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Self-Microemulsifying Drug Delivery Systeam: Special Emphasis on Various Oils Used In Smedds.

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ABSTRACT
In pharmaceuticals, poorly aqueous soluble drug candidates are becoming a challenging to administer into a dosage form, as 40-50% new chemical entities discovered are found to be poorly aqueous soluble which leads to allow their adequate absorption from GIT followed by oral administration. Due to ease of administration & painless approach oral administration remains favoriteamong other routes of administration. The main problem in oral drug formulations is poor bioavailability due to poor aqueous solubility. So formulation scientists are adopting different strategies to enhance the absorption & to improve the bioavailability of the poorly aqueous soluble drug which is a challenging one. The different strategies used are nano-suspensions, complexation, pH modification, Solid dispersion, liposome, solid lipid nanoparticle (SLN), Self-Emulsifying Drug Delivery systems (SMEDDS) etc. In last few decades, Pharmaceutical research area is highly diversified for self-emulsifying systems: from micron to nano size. Therefore, nowadays (SMEDDS) has gained much attention as it requires low dose and the drug can be protected into the hostile environment in the gut also it forms the droplet size <100 nm.
This article aims to review (SMEDDS) their pharmaceutical application in the delivery of drug with special emphasis on various oils used in (SMEDDS).

Keywords: - SMEDDS, Oils, Poorly Water-Soluble Drug

I. INTRODUCTION

As 40% of new chemical entities found are poorly aqueous soluble which resulted into the poor bioavailability of drug. So for the therapeutic drug delivery of those drugs in recent years SMEDDS is considered to be the reliable option. In 1943 T.P. Hoar & J.H. Shulman professors of chemistry at Cambridge University coined the term microemulsion [1]. Most preferred and convenient route over the other route is oral route of administration, but limitations are poor solubility & poor bioavailability of the drugs along with the rapid metabolism and lack of constant level in blood/plasma level [2].SMEDDS are isotropic mixtures of the oil, surfactant, co. surfactant & co-solvents. When SMEDDS administered orally upon mild agitation it undergoes spontaneous emulsification & forms fine O/W emulsion. Where this emulsified oil stimulates bile's secretion and drug containing oil droplets further emulsified by bile salts. Lipid droplets are then metabolized by lipases which are secreted by salivary gland, gastric mucosa, pancreas, which further hydrolyze the oil (triglycerides) into mono/di glycerides & free fatty acids. Upon further Solubilization of these molecules occurs during the passage of GIT forms the emulsion droplets, vesicular structure and micelles containing phospholipids and cholesterol [3].

ADVANTAGES

1. It enhances oral bioavailability of poorly soluble drug also reduces the dose of drug.
2. It reduces the irritation caused by the prolonged contact between the drug &wall of GIT.
3. SMEDDS protects the drugs from the hostile environment into the GI tract.
4. Excipients used in Smedds are mainly having the inhibitory effect on efflux transporters which leads to the increase in the bioavailability of the drug. E.g.- tween-80, spans, Cremophor (EL & RH)[1].
5. It delivers protein delivery which is prone to the enzymatic hydrolysis in the GIT.
6. It reduces variability including food effects.

TYPES OF SELF EMULSIFYING SYSTEMS:

Majorly these are of following types: Self emulsifying System, Self-micro emulsifying

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System, Self-nano emulsifying System (SEDDS, SMEDDS, and SNEDDS). These are stable isotropic mixture of (natural/synthetic) oil, (solid /liquid) surfactant & co. surfactant that form the fine O/W emulsion, micro-emulsion, and nano-emulsion respectively when introduced to aqueous medium under gentle agitation. Thus these formulations readily dispersed into the GIT, where the motility of the stomach provides the necessary agitation for self-emulsification.

SEDDS are the thermodynamically unstable (in aqueous or physiological conditions) simple binary composition of (lipophilic phase & drug) or (lipophilic phase, surfactant & drug). SEDDS formulations provide lipid droplets in the range 200 nm- 5 um providing a larger surface area for absorption. Dispersion having appearance turbid and development of SEDDS is mainly done by using of ternary phase diagram. Surfactant used in sedds is having the HLB value below 12.

SMEDDS requires the use of a co-surfactant to generate a microemulsion and defined as the isotropic mixture if the oil, surfactant &co. surfactant which forms O/W emulsion upon gentle agitation and forms the droplets size in between 100-300 nm. This droplet provides the larger surface area for the absorption of the drugs. Formed dispersion having appearance optically clear to translucent and the development is mainly done by using of the pseudo ternary phase diagram. Surfactant used in sedds is having the HLB value above 12[4].

SNEDDS are defined as the isotropic mixture if the oil, surfactant &co. surfactant which forms O/W emulsion upon gentle agitation and forms the droplets size below <50 nm. Snedds involves the digestion of the excipients which forms nanodroplets. This droplet formed with increased surface area due to the decrease in the interfacial tension which are available for the absorption of poorly aqueous soluble drugs. Research also reveals that Snedds facilates transcellular and paracellualar absorption thereby the drug is absorbed through the lymphatics via chylomicron synthesis of components of the oil phase of the emulsion, thus inhibits the first pass metabolism of drug. Besides that, Smedds / sedds require higher conc. of the surfactant while Snedds requires the (3-10%) of the surfactant which is having HLB value above 12[5, 6].

Lipid formulation classification system

Due to the large no excipients combinations used to formulate lipid based formulation especially self-emulsifying system, the lipid formulation classification system (LFCS) was introduced by Pouton in 2000 and recently updated into 2006 for the stratify the formulations with the similar components parts. The different lipid drug delivery systems are there which include lipid emulsion, lipid solution, lipid microemulsion etc. Based on the composition, effect of dilution and digestion ability to prevent drug precipitation, the LFCS classified lipid-base formulation into four major parts [7].

Type I: This systemconsists of formulations which comprise drug in solution of triglycerides or mixed glycerides or in oil water emulsion which further stabilized by low amount of emulsifiers as 1% w/v polysorbate 60 and 1.2% w/v lecithin. This system possesses a coarse dispersion particle. Generally, this system has poor initial aqueous dispersion which needs digestion by pancreatic lipase/co-lipase in GIT for more amphiphilic lipid digestion products and then the transfer of drug into colloidal aqueous phase is promoted. This system is represented for the formulation of the potent drugs and highly lipophilic drug where the drug solubility in oil is sufficient for the incorporation of the required dose [8].

Type II: This lipid formulation system also known as non-water soluble component system. In this system self-emulsification is obtained at range surfactant above 20-25% w/w, but higher surfactant content of 50-60% w/w cause formation of viscous liquid crystalline gels at oil/water interface. Type II system provide the advantage of overcoming the slow dissolution step typically observed with solid dosage forms.

Type III: This lipid based formulation known as SMEDDS and defined by inclusion of hydrophilic surfactant having HLB>12 and co-solvent like PEG. These systems are further differentiating into type IIIA and type IIIB formulation in order to known specific hydrophilic system. Where III B content of hydrophilic surfactant& co surfactant increases and lipid content get decreases.

Type IVsystem is recently added system to LFCS which exclude natural lipid from the formulation and represent hydrophilic formulation. Due to maximum solubility of drug in surfactant and co-solvent, the drug payload is increased in these formulations. These systems produce very fine dispersion in aqueous media as compared to simple glycerides containing formulation [4].

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Self-emulsification mechanism

The actual mechanism of SMEDDS is still not well understood. But some of the scientist suggested that when the entropy changes in the system self-emulsification process occurs, which favors dispersion is greater than the energy required to increase surface area of the dispersion[9]. Moreover free energy of the conventional emulsion is directly proportional to the energy required to form a new surface between the two phases which is given by the following equation:

$$\Delta G = \Sigma N\pi r2\sigma$$

Where:

ΔG = free related to the process (ignoring the free energy of the mixing)

N = no. of droplets with the radius 'r'

σ = interfacial energy associated with process.

The two phases of the emulsion will tend to separate with the time in order to decrease the interfacial energy and subsequently free energy associated with system. Thus emulsion resulting from the aqueous dilution stabilized by the emulsifying agent. This agents form monolayer of the emulsion droplets hence reduces the interfacial energy, as well as acts as barrier to prevent coalescence [10].

COMPOSITION OF SMEDDS:

1. **API:** According to the BCS classification system mainly there are four types; among them BCS class II drugs are having low solubility, high permeability. Therefore, these classes are employed in the preparation of the SMEDDS. Mainly drugs having dose are not suitable candidates of SMEDDS unless they are showing high solubility into one of the components of the Smedds. Also drugs should not have its log P value near about 2.

BCS Class IIExamples:ketoconazole, glibenclamide, cyclosporine-A, Itraconazole etc.

2. **Lipids (oils):**Solubilization and access of the drug to the lymphatic circulation of poorly aqueous soluble drug is mainly depending upon the type and concentration of oil is used in the formulation therefore oil is considered to be the important component of the SMEDDS. For the selection of oil regulatory guidelines should be considered depending on route of administration.
3. **Surfactant:**

Mainly to adopt the self-emulsification process by Smedds surfactant are to be added which is prime process to form microemulsion and to solubilize hydrophobic drug which leads to improve the dissolution rate of the drug. Surfactant is the amphiphilic in nature which is composed of both hydrophilic (polar) and lipophilic (non-polar) group. By selecting suitable surfactant low ultra-tension at the oil-water interface can be attained. Selection of the surfactant is depending upon following parameter:

a) Mainly selection of surfactant is depending upon the HLB value, surfactant having high HLB forms the O/W microemulsion.

b) Efficiency and rapidity to micro emulsify the selected oil,

c) Type of emulsion to be formulated,

d) Safety (depends upon the route of administration),

e) Solubilizing capacity if the drug,

f) Ability to inhibit p-gp (if API is p-gp substrate) which leads to improve the oral bioavailability of the drugs which are p-gp substrate transporters due to which surfactant gained so much attention to be used in Smedds[11].

Also surfactants also helpful for the enhancement of the permeability of as it disrupt the intestinal cell membrane which is comprised of the lipid [12].Surfactant also enhances the permeability by opening the tight junctions; this study was conducted by [Sha et al], wherePermeability of the drug was enhanced & observed with surfactant labrasol due to opening of tight junctions [13].Utility range of surfactant used in the Smedds is about 30-60%, however high (% of the surfactant) causes GI irritation due to tissue damage also self-emulsification efficiency get decreased.

TABLE NO. 1: Commonly Used Polyoxyethylene Surfactants:

Chemical name	Commercial name	HLB
POE Sorbitanmonolaurate	Tween 20	17
POE Sorbitanmonopalmitate	Tween 40	15.6

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POE Sorbitanmonostearate	Tween 60	15.0
POE Sorbitanmonooleate	Tween 80	15.0
POE glycerol trioleate	Tagat TO	11.5
POE- 40- Hydrogenated castor oil	Cremophor RH 40 (solid)	14.0-16.0
POE- 35- Castor oil	Cremophor EL (liquid)	12.0- 14.0

Cosurfactant:

Along with required conc. of surfactant (>30%) cosurfactant is aids into the self-emulsification. Presence of the cosurfactant decreases bending stress of interface which provides flexibility to the interface to form microemulsion. If nonionic surfactant is used into SMEDDS then co. surfactant is not used. Both surfactant &co. surfactant are to be used into smedds not only for formulation but also for the solubilization of drug into SMEDDS. Some of the organic solvents such as (propylene glycol) PG, (polyethylene glycol) PEG, ethanol also Transcutol P are helpful to dissolve the large amounts of drug / hydrophilic surfactants into the lipid base and acts as co. surfactant. Higher conc. of the co. surfactant resulted into the precipitation of the drug as upon dilution of smedds partitioning of the co. surfactant into aqueous phase.

OILS USED IN SMEDDS:

In Smedds oil is mainly used for the purpose of too solubilize the hydrophobic/lipophilic drug to enhance the bioavailability of the drug. Lipids are naturally occurring oil /fats which are composed of triglycerides and fatty acids of varying chain length of the degree of unsaturation. Selection of the oil mainly plays a vital role in SMEDDS as it mainly as it determines the amount of the drug that dissolves in the system [14].Generally lipids are classified on the basis of their structure, polarity, degree of interaction with water. Polarity of the lipid highly influences the release of the drug if as lipid having higher polarity which indicate quick release of drug into the aqueous state. A study shows that the rate of release of the **idebenone** from Smedds formulation was duly depended on the basis of the polarity of the oil used in the formulations which has the highest polarity with (labrafil 2609 HLB > 4) [15].

A lipid molecule with large hydrophobic portion is desirably used in the Smedds as it maximizes amount of the drug that can be solubilized in Smedds than hydrophilic portion. The lipid part of the Smedds mainly forms the core of the emulsion particle which are composed of the non-polar/polar lipids according to the Class-I lipid classification system [16].The most common lipid excipient used in the Smedds is triglycerides vegetable oils derivative as they are not having any safety issue, fully digested and absorbed [17].Triglycerides are mainly classified into the long chain triglycerides **(LCT**), medium chain triglycerides **(MCT)**. The capacity of the solvent is mainly based on the effective concentration of the ester groups [16].Stability of the emulsion is mainly depend upon the rheological behavior of the oils as non-digestible lipids (mineral oil) e.g. liquid paraffin & sucrose polyesters mainly remain unabsorbed into the intestinal lumen and reduce the absorption of the drug by retaining certain amount of co. administered drug. Digestive lipids such as triglycerides, diglycerides, fatty acids, phospholipids, cholesterol, and other lipid based synthetic derivative helps in the improvement of the bioavailability of the drug. Edible oils based on the natural origins are favored but they do not possess the high solubilization property for the lipophilic drug also not having the sufficient capacity for the self-emulsification also possess a large molecular volume. Therefore, instead of the edible oils mainly hydrolyzed or modified oils of the vegetable oils are used as they are having the superior self-emulsification.

Various types of oils used are:

Fixed oils (long- chain triglycerides): Soybean oil, arachis oil, cottonseed oil, maize (corn) oil, hydrolyzed corn oil, olive oil, sesame oil, sunflower oil, palm oil, peanut oil, triolein etc.

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Medium- chain triglycerides and related esters: Caprylic/capric triglycerides (Akomed E, Akomed R, Miglyol 810, and Captex 355, Crodamol GTCC), fractionated coconut oil (Miglyol 812), Captex 300, Labrafac CC, Triacetin

Medium- chain mono and di- glycerides: Mono and diglycerides of capric/caprylic acid. (Capmul MCM and Imwitor)

Long- chain mono glycerides: Glycerylmonooleate (Peceol, Capmul GMO), glycerylmonolinoleate (Maisine - 35)

Propylene glycol (PG) fatty acid esters:
PG Diester of caprylic/capric acid (Labrafac PG),PG monocaprylic ester (Sefsol- 218),PG monolaurate (Lauroglycol FCC, Lauroglycol90, Capmul PG- 12)PG dicaprylate (Miglyol 840)

Caprylic/capric/diglyceryl succinate: Miglyol 829

Fatty acids: Oleic acid (Crossential O94), Caprylic acid

Fatty acid esters: Ethyl Oleate (Crodamol EO), Ethyl butyrate, Isopropyl myristate, Isopropyl palmitate

Vitamins: Vitamin E

Mineral oil: Liquid paraffin

(Long-chain triglycerides):

Fixed oils i, e vegetable oils containing the mixture of the esters of the unsaturated long chain fatty acids [18].Fixed oils are considered to the safe for digestion and available into the daily food. Long chain triglycerides are lipids which are consisting of the 14-20 long fatty acid chain of the carbon atoms [19].Large hydrophobic portion of triglycerides are mainly having high solvent capacity of lipophilic molecule. Some of the marketed formulations consisting of the LCT e.g. (Neoral® consist of the olive oil which shows improved bioavailability) &Topicaine® gel (consist of Jojoba oil for transdermal application) have been successfully used in the formulation of microemulsion using LCT [20].Long chain triglycerides like **cottonseed** and **soybean** are reported to enhance the bioavailability by stimulation of lymphatic transport of the drug [21].When drugs like Mepitiostane (pro-drug of the epitiostanol) and Mepitiostaneolefin with octanol: water partition coefficients of 6 and 5.1 respectively, when given with the LCT are proved to be undergoing the significant lymphatic transport of drug [22].It is well known that long hydrocarbon chains (high molecular volume) such as soybean oil, castor oil are difficult to prepare microemulsion compared to MCT (low molecular volume) such as capmul MCM and Miglyol. As the solubilizing capacity of oil for lipophilic moiety increases with chain length (hydrophobic portion) of the oil. Hence the selection of oil is a compromise between the solubilizing potential and ability to facilitate the formation of microemulsion [21].Drug substance should possess minimum solubility of 50 mg/ml in LCTs for lymphatic absorption [16].

Medium chain triglycerides and related esters:

Lipids which are having fatty acid chain in the range of 6-12 carbons are categorized as MCT [19].MCT are the most commonly used oil for SMEDDS as they are resistant to oxidation and possess high solvent capacity compared to LCT because of their high effective concentration of ester group. MCT which are produced from the distillation of coconut oil are known as glyceryl tricaprylate and comprises of saturated C8 and C10 fatty acids in the liquid state [23].(Labrafac CM 10), a MCT, has shown enhancement in the solubility for fenofibrate and produced large microemulsion region at all surfactant/co-surfactant combinations than Maisine 35, which, is a LCT.

Oils used into various routes of administration:

As the different oils are to be used into the SMEDDS/ SNEDDS formulation mainly belonging to the various categories like: LCT, MCT etc. A new trend is coming up which involves the formulation of the microemulsion based drug delivery. For example it comprises microemulsion based topical gel, microemulsion based in-situ gel,microemulsion based nasal drug delivery or microemulsion also incorporated into vaginal route etc. So the selection of oil is mainly gets important as they will be using for different route of administration.

1. **Oils used in oral drug delivery:**
Example are: Capmul® MCM), Castor Oil, Capryol 90, Triacetin (SCT), Glycerol Mono Oleate, Sunflower Oil, Ethyl Oleate, Capmul PG 8 NF, Gelucire (44/14), Labrafil WL 2609, Sesame Oil, Triethyl Citrate Benzyl Alcohol, Captex 355, Caprylic Acid: Labrafil, Mixture Of Labrafil®/Capmul, Capmul MCM C8, Propylene Glycol Monocaprylate, Cremophor RH40, Maisine 35-1 etc.
2. **Oils used in topical drug delivery:**Example: Isopropyl myristate, Oleic Acid, Isopropyl Palmitate, Transcutol P etc.

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3. **Oils used in occular drug delivery:**Example: Capryol 90,oleic acid, olive oil, Castor Oil, soybean oil etc.
4. **Oils used in vaginal drug delivery:**Example: Capryol 90, Linseed oil, Oleic Acid, lauric acid, myristic acid, capric acid, oleic acid, linoleic acid, linolenic acid etc.

OILS USED FOR VARIOUS DRUGS:

Table 2: oils used in the formulation of Microemulsion of various drugs.

Sr. No	Name Of Article	Author	Journal	Drug	Oils Used	Route Of Administration	Ref. No
1	Development of a solidified self-microemulsifying drug delivery system (SSMEDDS) for atorvastatin calcium with improved dissolution and bioavailability	Dong WY, Sona HY, Kima JH, "et al".	International Journal Of Pharmaceutics	Atorvastatin Calcium	Capmul® MCM),	Oral Route	24
2	Development and evaluation of a self-emulsifying drug delivery system of amphotericin B	Bhattacharyya A, Bajpai M.	Asian Journal Of Pharmaceutics	Amphotericin B	Glycerol Mono Oleate,	Oral Route	25
3	Novel Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS) for Oral Delivery of Olmesartan Medoxomil: Design, Formulation, Pharmacokinetic and Bioavailability Evaluation	Ali N, Ahmed G, Mamdouh G.	Pharmaceutics	Olmesartan Medoxomil	Capryol 90	Oral Route	26
4	Preparation and Evaluation of Self-micro Emulsifying Drug Delivery Systems of Lercanidipine hcl using Medium and Short Chain Glycerides: A Comparative Study	Suthar V.C, Butani S.B.	Asian Journal Of Pharmaceutics	Lercanidipine Hcl	Triacetin (SCT)	Oral Route	27
5	Microemulsion-loaded hydrogel formulation of butenafine hydrochloride for improved topical delivery	Pillai AB, Nair JV, Gupta NK, Gupta S.	Arch Dermatol Res	Butenafine	Isopropyl Palmitate	Topical Route	28

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6	Preparation and evaluation of novel microemulsion-based hydrogels for dermal delivery of benzocaine	Okur NU, Caglar ES, Arpa MD, Karasulu HY.	Pharmaceutical Development And Technology	Benzocaine	Isopropyl myristate	Topical Route	29
7	Formulation and evaluation of microemulsion-based hydrogel for topical delivery	Sabale V, Vora S.	International Journal Of Pharmaceutical Investigation	Bifonazole	Oleic Acid	Topical Route	30
8	Preparation and Pharmacokinetics Evaluation of Solid Self-Microemulsifying Drug Delivery System (S-SMEDDS) of Osthole	Sun C, Gui Y, Hu R, Chen J, Wang B, Guo Y, "et al".	AAPS Pharm Scitech	Osthole	Castor Oil	Oral Route	31
9	Development of SMEDDS using natural lipophile: Application to - Artemether delivery	Mandawgadea SD, Sharmab S, Pathakb S, Patravale VB	International Journal Of Pharmaceutics	Artemether	N-LCT, Capryol 90	Oral Route	32
10	Development and Evaluation of New Microemulsion-Based Hydrogel Formulations for Topical Delivery of Fluconazole	Coneac G, "et al".	American Association Of Pharmaceutical Scientists	Fluconazole	Transcutol P	Topical Route	33
11	Oral Bioavailability Enhancement of Acyclovir by Self-Microemulsifying Drug Delivery Systems (SMEDDS) Oral Bioavailability Enhancement of Acyclovir	Patel D, Sawant KK.	Drug Development And Industrial Pharmacy	Acyclovir	Sunflower Oil	Oral Route	34
12	Development of a solid self-microemulsifying drug delivery system (SMEDDS) for solubility enhancement of naproxen	Erpnjak KC, Zvonar A, Vrecer F, Perlin MG.	Drug Development And Industrial Pharmacy,	Naproxen	Miglyol 812/Peceol (1:1)	Oral Route	35

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13	Quality-by-design based development of a self-microemulsifying drug delivery system to reduce food effect of Nelfinavir mesylate	Kamboj S, Rana V.	International Journal Of Pharmaceutics	Nelfinavir Mesylate	Maisine 35-1	Oral Route	36
14	Spontaneous Emulsification of Nifedipine-Loaded Self-Nanoemulsifying Drug Delivery System	Weerapol Y, Limmatvapirat S, Vollrath MK, Sriamornsak P.	American Association Of Pharmaceutical Scientists	Nifedipine	Cremophor RH40,	Oral Route	37
15	Oral solid self-nanoemulsifying drug delivery systems of candesartan citexetil:formulation, characterization and in vitro drug release studies	Ali HH, Hussein AA.	American Association Of Pharmaceutical Scientists	Candesartan Citexetil	Cinnamon Oil	Oral Route	38
16	Response Surface Methodology for the Optimization of Celecoxib Self-microemulsifying Drug delivery System	Shaji J, Lodha Shital.	Indian Journal Of Pharmaceutical Sciences	Celecoxib	Labrafil WL 2609	Oral Route	39
17	Formulation Optimization and pharmacokinetics evaluation of oral self-microemulsifying drug delivery system for poorly water soluble drug cinacalcet and no food effect	Cao M, Xue X, Pei X, Qian Y, Liu Lan "et al".	Drug Development And Industrial Pharmacy	Cinacalcet	Ethyl Oleate	Oral Route	40
18	A-Tocopherol as functional excipient for Resveratrol and Coenzyme Q10 loaded SNEDDS for improved bioavailability and prophylaxis of breast cancer	Jain S, Garg T, Kushwah V, Thanki K, Agrawal AK, Dora CP.	Journal Of Drug Targeting	Resveratrol	Capmul MCM EP	Oral Route	41

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19	Self-microemulsifying drug-delivery system for improved oral bioavailability of pranlukast hemihydrate: preparation and evaluation	Baek Mk, Lee Jh, Cho Yh, Kim Hh, Lee Gw.	International Journal Of Nanomedicine	Pranlukast Hemihydrate	Triethyl Citrate Benzyl Alcohol	Oral Route	42
20	In vivo Evaluation of Self Emulsifying Drug Delivery System for Oral Delivery of Nevirapine	Chudasama AS, Patel VV, Nivsarkar M, Vasu KK, Shishoo CJ.	Indian Journal Of Pharmaceutical Sciences	Nevirapine	Caprylic Acid:	Oral Route	43
21	Ultra fine super self-nanoemulsifying drug delivery system (SNEDDS) enhanced solubility and dissolution of indomethacin	Shakeel F , Haq Nazrul, El-Badry M, Alanazi FK, Alsarra IA.	Journal Of Molecular Liquids	Indomethacin	Labrafil,	Oral Route	44
22	SNEDDS containing bioenhancers for improvement of dissolution and oral absorption of lacidipine. I: Development and optimization	Basalious EB, Shawky N, Badr-Eldin SM.	International Journal Of Pharmaceutics	Lacidipine	Mixture Of Labrafil® /Capmul	Oral Route	45
23	Statistical modeling, optimization and characterization of solid self-nanoemulsifying drug delivery system of lopinavir using design of experiment	Patel G, Shelat P, Lalwani A.	Drug Delivery	Lopinavir	Capmul MCM C8	Oral Route	46

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24	Design, optimization and evaluation of glipizide solid self-nanoemulsifying drug delivery for enhanced solubility and dissolution	Dash RN, Habibuddin M, Humaira T, Ramesh D.	Saudi Pharmaceutical Journal	Glipizide	Captex 355	Oral Route	47
25	Solid self-microemulsifying dispersible tablets of celastrol: Formulation development, characterization and bioavailability evaluation	Qi X, Qin J, Maa N, Chou X, Wua Z.	International Journal Of Pharmaceutics	Celastrol	Masine-1, Ethyl Oleate And Olive Oil	Oral Route	48
26	Solid super saturated self-nanoemulsifying drug delivery system (sat-SNEDDS) as a promising alternative to conventional SNEDDS for improvement rosuvastatin calcium oral bioavailability	Abo Enin HA, Abdel-Bar HM.	Expert Opinion On Drug Delivery	Rosuvastatin Calcium	Garlic /Olive Oil	Oral Route	49
27	Design and Development of Oral Lipid Based Solid Self Micro emulsified Drug Delivery System	Chaudhari SP, Kolhe S, Ranpise AA, Ratnaparkhi MP.	American Journal Of PharmTech Research	Nimorazole	Capmul PG 8 NF	Oral Route	50
28	Design and Evaluation of Self-Emulsifying Drug Delivery Systems (SEDDS) of Nimodipine	Kale AA, Patravale VB.	American Association Of Pharmaceutical Scientists	Nimodipine	Gelucire (44/14)	Oral Route	51
29	Development of Self-microemulsifying Drug Delivery System for Oral Delivery of Poorly Water-soluble Nutraceuticals	Shah A, Desai H, Thool P, Dalrymple D, Serajuddin A.T.M.	Drug Development And Industrial Pharmacy	Vitamin A, Vitamin K2, Coenzyme Q10, Quercetin And Trans-Resveratrol	Capmul McmNf: Captex 355 Ep/Nf (1:1)	Oral Route	52

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30	Self-nanoemulsifying drug delivery systems (SNEDDS) for oral delivery of protein drugs I. Formulation development	Rao SVR, Shao J.	International Journal Of Pharmaceutics	Beta-Lactamase	Laurogly col FCC,	Oral Route	53
31	Design and Evaluation of Self-Nanoemulsifying Drug Delivery System of Flutamide	Jeevana J.B, Sreelaks hmi K.	Journal Of Young Pharmacists	Fluttamid e	Sesame Oil	Oral Route	54
32	Design, development and optimization of selfmicroemulsifying drug delivery system of an anti-obesity drug	Desai J, Khatri N, Chauha n S, Seth A.	Journal Of Pharmacy And Bioallied Sciences	Orlistat	Propylen e Glycol Monocap rylate	Oral Route	55
33	Solid self-microemulsifying drug delivery system of ritonavir	Deshmu kh A, Kulkarn i S.	Drug Development And Industrial Pharmacy,	Ritonavir	Imwitor 988	Oral Route	56
34	Food grade microemulsion systems: Canola oil/lecithin:n-propanol/ water	Abbasi S, Radi M.	Food Chemistry	-	Canola oil	Oral Route	57
35	Formation and Investigation of Microemulsions Based on Jojoba Oil and Nonionic Surfactants	Shevach mana M, Shania A, Gartib N.	Journal of American Oil Chemists Society	-	Jojoba Oil	-	58
36	Rats given linseed oil in microemulsion forms enriches the brain synaptic membrane with docosahexaenoic acid and enhances the neurotransmitter levels in the brain	Dhavam ani S, Belur R.L	Nutritional Neuroscience	Docosahe xaenoic acid	linseed oil	Oral Route	59

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37	The use of orange peel essential oil microemulsion and nanoemulsion in pectin-based coating to extend the shelf life of fresh-cut orange	Mohsen R, Sara AD, Hamid RA, Sedigheh A.	Journal of Food Processing and preservation	-	Orange oil	Oral route	60

II. CONCLUSION:

Lipid based drug delivery system are becoming promising approach for increasing bioavailability, solubility of the various drugs. The effect of the lipids on the orally administered drug is highly complex due to the various mechanism through which lipid can alter the biopharmaceutical aspects of the given drug. So the understanding the role of various components used in lipid based formulation is very important. Therefore this review focused on the basics of the smedds and various oils used in the lipid based drug delivery system also their mechanism with the oils used according to the various routes of administration.

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