REVIEW ARTICLE

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A Review on Solid Self Emulsifying Drug Delivery Systems and Dosage Forms

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Abstract: Combinatorial chemistry and high-throughput screening used in drug discovery have resulted in a 70% of new drug candidates shown poor aqueous solubility in recent years which leads to low oral bioavailability. In clinical use, the poor bioavailability of a drug substance might result in limited therapeutic potential, thereby leading to insufficient clinical outcomes. Among the approaches of solubility and bioavailability enhancement, self emulsifying formulations have great potential for hydrophobic drugs. Conventionally SEDDS were prepared in liquid forms which have various disadvantages of liquid dosage forms. Accordingly, solid SEDDS were prepared by various solidification techniques. This article reviews the recent advancement in solid SEDDS with emphasis on solidification technique, solid SEDDS dosage forms, their associated problems and future directions for the research.

INTRODUCTION

Oral intake has been the most sought-after route of drug delivery by both patients and drug manufacturers for the treatment of most pathological states. Despite tremendous strides made in novel non oral drug delivery systems (DDS) to date, the majority of the drugs available commercially are oral formulations. Nevertheless, with oral delivery, over one-half of the drug compounds are diminished in the gastrointestinal (GI) tract because of their high lipophilicity and consequently poor aqueous solubility. Oral bioavailability of such drugs, being primarily a function of their solubility and dissolution tends to exhibit inadequate magnitude with high intra- and intersubject variability. [1, 2, 3]

Combinatorial chemistry and high-throughput screening used in drug discovery have resulted in an increase of poorly water soluble drug candidates. In drug discovery, the number of drug candidates defined as having low solubility has increased. 70% of new drug candidates have shown poor aqueous solubility in recent years. [4, 5]

In clinical use, the poor bioavailability of a drug substance might result in limited therapeutic potential, thereby leading to insufficient clinical outcomes. Various approaches to overcome the poor aqueous solubility of drug candidates have been investigated in drug research and development. Figure 1 review viable formulation options based on the biopharmaceutical properties of drug substances. [4]

LIPID BASED DRUG DELIVERY SYSTEM

Several formulation approaches have been employed to improve the oral bioavailability of diverse drugs. Amongst these, oral lipid-based DDS have proved their immense potential in improving the poor and inconsistent drug absorption of many poorly water-soluble drugs, especially following their administration after meals because they can keep the drug in the dissolved state until it is absorbed, thus overcoming the barrier of slow dissolution rates. These include various types of lipid suspensions, solutions and emulsions. With applications in specific domains, the lipidic formulations, thus, have carved a significant niche in oral drug delivery. [1, 6]

These formulations can also enhance drug absorption by a number of ancillary mechanisms, including inhibition of P-glycoprotein-mediated drug efflux and preabsorptive metabolism by gut membrane-bound cytochrome enzymes, promotion of lymphatic transport, which delivers drug directly to the systemic circulation while avoiding hepatic first-pass metabolism and by increasing GI membrane permeability [1, 6] as depicted in Figure 2. [7]

Typically, lipid-based delivery systems are composed of oil, surfactant, cosurfactant and water-soluble organic solvents. The preferred choice of each of these components varies with the formulation (oral, injectable, topical, transdermal, pulmonary, ocular) desired and the physicochemical properties of the drug. [6]

SELF EMULSIFYING DRUG DELIVERY SYSTEMS

Self-emulsifying drug delivery systems (SEDDS) are relatively newer, lipid-based technological innovations with immense promise in enhancing the oral bioavailability of drugs. These formulations have been shown to reduce the slow and incomplete dissolution of a drug, facilitate the formation of its solubilized phase, increase the extent of its transportation via the intestinal lymphatic system, and bypass the P-gp efflux, thereby augmenting drug absorption from the GI tract. [1]

Self-emulsifying formulations are isotropic mixtures of drug, lipids (natural or synthetic oils), and emulsifiers (solid or liquid), usually with one or more hydrophilic co-solvents/co-emulsifiers. Upon mild agitation followed by dilution with aqueous media, these systems can form fine (oil in water) emulsion instantaneously. SEDDS is a broad term encompassing emulsions with a droplet size ranging from a few nanometers to several microns. Depending upon the size of globules, these emulsions are characterized as concentrated microemulsions, nanoemulsions, or pre-concentrates. Self- microemulsified drug delivery system (SMEDDS) are formulations forming transparent microemulsions with an oil droplet size rangingbetween 100 and 250 nm. Self-nanoemulsified drug delivery system (SNEDDS) is relatively a recent term indicating formulations with aglobule size less than 100 nm. [1, 8, 9]

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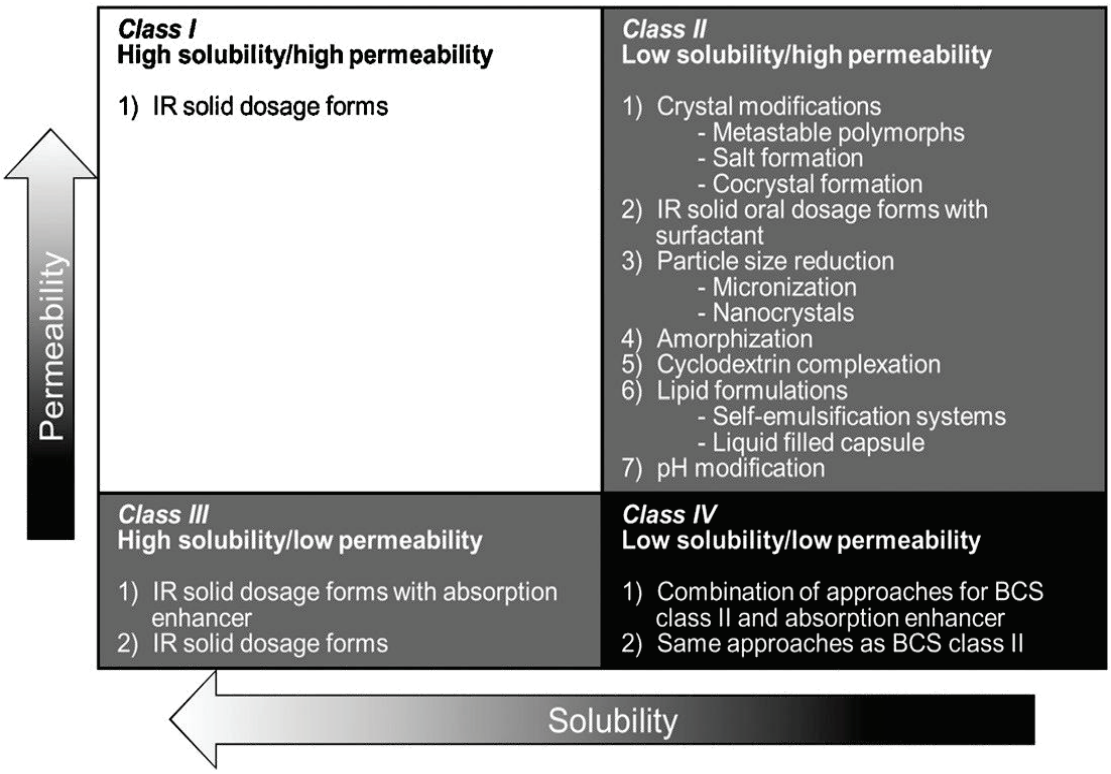

Figure 1: Biopharmaceutics classification system (BCS) and viable formulation options based on the BCS

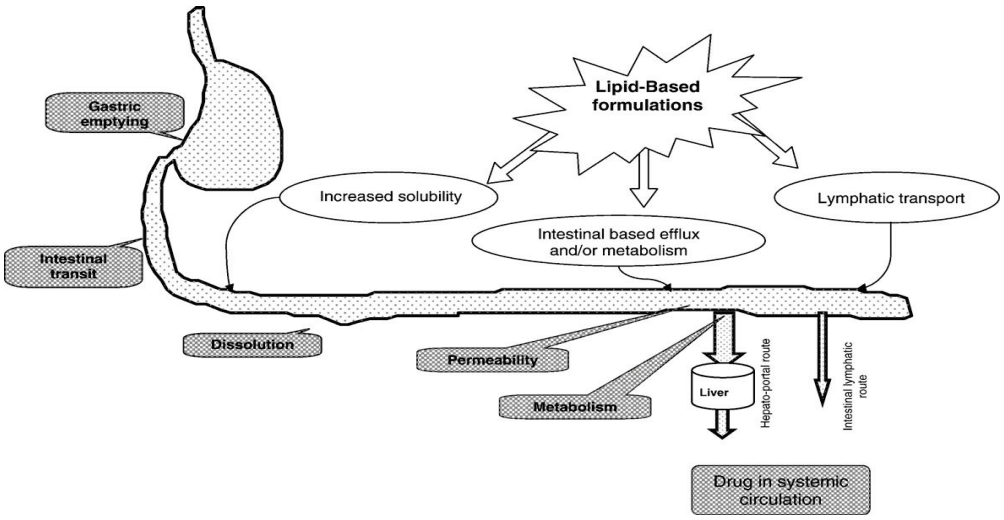

Figure 2: Schematic representation of the critical steps in oral drug absorption and the possible influences of lipid-based formulations

These systems can help in solving the under-mentioned problems of all the categories of BCS class drugs, as depicted in Figure 3. [10, 11]

Potential Advantages of SEDDS Include: [10, 12, 13]

1. Enhanced oral bioavailability enabling reduction in dose
2. More consistent temporal profiles of drug absorption
3. Selective targeting of drugs toward specific absorption window in GIT,
4. Protection of drugs from the hostile environment in gut.
5. Control of delivery profiles
6. Reduced variability including food effects
7. Protective of sensitive drug substances
8. High drug payloads
9. Liquid or solid dosage forms

SOLID SEDDS

SEDDS are usually prepared in liquid form and transforming liquid active ingredients and liquid pharmaceutical preparations into solid dosage forms is a challenging task. Soft gelatin capsules have been used as unit dose containers for liquids for many years. As new equipment has become available that allows sealing of hard capsules, it has also become possible to prepare liquid formulations in two-piece hard capsules. However, the capsule technologies are associated with a range of problems such as leaking, leaching of components through the capsule shell, incompatibilities with capsule material, and slower manufacturing rate compared with tablet production. The soft capsules furthermore require specialized manufacturing equipment and the

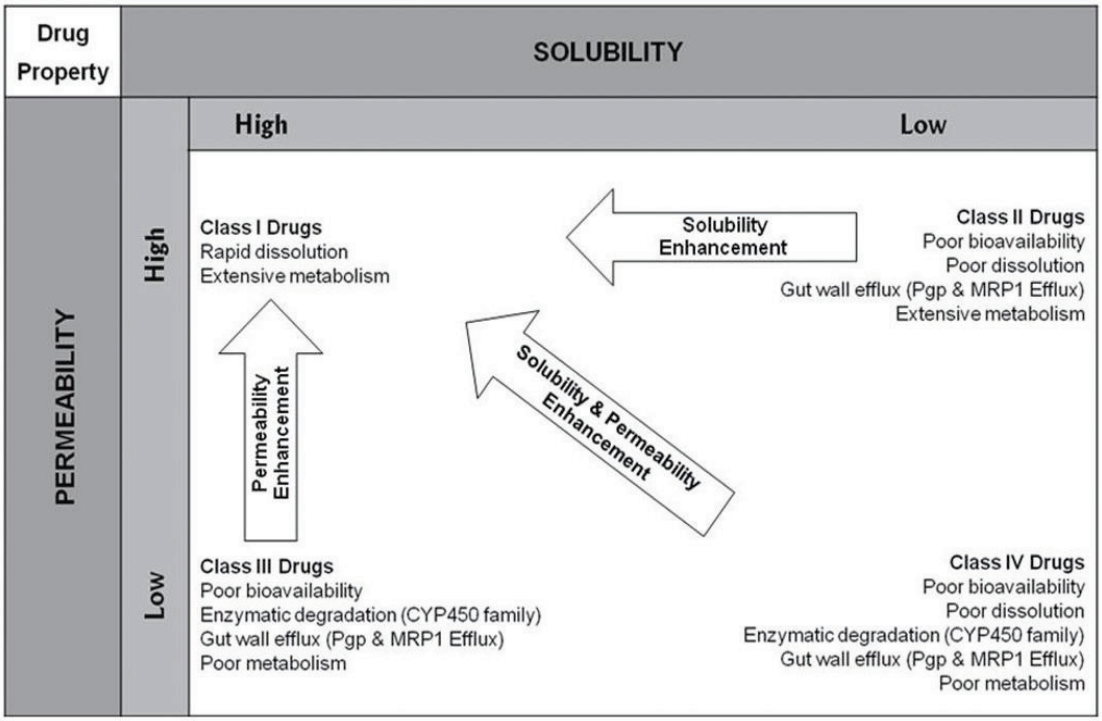

Figure 3: Overcoming the problems of solubility and/or intestinal permeability of BCS class II to IV drugs employing SEDDS

Table 1: Various Recent Literature Reports on Solid SEDDS

Drugs/Dosage Forms	Oils/Lipids	Surfactants/Co-Surfactants	Carriers	Reference No.
Glyburide/SMET	Labrafac WL1219	Tween 20/Transcutol	Neusilin US2	16
Valsartan/SNET	Capmul MCM	Labrasol/Tween 20	Neusilin US2	17
Ibuprofen/SET	Capryol 90	Cremophor EL/ Labrasol	Fujicalin	18
Carvedilol/SSNEG	Capmul MCM	Nikkol HCO 50	-	19
OndasetronHCl/SSNEG	Capmul MCM	Labrasol/Tween 20	Neusilin US2/ Sylsia 350	20
LercanidipineHCl/SEP	Capmul MCM L8	Tween 80/PEG 400	Neusilin US2	21
Silymarin/SE pellets	Akoline MCM	Miglyol 812/Tween 80/PG	MCC pH 101/Lactose	22
Puerarin/SE pellets	Castor oil	Cremophor EL/1,2-propanediol	MCC/HPMC	23
Carvedilol/Superporous Hydrogel	HCO-40	Miglyol/Transcutol	HPMC 15 cps	24

manufacturing cost is higher compared with tablet production. [11, 14] This problem led to the development of solid SEDDS, which combine the advantages of conventional SEDDS (i.e., enhanced solubility and bioavailability) with those of solid dosage forms (e.g., low production cost, convenience of process control, high stability and reproducibility, and better patient compliance). [8, 15]

Various disadvantages of liquid SEDDS are:

1. High production costs
2. Low stability and portability
3. Low drug loading
4. Few choices of dosage forms
5. Irreversible drugs/excipients precipitation may also be problematic
6. Large quantity (30–60%) of surfactants in the formulations can induce GI irritation

The solid SEDDS focus on the incorporation of liquid/semisolid ingredients into powders, employing diverse solidification techniques such as spray drying, melt granulation, molding, melt extrusion and nanoparticle technology. The Self-emulsifying Drug Delivery Systems powders can then be formulated as solid dosage forms such as self-emulsifying tablets and self-emulsifying pellets. Alternative approaches for the development of solid SEDDS include adsorption by solid carriers such as microcrystalline cellulose, colloidal silica and various viscosity grades of HPMC and the use of high melting-point solid excipients such as Lutrol® and Gelucire®. As melt extrusion/extrusion spheronization is a solvent-free process allowing high drug loading and content uniformity, it has been most extensively employed for solidification of SEDDS. [1, 8, 10, 11] Table 1 represents an updated comprehensive account of the solid SEDDS formulation of various drugs along with their excipient composition.

The main techniques for transforming liquid and semi-solid formulations into solid lipid-based particles or

Table 2: Considerations in Selection of Formulation Techniques for Bioavailability Enhancement with Lipid-based Excipients [25]

Formulation Techniques for Solid and Semi-solid Formulations	Physical Property of the Lipid Excipients Applied		Formulations Advantages and Limits	
	Liquid to Solid	Semi-solid	Maximum Lipid Exposure* (%, w/w)	Maximum Drug Loading (%, w/w)
Capsule filling	X	X	99	50
Spray-cooling	X		99	30
Spray drying	X	X	60	50
Adsorption on solid carrier	X		80	10
Melt granulation	X		50	80
Melt extrusion	X		50	60
Super critical fluid based methods	X		99	20
Solid lipid nanoparticles	X	X	99	50

granules has been described hereunder with a discussion of current practices pertaining to bioavailability enhancement with lipids. Table 2 sorts out these techniques according to physical nature of the excipients used, lipid exposure capacity, and maximum drug loading reported in the literature. [8, 11, 15]

Spray Cooling

Spray cooling can be renamed as a spray congealing and it is a process where the molten formula is sprayed into a cooling chamber. The molten droplets congeal and re-crystallize into spherical solid particles on contact with cool air; these solid particles fall to the bottom of the chamber and subsequently collected as fine powder. These fine powders can be used for development of solid dosage forms or direct filling into hard shell capsules or for development of various solid dosage forms like tablets. Parameters that are critical for spray cooling are the melting point of the excipient that should range between 50 and 80°C. Rotary, pressure, two-fluid or ultrasonic atomizers are the equipments available to atomize the liquid mixture and for generation of droplets. The spray cooling technique has various advantages like bioavailability enhancement and or sustained release formulations that ultimately depends on the choice of lipid matrix, and the drug behavior in that matrix (solution or dispersion). The drug loading capacity is limited by formulation viscosity as dispersions generally tend to be more viscous than solutions. It has a maximum of 30% drug loading capacity. [15, 25]

Spray Drying

In spray drying liquid solution is sprayed into a hot air chamber to evaporate the volatile fraction that may be organic solvent or the water contained in an emulsion. After evaporation of liquid this process yields solid microparticles. Equipment for spray drying is same that of spray cooling except the main difference relating to the temperature of the air circulating in the atomizer chamber. For sample preparation, drug and excipients are mixed together followed by solubilization of mixture in organic solvent. Dichloromethane is the conventional solvent used in spray drying as it is harmful solvent and carcinogenic, hence other solvents can be used in this technique. The drying condition, the key parameters for this process, which depends on the formulation and the solvent system. This technique has also been used in preparation of dry emulsions and obtained dry microparticles can be filled into hard gelatin capsule or converted into the other solid dosage forms like tablets. [8, 15, 25]

Adsorption on Solid Carriers

Free flowing powder can be obtained by adsorption of liquid formulation on solid carriers which have larger interfacial area. The adsorption process is simple and involves addition of the liquid formulation onto the carrier of choice by mixing in a blender. Selection of the appropriate carrier and its amount is a key parameter in this technique. Carriers are selected on the basis of greater adsorption capacity as higher adsorption allows drug loading, higher lipid exposure and also for better flowability of adsorbed powder. Similarly as in above technique, the resultant free flowing powder can be directly filled into capsule or after mixing with appropriate excipients compressed into tablets. Good content uniformity and higher lipid exposure (i.e. 70% w/w of SMEDDS may be adsorbed onto suitable carrier) are the significant benefits of this technique. Some pros of this technique are process is simple, requires minimal investment in equipments and facilitates formulation of preferable conventional dosage forms like tablets. The cons of this technique is reduced drug loading capacity in the final dosage form primarily due to dilution of lipid formulation during mixing with solid carrier and subsequent dilution by addition of various excipients for tabletting. [8, 15, 25]

Solid carriers can be microporous inorganic substances, colloidal inorganic adsorbent substances, cross-linked polymers or nanoparticle adsorbents, for example, silica, silicates, magnesium trisilicate, magnesium hydroxide, talcum, crospovidone, cross-linked sodium carboxymethyl cellulose and cross linked polymethyl methacrylate. Cross-linked polymers creates favorable environment to sustain drug dissolution and also assist in slowing down drug reprecipitation. Nanoparticle adsorbents comprise porous silicon dioxide (Sylysia 550), Neusilin US2 (Aluminium magnesium silicates), Fujicalin (Dibasic calcium phosphate), carbon nanotubes, carbon nanohorns, fullerene, charcoal and bamboo charcoal. [8, 15]

Melt Granulation

It can be also termed as pelletization and is a one step process which produces a granules or spheronized pellets from powder mixture containing drug. This technique necessitates high shear mixing for production of granules or pellets. There are two types of technique on the basis addition of binder in molten or solid/semi solid forms. A meltable binder was sprayed onto the powder mixture in molten state as in wet granulation hence referred as "pump-on" technique. Alternatively, the binder also be blended with the powder mix in its solid or semi-solid state and allowed to melt (partially or completely) by the heat generated from the friction of particles during high shear mixing referred to as "melt-in" process. After melting of binder it creates bridges with the powder particles that produce small agglomerates (granules) which can be transformed to spheronized pellets by mixing at specialized conditions. Impeller speed, binder particle size, binder nature, viscosity of binder and mixing time are the key parameters as it affects the granulation critically. Various pros of these techniques are simple process, single step, absence of solvents and higher drug loading i.e. 85% theoretically and 65% reported in literature. [8, 15, 25]

Melt Extrusion/Extrusion Spheronization

Extrusion spheronization technique produces uniform shaped spherical particles. In this process, raw material having plasticity is suitable for extrusion as it is forced through a die under controlled temperature, product flow and pressure conditions and initially produces a rod shaped extrusions which can be converted or cut into spherical particles by spheronization. In classic spheronization technique, lipid based excipients were used such as microcrystalline cellulose which enhances the dissolution or bioavailability of drugs. [8, 15, 25]

Supercritical Fluid Based Methods

In this technique, lipids may be used either for coating of drug particles or for producing solid dispersions. One or more coating materials are dissolved in supercritical fluid; to this drug particles are dispersed. Initially solubility of coating material in supercritical fluid is maintained by elevating temperature and pressure. Subsequently temperature and pressure are reduced gradually to decrease solubility of coating material in supercritical fluid hence coating material get deposited on drug particles to form coating layer. As various supercritical fluids are environmentally hazardeous so carbon dioxide is preferred. The process in this technique involves dissolving drug and lipid based excipient in an organic solvent such as alcohols and then in supercritical fluid which is followed by decreasing the temperature and pressure conditions to decrease the solubility in the supercritical fluid. It has highest potential for 99% lipid exposure and lower drug loading capacity compared to other methods hence best suiuted for high potency low dose drugs. [15, 25]

Solid Lipid Nanoparticles and Nano-structured Lipid Carriers

SLN and NLC are two types of solid state submicron particles (50-1000 nm) which are composed of physiologically tolerated lipid components. Main difference between SLN and NLC is that former have solid core. SLN are produced by high pressure homogenization of solid matrix usually made up of glyceryl dibehenate (Compritol 888 ATO) and drug with an aqueous solution of surfactant (Poloxamer 188 or polysorbates 80). On the other hand NLC is reservoir systems to increase the drug loading capacity and derived from SLN. NLC contain same component as that of SLN with liquid lipid material such as medium chain triglycerides. An application of such system includes controlled release drug delivery for oral, intravenous or topical route and additionally enhancement of oral bioavailability. SLN has advantage of free from organic solvents, wide range of lipid materials having different properties can be used and can be useful for the drug requiring high lipid exposure (90%), for high content uniformity and high drug loading. [15, 25]

DOSAGE FORM DEVELOPMENT OF S-SEDDS

Dry Emulsions

Dry emulsions are the powder form of liquid emulsion and it forms emulsion spontaneously on exposure to GI fluid or aqueous medium. Dry emulsions can be further use for the conversion into tablets or capsules. Dry emulsions are prepared from o/w emulsion containing a solid carrier like Lactose, maltodextrin, etc in the aqueous phase by rotary evaporation, freeze drying or spray drying. In freeze drying heat treatment before thawing decreases the stability while slow cooling rate and addition of amorphous cryoprotectant have the best stabilizing effect. Spray drying is frequently and mostly used technique for preparation of dry emulsion. Recent development in dry emulsion is development of enteric coated dry emulsion formulations which is commonly used for protein and peptide drug delivery for oral use. This formulation consisted of a surfactant, a vegetable oil and a pH-responsive polymer, with lyophilization used. [8, 15]

Self-emulsifying Capsules

Conventionally liquid SE systems are administered in the body by filling in capsule which on contact with body fluid dispersed to form microemulsion. If there is irreversible phase separation occurs leads to decrease/changes in drug absorption from absorption site. To overcome this problem Sodium Dodecyl Sulphate was added into the SE formulation or alternatively super-saturable SEDDS was designed using HPMC as precipitation inhibitor by enhancing viscosity of system which maintains the supersaturated state in vivo. Super saturated systems further have one more advantage that it contain reduced amount of surfactants, thereby minimizing GI side effect as well as irritation effect. Besides liquid filling, solid or semi solid forms of Liquid SE can be filled after its solidification by any teachnique. Oral administration of capsule enhances the patient compliance compared to intravenous/parentral administration. [8, 15]

Self-emulsifying Sustained/Controlled-release Tablets

Combinations of lipid, surfactant and co-surfactant have great potential of preparing self emulsifying tablets that have been used recently for various research works. For preparation of SE tablets, higher amount of solidifying agents are required so to overcome this gelled formulation was developed by Patil *et al*. In their study they had used an Aerosil 200 as gelling agent and it also aids in slowing down the release of drug. [8, 15]

Selection of different matrices for solidifying purpose depends on the type of release mechanism required for drug such as polyethylene oxide for controlled release, Fujicalin for immediate release, etc. SE tablets maintain higher drug concentration in plasma compared to conventional non-emulsifying tablet. The recent advance in the field of SE tablet is the self emulsifying osmotic tablet, where elementary osmotic pumps were selected as the carrier of SE system. This system has an outstanding achievement of stable plasma concentration and controlled drug release rate, allowing the relative bioavailability of 156.78% compared to commercial Carvedilol tablets. Liquisolid technique for the preparation of SE tablets is widely used technique as it aids in simple and rapid selection as well as sufficient amount of carrier and coating materials. [8, 15]

Self-emulsifying Sustained/Controlled-release Pellets

A pellet are the multiple unit dosage forms and offers various advantages over conventional solid dosage forms like flexibility of manufacturing, reducing intra-subject and inter-subject variability of plasma profile of drugs and minimizing GI irritation without compromisation of drug bioavailability. Hence this dosage form amalgamets the advantages of pellets with those of SEDDS by Se pellets. [3, 8, 15]

Self-emulsifying Solid Dispersions

Solis dispersion is widely used technique for enhancement of solubility, dissolution rate and bioavailability of poorly water soluble drugs although there are manufacturing difficulty and stability problems exists with this technique. These difficulty can be surmounted by SE excipients as these excipients have potential to further increase in drug absorption of poorly water soluble drugs relative to solid dispersion, also be filled directly into capsule in molten state, thus obviating the former requirement for milling and blending. Various widely used SE excipients in this field are Gelucire 44/14, Gelucire 50/02, Labrasol, Transcutol and TPGS (tocopherylpolyethyleneglycol 1000 succinate). [8, 15]

Self-emulsifying Beads

In an attempt to transform SES into solid form with minimum amount of solidifying excipients, Patil and Paradkar developed microbeads by loading SES into the microchannels of porous polystyrene beads (PPB) by solvent evaporation technique. PPB has complex internal void structures are prepared by copolymerization of styrene and divinyl benzene and are potential carrier for solidification SES. PPB is inert, stable over a wide range of pH and exaggarated conditions of temperature and humidity. High SES to PPB ratio is required to obtain the solid form. Drug loading efficiency and in vitro drug release from SES loaded PPB are mainly governed by Geometrical features such as bead size and pore architecture of PPB. [8, 15]

Self-emulsifying Sustained-release Microspheres

Similar to the beads, microsphere is also having great potential for the solidifying of SES. You et al prepared solid sustained release microsphere by quasi emulsion solvent diffusion method of spherical crystallization technique by using Zeodary turmeric oil (ZTO) as an oil phase. Zeodary turmeric oil exhibits potent pharmacological actionds including tumor suppressive, antibacterial and antithrombotic activity. ZTO release behavior was controlled by the ratio of HPMC acetate succinate to aerosil 200 in the formulation. [8, 15]

Self-emulsifying Nanoparticles

Various techniques have been used in the production of SE nanoparticles. Out of this, solvent injection is one of these technique has immense importance due to simplicity of method. In this method, lipid, surfactant and drugs are melted together and injected dropwise into a non- solvent with continuous stirring, thereafter resulted nanoparticles are filtered out and dried. This approach yields nanoparticle having size range about 100 nm and with drug loading efficiency of 74%. A second technique used for same is sonication emulsion diffusion evaporation. [8, 15]

Self-emulsifying Suppositories

Solid SEDDS could not increase only GI absorption but also enhance rectal/vaginal absorption. Various drugs could not achieve therapeutic plasma concentration after oral administration and required vaginal or rectal route and for this route suppository is the best dosage forms, for example Glycyrrhizin. Hence Glycyrrhizin is prepared as SES and then suppository were prepared by using mixture of a C6–C18 fatty acid glycerol ester and a C6–C18 fatty acid macrogol ester. [8, 15]

Self-emulsifying Implants

Research into SE implants has greatly enhanced the utility and application of S-SEDDS as it combines advantages of SEDDS and implants. For example, 1, 3-bis (2-chloroethyl)-1-nitrosourea (carmustine, BCNU) is a chemotherapeutic agent used to treat malignant brain tumors. However, its effectiveness was hindered by its short half-life. In order to enhance its stability compared with that released from poly (d, l-lactide-co-glycolide)(PLGA) wafer implants, SES was formulated with tributyrin, Cremophor RH 40 (polyoxyl 40 hydrogenated castor oil) and Labrafil 1944 (polyglycolyzed glyceride). Then the self-emulsified BCNU was fabricated into wafers with flat and smooth surface by compression molding. Ultimately, SES increased *in-vitro* half-life of BCNU up to 130 min contrasted with 45 min of intact BCNU. *In-vitro* release of BCNU from SE PLGA wafers were prolonged up to 7 days. Such wafers had higher *in-vitro* antitumor activity and were less susceptible to hydrolysis than those wafers devoid of SES. [3, 8, 15]

CONCLUSION

As mentioned above, numerous studies have confirmed that SSEDDS substantially improved solubility/dissolution, absorption and bioavailability of poorly water-soluble drugs. As improvements or alternatives of conventional liquid SEDDS, S-SEDDS are superior in reducing production cost, simplifying industrial manufacture and improving stability as well as patient compliance. Most importantly, S-SEDDS are very flexible to develop various solid dosage forms for oral and parenteral administration. Moreover, GI irritation is avoidable and controlled/sustained release of drug is achievable. There may be only a few solid SE dosage forms (except for SE capsules) appear on the market because there is some fields of S-SEDDS to be further exploited such as human bioavailability and *in-vitro in-vivo* correlation. Moreover, the researches of S-SEDDS lose their balance, that is, SE implants/suppositories/microspheres have not been as extensively studied as SE tablets/ pellets/ capsules. It is also worth pointing out some issues to which much attention should be paid, for example physical aging phenomenon associated with glyceride, oxidation of vegetable oil. Selection of suitable excipients is the main hurdle of developing S-SEDDS. Thus, these aspects should represent the major future working directions for S-SEDDS.

REFERENCES AND NOTES

1. Singh B, Bandopadhyay S, Kapil R, Singh R, Katare O P. Self-Emulsifying Drug Delivery Systems (SEDDS): Formulation Development, Characterization, and Applications. Critical Reviews in Therapeutic Drug Carrier Systems, 26(5):427–52, 2009.
2. Tatyana G, Simon B. Self-dispersing lipid formulations for improving oral absorption of lipophilic drugs. European Journal of Pharmaceutics andBiopharmaceutics.50:179-188 2000.
3. Wadhwa J, Nair A, Kumria R. Emulsion Forming Drug Delivery System for Lipophilic Drugs. Acta Poloniae harmaceutica-Drug Research, 69(2):179-191, 2012.
4. Yohei K, Koichi W, Manabu N, Shizuo Y, Satomi O. Formulation design for poorly water-soluble drugs based on biopharmaceutics classification system: Basic approaches and practical applications. International Journal of Pharmaceutics, 420:1– 10, 2011.
5. Hauss D J. Oral lipid-based formulations. Advanced Drug Delivery Reviews, 59:667–676, 2007.
6. Rane S S, Anderson B D. What determines drug solubility in lipid vehicles: Is it predictable? Advanced Drug Delivery Reviews, 60:638–656, 2008.
7. Driscoll C M, Griffin B T. Biopharmaceutical challenges associated with drugs with low aqueous solubility—The potential impact of lipid-based formulations. Advanced Drug Delivery Reviews, 60:617–624, 2008.
8. Tang B, Cheng G, Gu J C and Xu C H. Development of solid self-emulsifying drug delivery systems: preparation techniques and dosage forms. Drug Discovery Today, 13(13/14):606-612, 2008.
9. Porter C J, Pouton C W, Cuine J F, Charman W N. Enhancing intestinal drug solubilisation using lipid-based delivery systems. Advanced Drug Delivery Reviews, 60:673–691, 2008.
10. Sarpal K, Pawar Y B, Bansal A K. Self emulsifying drug delivery systems: Astrategy to improve oral bioavailability. Current Research and Information on Pharmaceutical Sciences, 11(3):42-49, 2010.
11. Kohli K, Chopra S, Dhar D, Arora S, Khar R K. Self-emulsifying drug delivery systems: An approach to enhance oral bio-availability. Drug Discovery Today, 15(21/22):958-965, 2010.
12. Patel P A, Chaulang G M, Akolkotkar A, Mutha S S, Hardikar S, Bhosale A V. Self Emulsifying Drug Delivery System: A Review. Research Journal of Pharmaceutical Technology, 1(4):313-323, 2008.
13. Dahan A and Hoffman A. Rationalizing the selection of oral lipid based drug delivery systems by an in vitro dynamic lipolysis model for improved oral bioavailability of poorly water soluble drugs. Journal of Controlled Release, 129:1–10, 2008.
14. Sander C and Holm P. Porous Magnesium Aluminometasilicate Tablets as Carrier of a Cyclosporine Self-Emulsifying Formulation. AAPS PharmSciTech, 10(4):1388-1395, 2009.
15. Katteboinaa S, Chandrasekhar V S R, Balaji P. Approaches for the development of solid self-emulsifying drug delivery systems and dosage forms. Asian Journal of Pharmaceutcal Sciences, 4(4):240-253, 2009.
16. Mura P, Valleri M, Cirri M, Mennini N. New solid self-microemulsifying systems to enhance dissolution rate of poorly water soluble drugs. Pharmaceutical Development and Technology, 17(3):277–284, 2012.
17. Beg S, Swain S, Singh H P, Patra N, Rao B. Development, Optimization, and Characterization of Solid Self-Nanoemulsifying Drug Delivery Systems of Valsartan Using Porous Carriers. AAPS PharmSciTech, 13(4):1416-1427, 2012.
18. Kang M J, Jung S U, Song W H, Park JS, Choi S, Taek K, Choi H K, Choi Y W, Lee J. Immediate Release of Ibuprofen from Fujicalin-based Fast dissolving Self-emulsifying Tablets. Drug Development and Industrial Pharmacy, 37(11):1298–1305, 2011.
19. Singh B, Singh R, Bandopadhyay S, Kapil R, Garg B. Optimized self nanoemulsifying systems of Carvedilol. Colloids and Surfaces B: Biointerfaces, 101:465–474, 2012.
20. Beg S, Jena S S, Patra N, Rizwan M, Swain S, Sruti J, Rao M E B, Singh B. Development of solid self-nanoemulsifying granules (SSNEGs) of ondansetron hydrochloride with enhanced bioavailability potential. Colloids and Surfaces B: Biointerfaces, 101:414–423, 2012.
21. Kallakunta V R, Bandari S, Jukanti R, Reddy P, Reddy V. Oral self emulsifying powder of lercanidipine hydrochloride: Formulation and evaluation. Powder Technology, 221:375–382, 2012.
22. Iosioa T, Voinovicha D, Perissuttia B, Serdoza F, Hasaa D, Grabnarb I, Zarad G P, Muntonid E, Pintoe J F. Oral bioavailability of silymarin phytocomplex formulated as self-emulsifying pellets. Phytomedicine, 18:505–512, 2011.
23. Zhanga Y, Wanga R, Wua J, Shena Q. Characterization and evaluation of self-microemulsifying sustained-release pellet formulation of puerarin for oral delivery. International Journal of Pharmaceutics, 427:337–344, 2012.
24. Mahmoud E, Bendas E R, Mohamed M I. Effect of Formulation Parameters on the Preparation of Superporous Hydrogel Self-nanoemulsifying Drug Delivery System (SNEDDS) of Carvedilol. AAPS PharmSciTech, 11(1), 2010.
25. Jannin V, Musakhanian J, Marchaud D. Approaches for the development of solid and semi-solidlipid-based formulations. Advanced Drug Delivery Reviews, 60:734–746, 2008.
26. Chambin O. Influence of cryogenic grinding on properties of a self-emulsifying formulation. International Journal of Pharmaceutics, 278:79–89, 2004.

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