipid based oral modified released dosage forms. This review summaries the overview of the lipid excipients in terms of their classification, methods of absorption, and lipid-based product development. The manufacture of solid and semi-solid lipid formulations using various methodologies, applications, phase behaviour, and the regulatory outlook of lipid excipients are covered.

Keywords: Solid lipids, Lipid classification, solidification techniques, modified released.

1. Introduction

Since its introduction to the market in 1981, oral lipid-based drugs have grown to comprise around 3% of all oral formulations sold commercially. Drugs having poor bioavailability and solubility can be delivered using formulations based on lipids. Also this lipid based formulations gives therapeutics advantages. As lipids are metabolized and absorbed by the digestive system, many substances that are similar to lipids are absorbed by the lymphatic system instead of the liver and pass out of the body via the thoracic lymph duct. Vegetable oils, Fatty acids, triglycerides, also their derivatives are examples of lipids that can exist in the form of numerous particles that are solid, semisolid, or liquid. Those lipids that have higher melting points it means above body temperature they will be easily converted to solid dosage form, where as those lipids that are liquid as well as semisolid that will be suitably converted to multiparticulate dosage forms by the adsorption process on compatible pharmaceutical additives. Lipids are currently used extensively in the manufacturing of numerous formulations employing inventive adaptations and modifications of traditional machinery with a moderately simple method. Several methods are used, including spray cooling, adsorption on a solid support, pastillation, melt extrusion, melt granulation, and spheronization. These methods improve the flow of bulk lipids by dissolving lipids into certain size solid particles (powder, granules, or pellets) and then placing them in capsules, bags, or even in dispersible tablets.

Lipids are employed in a variety of ways in pharmacological dosage forms (Table 1), including:

1) Increasing the processing efficiency or maintaining the drugs preferred physical condition
2) Modification of the drug’s cellular or systemic absorption
3) Improved drug targeting
4) Extended or more controlled medication delivery.
Table 1: Benefits related to biopharmaceuticals

<table>
<thead>
<tr>
<th>Benefits related to biopharmaceuticals</th>
<th>Benefits Related to Product Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid melts help to increase the solubility as well as bioavailability of drugs.</td>
<td>Lipid materials can also be processed in a fixed dosage form by adsorbing them to the right additives.</td>
</tr>
<tr>
<td>The gastrointestinal tract’s absorption and digestion of lipids promotes the uptake of entrapped drugs into the lymphatic system, bypassing the liver.</td>
<td>Produced utilizing traditional methods and tools, with processing options that are flexible and contemporary techniques that enable cost-effective manufacture.</td>
</tr>
<tr>
<td>Enhanced drug micellar solubilization induced by bile</td>
<td>Increasing formulation flexibility and knowledge of functional excipients</td>
</tr>
<tr>
<td>lipids that are digestible and used for taste masking and non-digestible used for release retardants action</td>
<td>Helps to prevent modification in the release kinetics of drugs that are influenced by adsorption</td>
</tr>
</tbody>
</table>

2. Classification of lipid excipients

2.1 Fatty Acids and their Related Derivatives

Long-chain fatty acids such as benzoic acid, stearic acid, and palmitic acid are used to deliver continuous release in oral medication. Because they react chemically with other solids and have the best processing properties, such as uniform distribution of particles, enhanced compression, and control the final release of active compounds, fatty acid salts such as aluminum, calcium, and magnesium are often used on tablets.

2.2 Wax, neutral lipids, and oils

Mono, di, as well triglycerides are produced through the esterification of fatty acids to glycerol. Chemically altered natural triglycerides contain substances that can be used to create medication delivery systems such as glyceryl distearate, mineral oil, stearoyl polyoxyl-6 glycerides, olive oil as well as ethyl ester, glycerol monostearate, and hydrogenated vegetable oils.

2.2.1 Phospholipids

In order to form phospholipids, glycerides must undergo a more complicated change of their terminal hydroxyl. The common phospholipid heads include glycerol and glycerol esters, as well as ethanolamine, serine, choline, inositol, and inositol phosphate. Amphipathic phospholipids are utilized as an oral capsule medication and combine easily with emulsifiers and dispersants.

2.2.2 Glycolipids

Glycolipids are compounds that develop as the sugar mixture attaches to the glyceride’s backbone. Traditional glycol lipids, which include glycosyl glycerides as well as ceramides, are uncommon in pharmaceutical products due to their scarcity and expensive cost, however, glycosyl modifications may be employed to incorporate targeting mechanisms into lipid formulas.

3. Advantages of lipids use as drug carrier

Lipid-based formulas increase the bioavailability of drugs. Pharmacological half-life can be extended through lipiddation therefore the use of lipid carriers, enhancing pharmacokinetics and enabling less frequent dosing. When lipids are present in the digestive tract, bile salts are encouraged to be released, simulating a partially fed state. Bile salts cause the drug to emulsify, improving its in vivo solubility as it is only moderately soluble in gastrointestinal fluid. The solubilized compounds’ digestion is then accelerated, which inevitably raises oral bioavailability. Due to their stability across a range of pH and moisture levels, lipids constitute an effective barrier for certain sensitive drugs towards gastrointestinal or environmental conditions. Lipids substances are non-cytotoxic and biodegradable, they have a long history of being safe for use. Solid lipids have the additional advantage of maintaining their structural integrity, which enables them to resist the effects of enzymes in vivo for an adequate period of time. Lipids offer an environment that is hydrophobic and resistant to enzymes, which help to delay the release of the drug that has been loaded and result in a regulated drug release.

4. Manufacturing benefits of lipids substances as drug carriers

Lipids have significant advantages in formulation development and manufacturing in addition to their therapeutic benefits. Especially since pharmaceuticals with very low melting points require high temperatures and high processing pressures (such as drying granules and tablet compression), it is difficult to process pharmaceuticals at very low melting points, especially if they are liquid at ambient temperature, or if they convert to their own crystal state (e.g., granule drying and tablet compression). To stabilize drugs, a combination of drugs and lipids can be directly absorbed into solid particulate carriers. During the melting granulation process, lipid-based compounds can aid in the solubility and dispersion of medicines in solid solutions.

5. Solidification techniques for lipid-based systems

The following techniques can be used to produce lipids to prepare solid oral lipid dosages forms such as pastilles, pellets, tablets, and capsules, also powders and granules, and others.

5.1 Melt solidification technique

Melt solidification is a crucial process for producing the state liquid phase to the solid phase so that the products come out in a condition that is suitable during their transportation, storage, and subsequent use. This should be accomplished with the least amount of resources and the simplest, smallest amount of tools. The transformation of the melt material into a solid state with a certain kind and specific physical properties is a vital operation in the chemical and industrial industries. (Figure 1) The primary characteristic of solidification is crystallisation without separation.
Crystallization occurs under certain processes that affect the size, shape, crystal composition, hardness, and concentration of dust of solidified solids. Over the past decades, numerous solidification processes have been developed for the final size and shape of various standards. Pastillation is a method of rapidly converting melting into dispersed solids. The process of directly converting a liquid into a single-sized volume is called pastillation melts. Dust is not present during the pastillation process, which frequently occurs during the mechanical cutting and breaking process.

5.2 Dropping method

The dropping method, a novel technique for forming spherical particles from melted solid dispersions, helps various compounds crystallize. Round particles made using the dropping method can either be utilized as a ready dose form or put into capsules. If required, round particles might be treated further for coating. The production process is made simpler by using this approach instead of the other melt methods, which include pulverization, sifting, and compressibility issues.
The dropping method is a brand-new technique for creating spherical particles from melted solid dispersions. Bülau and Ulrich created it to speed up the crystallization of various chemicals. Special tools created by Bülau and Ulrich were employed for this purpose (Figure 2). If a coating is preferred, the production process is made simpler by using this approach instead of the other melt methods, which include pulverization, sifting, and compressibility issues. Dropping is a green technology that doesn’t use things that are bad for the environment.

5.3 Pastillation

The process of pastillation, which solidifies dusty, hazardous powder materials of chemicals into pastilles (hemi-spherical solidified units), is one that is frequently employed in the chemical, petrochemical, and agrochemical industries. This method makes it easier to handle the formed pastilles. Pastillation is the process of creating uniform-sized pastilles by depositing or allowing falling drops of chemical compounds to fall over a stainless steel surface that has been allowed to cool. The drops flatten slightly depending on their weight and the physical parameters of the melt, like viscosity and surface tension. The formed droplet then displays the traditional “pastille” shape. A particular piece of machinery called a “Rotof orm er” is used to produce pastilles on a large scale. (Figure 3).

Figure 3: Schematic diagram of pastillation technique

5.4 Fabrication of melt solidification apparatus

Figure 4: In house Labscale Melt solidification apparatus
Assembling and set up of pastilles formulation apparatus

In-house apparatus was developed to generate pastilles at the lab scale depicted in (Figure 4) The apparatus consists of a glass syringe or metal syringe with a plunger setup, hypodermic metal needles, and a heating coil on the outside of the glass syringe controlled by a temperature controller. The syringe was mounted on a burette holder, which was then set up on top of the metal plate. For cooling the base plate ice bag placed below the base plate. The droplet of molten material that fell onto the metallic plate was scraped off with the use of a sharp metal scraper after it had solidified and become known as the pastilles. The hardened pastilles were filled with '0' capsules of the specified size. The step wise process of pastilles formulation given in (Figure 5)

The roughness of the cooling surface, falling height, cooling rate, and crystallisation behaviour of the carrier are the main parameters involved in this process. Physical characteristics that are taken into account during processing include viscosity, surface tension, and melt density of the lipid.

Compared to other techniques for producing melt and solidify processes, this one has significant advantages. This method is suitable for processing of hygroscopic drugs and excipients the reason is this method not needed the organic solvents as well as this method also eliminates water during processing of ingredients. It is possible to produce the pastilles in a various sizes such as from 1 mm to 30 mm in diameter, are in solid spherical in shape, free-flowing, that are ideal for handling, filling, and packaging. When compared to powders, pastilles offer a larger bulk density as well as better packing capabilities.

A large amount of molten liquid is converted into discrete solidified units, resulting in a dust-free and solvent-free working environment. The entire procedure, which comprised melting fat, mixing the drug and essential excipients, and then solidifying, used only one piece of equipment. The absence of accompanying operations such as grinding, crushing, and other types of breaking processes reduces the pastillation process's energy cost. While larger pastilles may be strip-packed or poured immediately into sachets or bottles, smaller pastilles can be easily inserted to capsules.

5.5 Direct Compression

Direct compression is just a two-step, simple, and continuous process that calls for mixing and lubricating powder materials before compaction. By cutting down on production costs and processing time, this approach may guarantee cost-effectiveness. Tablets are prepared through mixing API, a solid lipid and polymer agent, diluent, lubrication, and compressing the mixture in tablets. Lipids in smaller quantities than hydrophilic polymers may have a stronger retention effect, as their water-insolubleness reduces the penetration of liquids and, consequently, the dissolution and diffusion of drugs.

5.6 Granulation – Wet and Dry

Granulation is used to increase mix uniformity, compressibility, and powder flow characteristics. In addition to employing binder solutions and water also organic solvents, excipients such as lipid may also then granulated along with API in a dry form. Dry granulation creates thick granules using roller compaction, which, while less frequently used, is a continuous and energy-efficient technique that does not require solvents, which is beneficial for APIs that are hygroscopic or humidity-sensitive. Lipids can help hydrophilic matrices retain less water, resulting in medication release kinetics that are adequate. Because of their excellent binding qualities, hydrophilic polymers are typically used in wet granulation, which is a highly frequent technique in the pharmaceutical sector. These polymers, however, have a tendency to adhere in wet processing as well as cleaning when utilized in high quantities. Solid lipid excipients are substitute to the release rate retardant polymers used in wet granulation as they none swelling when in contact with liquids.

5.7 Melt Granulation/Melt Pelletization

Pelletization, also name for melt granulation, is a one-step, solvent-free method for producing formulations that sustained release and high drug loading requirements, as well as pharmaceuticals that cannot be freely water soluble. The components get preblended using high-shear mixers as the temperature gradually rises to attain the lipid melting point. The lipids melt, causing the particles to bond to generate free-flowing granules. An approach is to heat fatty excipients before adding them to a powder combination in a granulator.
to create granules as well as pellets that may then be placed inside of capsules or crushed into tablets. Melt-granulates enable a slower medication release over longer timespans than standard granulation methods. Drug loading, processability, and overall repeatability may all be improved by combining lipid excipients with various melting points.

5.9 Hot melt extrusion process

Hot melt extrusion is a continuous method that allows the creation of granules with extraordinarily high drug loadings (90-95%) without the need of solvents or protracted drying times. The conveying including kneading mechanism settings, temperature, or in-process controls are critical for improving process parameters or repeatability during extrusion. When lipid excipients are used as binders, drug bonding is promoted while dosage form wettability is reduced, resulting in a slower drug release. By remaining molecularly distributed within the molten lipid, the drug’s solubility as well as release time may be improved. This method has the benefits of being simple, scalable, and versatile enough to provide a wide range of dose forms.

5.10 Molding

The easiest method for creating lipid-based continuous medication delivery systems is molding. Before being put into ethyl cellulose cylinders, capsules, or cast into molds to make tablets, the drug is dissolves in the lipid melt. An insoluble, hydrophobic lipid excipient is created as an extremely dense, pore less, hydrophobic, and poorly wettable matrix. Mannitol and polyethylene glycols are examples of hydrophilic pore formers that can be employed to make these dosage forms more wettable. Despite being simple to use, this approach is over followed by the acceptability as well as popularity of the usual compressed tablet forms.

5.11 Spray Congealing Method or Chilling and Prilling Method

Drug microparticles are produced by processes such as spray congealing or prilling and then incorporated into the lipid matrix. When the lipid has completely melted, the drug will get dissolved or finely dispersed. After being atomized with a pneumatic nozzle in a cool chamber, this mixture is next dried. The method is not appropriate for formulations that are extremely drug-loaded because overly viscous mixes can result in nozzle obstruction, and irregularly shaped, or excessively large particles.

5.12 Hot-Melt Coating

Hot-melt coating eliminates the need for solvents by spraying molten lipid excipients on the surface of the medicine to create a lipid coating. The medicine can then be compacted into tablets or placed into capsules after being coated. The method is quicker and less expensive than traditional coating procedures, which calls for the expensive, tiresome, and time-consuming evaporation and/or recovery of solvent. Drawbacks include processing thermo-labile chemicals and a small selection of excipients.

The processing adaptability of lipid excipients is provided in (Table 2) for the production of sustained release dose.

<table>
<thead>
<tr>
<th>Characteristics of Drug</th>
<th>Related Process</th>
<th>Classes of Release Modifiers/fillers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs that are water insoluble</td>
<td>Effective techniques include dry/wet granulation and direct compression.</td>
<td>Diluents that are water-insoluble are best suited Surfactants for stabilization Polymers that are water soluble are best suited Disintegrating agents</td>
</tr>
<tr>
<td>Drugs that are water soluble</td>
<td>The following methods are appropriate: direct extrusion, melt extrusion, wet/alloy granulation, spray solidification, hot melt coating.</td>
<td>Diluents that are water-insoluble are best suited. Additionally, hydrophobic and hydrophilic swelling polymers are employed.</td>
</tr>
<tr>
<td>A drug that has low therapeutic dose</td>
<td>Melt and then mix capsule moulding and direct compression are suitable techniques.</td>
<td>Diluents that are hydrophilic polymers get swell when exposed to water, surfactants, sugars, and disintegrants</td>
</tr>
<tr>
<td>Drugs that have a high therapeutic dose</td>
<td>The best method is hot melt coating, which is followed by capsule moulding, melt extrusion, dry granulation, and wet granulation also the melt granulation.</td>
<td>Non-water soluble appropriately flowing and compressible Fillers and diluents</td>
</tr>
<tr>
<td>Drugs that are hygroscopic (water sensitive) in nature</td>
<td>It is appropriate to use the hot melt extrusion, direct compression, hot melt coating, spray cooling dry/melt granulation, and capsule moulding techniques.</td>
<td>Choice of diluents and fillers are non-hygroscopic</td>
</tr>
<tr>
<td>A drug that is thermo-labile (heat sensitive)</td>
<td>The appropriate method is Direct compression Wet granulation</td>
<td>All</td>
</tr>
</tbody>
</table>

6. Drug release mechanism from lipid matrices

Understanding the main release of drugs mechanism in depth is essential for proper product development as well as drug safety. However, little is known about how drugs are released from lipid-based preparations. There are numerous durable polymer-based drug delivery technologies that have undergone thorough analysis.
7. Mechanism by which drug releases sustained manner from lipid matrices

Solid dosage forms produced using insoluble lipid excipients have been shown to maintain their integrity during drug release without dissolving or gelling\(^49\). This shows a pure Fickian diffusion mechanism that involves (a) water permeates the matrix's interior, (b) the drug dissolves, (c) takes up pores resulting from the dissolution of drug particles, (c) generates water-filled channels thereby enhancing matrix porosity as well as drug mobility, and (v) ensures constant drug diffusion from the dosage form into the drug release medium. The importance of water diffusion into the device can be inferred from the aforementioned release mechanism, which assumes that the lipid matrix fully attempts to keep its geometric structure upon dissolution while drug release is based solely on Fickian diffusion. Such lipid matrices’ rate-limiting component for release. This is due to the fact that water in the matrix alone has the ability to dissolve drugs and form tiny pores for drug diffusion. As a result, lipids and pharmacological qualities have a significant impact on the matrix wettability’s characteristics. Some solid lipids and process used for formulation listed in (Table 3).

### Table 2: Solid lipid materials used to sustain the release of dosage forms\(^{41-44}\).

<table>
<thead>
<tr>
<th>Lipids class</th>
<th>Chemical configuration</th>
<th>Characteristics</th>
<th>Examples</th>
<th>Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waxy materials</td>
<td>Fatty acid esters and long chain alcohol</td>
<td>Water insoluble nature Melting point range 62-86(^\circ)C</td>
<td>Solid paraffin, candelilla wax, carnauba wax, and beeswax Cetyl palmitate</td>
<td>Cold, hot</td>
</tr>
<tr>
<td>Oils from Vegetable origin</td>
<td>combination of phospholipids, triglycerides, and free fatty acids</td>
<td>Digestible Melting Point: 60-71(^\circ)C</td>
<td>hydrogenated soyabean oil, castor oil, and cottonseed oil</td>
<td>Cold, hot</td>
</tr>
<tr>
<td>Poloxamers</td>
<td>combination of polyethylene glycols, glycerides, and fatty acid esters</td>
<td>In part digestible 50(^\circ)C for melting</td>
<td>Stearoyl poloxyl-32, Stearoyl poloxyl-6, and glycerides</td>
<td>hot</td>
</tr>
<tr>
<td>Triglycerides and fatty acids</td>
<td>Long chain fatty acids, triglycerides and monoacids Triglycerides, monoacids</td>
<td>Melting Point: 60-90(^\circ)C Melting Point: 46-73(^\circ)C</td>
<td>Behenic acid, Stearic acid, Palmitic acid, Glycerol tripalmitate and tristearate</td>
<td>Hot and Cold</td>
</tr>
<tr>
<td>Partially glycerides</td>
<td>mono-, di-, and triglyceride mixtures</td>
<td>Melting Point: 54(^\circ)C-74(^\circ)C</td>
<td>Glyceryl behenate, distearic acid, and monooesters of glycerol</td>
<td>Hot and Cold</td>
</tr>
<tr>
<td>Fatty alcohol</td>
<td>fatty alcohol mixture</td>
<td>Melting Point: 48(^\circ)C-56(^\circ)C</td>
<td>Alcohols from cetyl and cetostearyl</td>
<td>Hot and Cold</td>
</tr>
</tbody>
</table>

8. Drug release adjustment

To obtain the desired drug release, formulation factors might be considered in addition to how dosage form dimensions and compression forces affect matrix porosity and diffusion channel length. It has been shown that the potency of lipid-based dosage forms depends on the kind of drugs, the lipids, and the manufacturing procedures. The molding and spray congealing of insoluble lipids create a very incomprehensible system that releases extremely slow drugs so a very long period of time, but the compression of a physical powder mixture makes it easy for water to spread into the device. The inclusion of other components may be used to control and optimize the drug released from the lipid matrix\(^{45, 46}\). This modulation is caused by facilitation or inhibition of water input to the matrix. These soluble chemicals dissolve immediately when they meet the release medium, and then the drugs quickly diffuse through the matrix along the channel where they are designed. Thehydrophilic fillers such as mannitol and lactose dissolve very quickly in water media, forming these channels in matrix. When high water-soluble drugs or high drug concentrations are diluted with calcium phosphate in low-water rather than lactose or mannitol, the drug release rate may be significantly increased\(^{47-50}\). Pores can be made from hydrophilic surfactants, polymers, or other chemicals that perform the same role as hydrophilic diluents in to the tablet formulations\(^51\). Once exposed to the release media, the pores that form expand or leak out from the lipid matrix, increasing the amount of medication released\(^{52-54}\). Poloxamers have been added into the glyceryl distearate matrix formed via capsule molding. Drug release increased by the incorporation of increasing amounts of hydrophilic polymers, allowing control and optimization of drug release rates.

9. Benefits of multiparticulate system and its application

A multiparticulate system is a matrix or reservoir that contains a large number of small drug depots or drug release units. Multiparticulate are defined as a single administrable dose of a drug that is uniformly dispersed among numerous smaller units of a specific uniform size and dimension ranging from the nano- to the mill scale. The term “multiparticulate” means distinct, small, repeating drug particles that may or may not follow a similar pattern of drug release. It is also known as a “multiple unit dose forms.”

Depending on the polymer used in the manufacturing process, they can be made for delayed, pulsatile, controlled, or targeted drug release. They can be made by combining excipients or drug material into fine powders or granules with the proper processing equipment as well as technology. Pharmaceutical technology has previously noticed the full potential for this approach because of the adaptability in product development as well as design and excellent flow properties due to uniformity in size as well as sphere-shaped agglomerates, higher physical stability, excellent strength, low friability, narrowed distribution of particle sizes, excellent quality throughout coating application, compatible packing characteristics, along with therapeutic advantages it provides.
The best thing about multiparticulate systems is that the desirable dose units may be easily removed from them without modifying the formulation or manufacturing process, which has little to no influence on the relative amount of medication released. Depending on its surface area, every modified release dosage form having varying strengths releases drug in a different way. Identical to matrix-sustained release tablets, the surface area change that occurs with a change in tablet form is often not proportionate to the dosage strength, resulting in various drug release patterns.

10. Modified drug delivery system

The most reliable and frequently used dose forms are oral solid dosage forms. Tablets have been widely used since the latter half of the nineteenth century, and their appeal has not diminished. Because of the benefits offered to both pharmaceutical makers and patients, tablets are still a common dosage form. They include straightforward preparation and cost-effective packaging, precision of a single dosing regimen, portability and compactness, as well as administration simplicity and blandness, are all advantages of the drug manufacturing methods.

Figure 6: Categories of modified drug delivery system

Modified release dosage forms differ than immediate release dosage form by the fact that the substances that constitute the active ingredient are released at a different pace and/or place. This purposeful alteration is produced via unique formulation design as well as. This recommendation covers oral, intramuscular, subcutaneous, and transdermal delivery of modified release dosage forms. Many technological advances that have attempted to address the shortcomings of traditional drug delivery methods have resulted in the creation of modified release drug delivery systems.57, 58 Different categories can be easily created from the changed release distribution systems (Figure 6).

11. Rationale for developing dosage formulations with controlled or sustained releases

Pharmaceuticals intended for oral administration often use traditional drug delivery systems that are intended for instant drug release for quick/immediate absorption. The drug level in the blood is not kept at a constant level when the standard dosage form is administered extravascularly. Due to the typical dosage form’s inability to regulate temporal administration, the duration of effect is short59. The requirement for repeated administration of drugs with a half-life, which raises the risk of forgetting to take a dose and reduces patient compliance, is one disadvantage of the conventional dosage forms, which include solution, suspension, tablet, capsule, as well as suppository.

1. The typical peak-valley plasma concentration-time profile (Figure 7) makes it difficult to reach a steady state. The inherent drug concentration changes may cause undermedicating or overmedicating as the steady state concentration values decrease or increase outside of the therapeutic range.

2. When there is an overdose, the variable drug levels may have undesirable consequences, particularly for a substance with a low therapeutic index.

3. Controlled drug delivery systems, which have the potential to totally revolutionise the administration of medication and provide a variety of therapeutic advantages, have emerged in response to the drawbacks of conventional drug delivery systems.

New and creative drug delivery techniques have quickly replaced traditional drug dose forms during the past few years. The controlled release/sustained release dosage formulations are widely used in modern medicines. Controlled drug delivery mainly tries to change the physiological and/or molecular properties inherent in a specific route of administration in order to impact the pharmacokinetic as well as pharmacodynamics features of pharmacologically active components.

Figure 7: Graphical representation of plasma drug concentration profiles for different released mechanisms of formulations.

Modified drug delivery system

Controlled release

Delayed release

Prolonged release
12. Conclusion

The rapidly expanding pharmaceutical sector is constantly seeking out new active compounds, which eventually calls for an appropriate dosage form capable of efficiently delivering those molecules in the body. The production of oral formulations can use a variety of excipients, but lipids have the added benefit of increasing the bioavailability of medications that are highly metabolised and lipophilic. The use of specific lipid excipients in formulations for sustained release is primarily justified by their hydrophobicity and inertness, which allow the creation of matrices that effectively delay release. They have fascinating biopharmaceutical features in addition to performance that is equivalent to polymer-based matrices. Therefore, a focus on innovation, advancement, and solving issues related to lipid-based manufacturing technology should be given. Additionally, where other methods are constrained due to intellectual property restrictions, new dosage forms like pastilles, solid SMEDDS, and new technologies like freeze-pelletization may be employed to improve the therapeutic efficacy of some medications. Additionally, using lipids as the main excipient might assist reduce the dosage of the medicine, particularly those with a low water solubility. Therefore, such efforts of formulation scientists will considerably improve the current healthcare system and assist patients in leading healthier lives.

Conflict of Interest: None

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