WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.632
Volume 9, Issue 7, 2302-2314 Review Article ISSN 2278 – 4357

A REVIEW ON SELF NANO EMULSIFYING DRUG DELIVERY SYSTEM CONTAINING DRUGS OF NATURAL ORIGIN

Heena Farooqui* and Prashant Upadhyay

School of Pharmaceutical Sciences, IFTM University, Delhi Road, Moradabad (U.P) 244001, India.

Article Received on
22 May 2020,

Revised on 12 June 2020,
Accepted on 02 July 2020

DOI: 10.20959/wjpps20207-16684

***Corresponding Author**
Heena Farooqui
School of Pharmaceutical Sciences, IFTM University, Delhi Road, Moradabad (U.P) 244001, India.

ABSTRACT

The aim of this review is to study the development of Self Nano Emulsifying Drug Delivery System (SNEDDS) loaded with drugs of natural origin like Phytoconstiuents, Proteins, Enzymes and Biosimilars the drugs of biotechnological origin. It's a boon in pharmaceutical field when nanotechnology combines with natural drugs because nanocarriers might be able to increase the bioavailability, potentiate the plant extracts therapeutic effect and reduce the required dose, side effects. Lipid based nano carriers such as SNEDDS is manufactured to improve the solubility of poorly and low water soluble drugs or drugs that come under Biopharmaceutical classification system (BCS) class II and class IV. SNEDDS is mainly an isotropic mixture of oil, surfactant and co-surfactant and drug molecule which suddenly form oil in water nanoemulsion of size ranges 50-100 nm in efficient mixing. Various pseudoternary phase diagrams are constructed to identify the nano-emulsification region.

KEYWORDS: Poor Solubility, SNEDDS, BCS, Nanotechnology, Natural Origins.

INTRODUCTION

Novel drug delivery system (NDDS) is advance towards the delivery of drug in more efficient way with the help of new technologies and formulations. It was developed to deliver the chemical entity or active constituent in more effective way other than conventional dosage form, it is a mixture of latest techniques and new developed dosage forms which gives best outcomes compared to the conventional dosage forms.[1] The attention has been focused to achieve benefits of mixture of herbal and nanotechnology. It targets on engineering novel applications.[2] There are so many reasons to develop novel drug delivery system such as re-

patenting the successful drugs by applying the new method of drug delivery, to deliver the bio similar or genetically engineered drugs such as peptides and proteins to their site of action without changing immunogenicity or biological activation, treating the diseases of enzymes deficiency and by better targeting cancer therapies can be improved, it increases therapeutic efficacy and safety.[3] NDDS when combines with phyto-constituents provides two main advantages that is delivery of drug at a rate directed by the need of the body, over the treatment of period and it should deliver the active constituent of herbal drug direct to the site of action.[4] Moreover, NDDS improves the performance of some biotechnological strategies such as protein delivery, glycoprotein, gene therapy, peptide, RNA interface etc.[5]

Nanotechnology is now a day's becomes most essential elements of pharmaceutical sciences as it is the combination of science and technology at the nano scale ranges from 1 to 100nm.[6] Nano scaled drug delivery devices have been prepared as an important weapon to deliver recombinant proteins, vaccines, nucleotides to modify the kinetics, distribution and release of targeted drug. This delivery is also said to target delivery as the drugs target directly to the cell or tissue for quick response and reduce unwanted side effects.[7] Lipid based drug delivery system (LDDS) are also having recent advancement in pharmaceutical field as this system target to improve the solubility and increases bioavailability of poorly soluble drugs and to enhance the therapeutic efficacy. LDDS are divided into a micro and nano scale and are broadly classified into four types like solid lipid dosage forms, emulsion system, solid lipid tablets and vesicular system.[8] Self Emulsifying Drug Delivery System (SEDDS) are the type that comes under LDDS, SEDDS are further classified into Self Microemulsifying Drug Delivery System (SMEDDS) and Self Nano Emulsifying Drug Delivery system (SNEDDS) is based on the size ranges.[9]

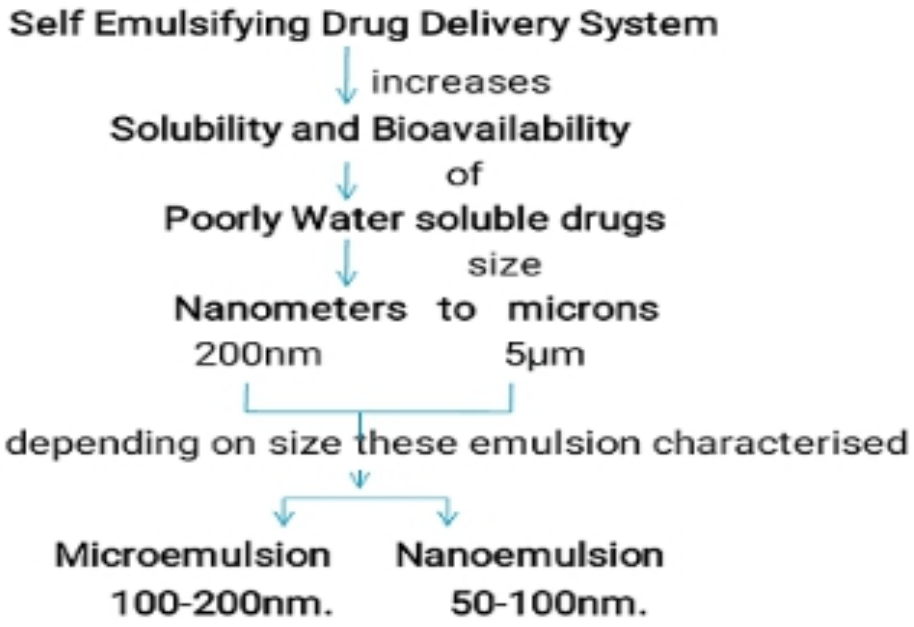

Fig. 1: Self emulsifying drug delivery system.

Many types of polymers/oils are used in the manufacturing of LDDS, these plays an important role in manufacturing of drug delivery technologies by providing controlled release of medicinal agent in fixed and constant manner over a long period. Polymers used are classified into two types such as synthetic polymer and natural polymer.

1. Synthetic polymers: Poly alkyl cyano acrylates are drug carrier for ophthalmic, parenteral and oral preparations. Poly lactic acid is a suitable carrier for sustained release of narcotic agonist, anti cancer agents such as cisplatin, cyclophosphamide, doxorubicin and narcotic antagonist. They are divided into two types:

a) Non- biodegradable polymers: Poly methyl methacrylate (PMMA), Glycidyl methacrylate, Epoxy polymers, Acrolein.

b) Biodegradable polymers: Lactides, Glycolides and their co-polymers, Poly alkyl cyano acrylates, Poly anhydrides.

2. Natural polymers: Albumin, Gelatin, Starch, Chitosan are naturally occurs and widely used in drug delivery system.[10]

It was found that SNEDDS loaded Andrographolide, which is isolated from *Andrographis paniculata* Nees that gives antibacterial, antiviral, antipyretic and anti-inflammatory effects was used to improve bioavailability and oral dissolution rate. The selection of oil, surfactant

and co-surfactant was done on the basis of solubility studies. Nano-emulsification are determined by different phase diagrams. From robustness to dilution, formulation containing Capryol-90, Tween 20 and PEG 400 (20: 70:10 and 20: 60: 20) was selected for the dissolution study. From the chosen formulation, transmittance, zeta potential, thermodynamic stability, droplet size, robustness to dilution, bioavailability and in- vitro release studies were determined.[11] Besides having the advantages, SMEDDS and SNEDDS have several disadvantages like high coast, low stability, portability, low drug loading, irreversible drug and excipients precipitation creates problem, surfactants in formulation can produce gastrointestinal irritation therefore to overcome these problems SMEDDS/SNEDDS are transforming into solid dosage form by adsorption onto porous carriers, by spray drying, by freeze drying, by melting granulation, by extrusion etc and that may enhanced solubility and bioavailability, forms low production cost, high stability, reproducibility, convenience of process control and for better patient compliance.[12] It is observed Recent years, lipid based systems are on prior interest of pharmacist because of having potential to act as therapeutic enzymes and peptide based drug delivery vehicles with incorporation of great range of active therapeutic protein and peptide molecules. These therapeutic molecules in microemulsion or nanoemulsion nurture protein drug distribution in the vehicles for enhanced drug solubilisation capacity, for easy preparation, increasing bioavailability and enhancing shelf life. Compatibility of proteins is studied along with characterization of microemulsion.[13]

SNEDDS of Cardamom (*Amomum Compactum*) essential oil, was successfully formulated by the optimum formula which contains mixture of oil component (*Amomum compactum* essential oil and Virgin coconut oil), tween 80 and poly ethylene glycol 400 (PEG 400) v/v with the help of Design Expert® software. The optimized formulation contains 10% *Amomum compactum* essential oil, 10% virgin coconut oil, 65.71% of tween 80, and 14.29% of PEG 400 and characterized by droplet size, viscosity, zeta potential, thermodynamic stability, morphology using Transmission Electron Microscopy (TEM), the results shows proper percent transmittance and emulsification time.[14] They are prepared to improve the solubility and oral bioavailability of Tetrandrine (Tet.), an alkaloid obtained from bisbenzylisoquinoline alkaloids. Research suggests that successful SNEDDS will improve the dissolution and oral bioavailability of Tet.[15] It was also found that SNEDDS was used to improve and increase the oral bioavailabilty and diminishes the food effect in fasted state[16] and also used to protect plantago lanceolata extract from hydrolysis and to improve its antioxidant effect. *Plantago lanceolata* L. leaves having components like catalpol, aucubin

and acteoside shows anti- inflammation, antioxidant, antineoplastic and hepatoprotective activity. Their formulations are investigated by their physical properties, in vitro cytotoxicity and by in vivo AST/ALT values. The anti-inflammatory effect of PL-SNEDDS was confirmed by ear inflammation test. PL-SNEDDS are manufactured to deliver active natural compounds in a stable, efficient and safe manner.[17] They are also formulated and evaluated for the establishment of the pharmacokinetic parameters and biodistribution of Artesunate (obtained from Chinese medicinal plant). Artesunate nanoemulsion was developed using lipid, surfactant and co-surfactant by spontaneous emulsification method. The characterization studies were performed include particle size distribution, poly dispersibility index, zeta potential, viscosity, refractive index, % transmission and conductivity.[18] Formulation of Noscapine (Nos) loaded in self emulsifying solid dispersible Microparticles (SESDs) was afforded by emulsification using an optimized formula of Labrafil M1944, Tween-80, and Labrasol was prepared by spray-drying with hydroxypropyl methylcellulose (HPMC), with and without mannosamine (Mann- Nos SMEDDS and Nos- SMEDDS respectively). SMEDDS and SESDs were optimized for size, polydispersity, surface charge, entrapment efficacy, in-vitro permeability, in vitro release kinetics and for oral pharmacokinetics.[19] Drugs that are classified as BCS class II and class IV with poor aqueous solubility and high membrane permeability. Oral route is the easiest way of drug administration, the oral bioavailability of poorly water soluble drug can be increased when co-administered with a meal rich in fat that also increases the interest in the lipid based drug delivery system (LBDDS) with emphasis on Solid-SNEDDS.[20] They are thermodynamically and kinetically stable that has globule size less than 100nm, it creates the chemical stability as well as solubility of drug product. The SNEDDS formulations are used for improving BCS Class II and Class IV drugs for improving solubility of poorly water soluble drugs and also to save the interfacial tension and improving the absorption rate of drug molecule.[21] It was defined that SNEDDS are isotropic mixture of oil, surfactant and co-surfactant forming o/w nano emulsion having droplet size range of 100-250 nm[22] 13. A study is done and found that the oral bioavailability and antioxidant potential by preparing the triple antioxidant SNEDDS i.e. Quercetin, resveratrol and genistein by QbD approach was enhanced[23] and are developed for increasing poor solubility and oral absorption of Akebia Saponin D. It was prepared by solvent evaporation method and was characterized by infrared spectroscopy, differential scanning calorimeter, solubility and morphological study. Pseudo ternary phase diagrams are constructed to determine the region of solubility and for optimization Akebia Saponin D-Phospholipid Complex (APC)-SNEDDS formulation, which was characterized by droplet

size determination, zeta-potential determination, morphology observation, robustness to dilution and thermodynamic stability were evaluated and in this pharmacokinetic parameters and oral bioavailability of Akebia Saponin D and APC- SNEDDS were investigated in rats.[24] Novel drug delivery system is an approach refers to formulation, technologies and system for transporting a pharmaceutical compound in the body as needed to safe achievement in desired therapeutic effects.[25] A plant polyphenol, Ellagic acid (EA) was known for its health benefits but are in limited use because of low oral bioavailability so SNEDDS formulation was prepared to overcome this problem.[26] SNEDDS can be used in ophthalmic, parenteral, intranasal and in cosmetics.[27] Increasing interest in nanopharmaceuticals had number of advancements in recent years with a target on engineering having novel applications. Nanophytomedicines, that was prepared from active phytoconstituents. The market of Nanomedicine was estimated to reach $ 30.9 billion in 2016. Nanotized herbal drug containing active principles of seawort, cassia twig and liquorice root was found effective in pulmonary, liver, skin cancer and bone. Also Nanotechnology has the ability to detect diseases at much earlier stages. Nanopharmaceuticals formulations knowledge has major impact on the nanotechnology of herbal medicines.[28] S-SNEDDS of Embelin was prepared, having capryol- 90 as oil phase. Box- Behnken experimental design was adopted to evaluate the formulation variables, X1 (amount of oil; capryol 90), X2 (amount of surfactant; Acrysol EL 135) and X3 (amount of co-surfactant; PEG 400). Optimised liquid formulations were formulated into free flowing S-SNEDDS by adsorption on the porous materials like Aerosil 200 and Neusilin and then compressed into tablet. FT-IR for drug and excipient interaction, characterization of S-SNEDDS by DSC and Powder XRD was performed for reduction in crystallinity which was further conferred by dissolution studies. TEM analysis was done for exhibited spherical globules and found that S-SNEDDS are stable for 6 months.[29] Naringenin (NRG), flavone present in grapefruit possesses anti-inflammatory, anti-carcinogenic, hepatoprotective and anti-lipid peroxidant effects. SNEDDS was prepared for enhancing the solubility and bioavailability of NRG. Preliminary screening was carried to select oil, surfactant and co-surfactant on the basis of solubilization and emulsification efficiency. Nano-emulsification region was identified by pseudoternary phase diagrams they were evaluated in terms of zeta potential, globule size, globule size distribution, zeta potential and surface morphology. TEM studies revealed nanoemulsion droplet size was less than 50 nm. Freeze thaw cycling and centrifugation studies are done for stability.[30] Herbal drugs are getting popular day by day. Most of herbal drugs are poorly soluble and have hydrophobic properties, leading to less bioavailability and therefore having

less efficacy in treatment and requires great amount of dose or requires several times dose administration so by keeping these points in mind SEDDS for herbal drugs are manufactured. Under gentle stirring SEDDS can be formed O/W micro/ nanoemulsion. The solubility studies, mechanism of self emulsification, construction of phase diagrams, optimization and characterization of herbal drugs in SEDDS formulation and in-situ absorption evaluation is done in rat intestine.[31] Impact of lipases on the release behaviour of a peptide drug from SNEDDS was evaluated. The lipophilic character of ion paired (octeriotide) with anionic surfactants (deoxycholate, decanoate, oleate and dodecylsulphate) complexes was characterized by determining the n-octanol/buffer pH 7.4 partition coefficient.[32] To improve the oral delivery of poorly soluble compounds on different lipid based formulations like SEDDS and SNEDDS attention has been paid. SNEDDS are used to prepare with lipids and lipophilic excipients, it affect bioavailability, drug absorption. SNEDDS have potential to increase bioavailability by multi-concerted mechanisms such as reduced intra-enterocyte metabolism by CYP-P450 enzymes, reduced P-glycoprotein (P-gp) efflux activity and hepatic first pass metabolism bypass via lymphatic absorption.[33] Natural products are the compounds that are derived from plants, animals and micro-organisms. The BCS predicts the importance of transporters and enzymes for obtaining drug bioavailability and disposition. According to water solubility and metabolism, BCS categorizes drugs into one of four classes. From review on 109 drugs of natural products, 29% of drugs are found belongs to class 1 that are having high solubility and extensive metabolism, 22% belongs to class 2 that are having low solubility and extensive metabolism, 40% belongs to class 3 that are of high solubility and poor metabolism and 9% of drugs belongs to class 4 that are low solubility and poor metabolism. Based on Biopharmaceutical drug disposition classification system, it serves as useful adjunct in evaluating the potential characteristics of new natural products.[34] From the ancient times, herbal medicines are broadly used recently all over the world. The biologically active compounds like flavonoids, tannins and terpenoids are very much soluble in water but have less absorption and are not able to cross the lipid membrane of the cells as they are having high molecular size, resulting in loss of bioavailability and efficacy. The combination of nanotechnology and herbal medicine is widely proposed to overcome these problems, because nanostructured systems might highly potentiate the action of plant extracts, reducing the dose and side effects and improves activity. During the entire treatment period nanosystems can deliver the active constituent at a required concentration, directing to the desired site of action.[35] In comparison, SMEDDS contain a higher quantity of hydrophilic surfactants and co-surfactants, where in the lipid content is reduced. They form

homogeneous, transparent, isotropic and thermodynamically stable microemulsion with droplet size of less than 100 nm after dispersion in aqueous media.[36] Morin (flavonoid) containing SNEDDS was developed to improve its oral bioavailability. Morin-phospholipid complex (MPC) was formulated by solvent evaporation technique and characterized by infrared spectroscopy and X- Ray diffraction. After formations of SNEDDS of MPC, the lipo-solubility of morin was significantly increased as per its solubility studies. To screen the blank SNEDDS, orthogonal design was employed. Ternary phase diagrams were constructed to identify the region of drug incorporated on the self-emulsifying performance of optimized blank SNEDDS.[37] SNEDDS based on melon oil was also formulated and its admixture with homolipid from cow fat that is Bos indicus by loading Indomethacin (anti-inflammatory agent). The formulation was encapsulated in hard gelatin capsules and evaluated in respects of isotropicity tests, dilution stability tests, precipitation propensity, absolute drug content, emulsification time, in- vitro drug release and anti-inflammatory activity in animal model.[38] SNEDDS of Zedoary turmeric oil (ZTO) an essential oil that was isolated from dry rhizome of Curcuma zedoaria was prepared and various phase diagrams were constructed to detect the self- emulsification region. As the surfactant concentration increases there is reduction in the droplet size but increased emulsification time. Depends on the emulsification time, droplet size and zeta potential after dispersion into aqueous phase, an evaluated formulation consists of ZTO, ethyl oleate, Tween 80, transcutol P and loaded with 30% of drug, was prepared. The active components should remain stable in the optimized.[39] SNEDDS based on fluorescent labeled β- lactamase (FITC- BLM) which is a model protein, was formulated through solid dispersion technique and to incorporate FITC- BLM into the oil phase which can form self O/W nano emulsion upon the expansion of water.[40] For coming up poor solubility and oral bioavailability of drugs lipid based nanocarriers it was found that SMEDDS and SNEDDS had lot of attention in recent times, these systems are simultaneously emulsified when exposed to gastro intestinal tract fluids.[41]

Table 1: Potential Differences between SMEDDS and SNEDDS.

Features	**Smedds** Self- micro emulsifying drug delivery system.	**Snedds** Self nano emulsifying drug delivery system.
Size range of globules	Size ranges from 100-200nm	Size ranges from 50-100nm
Appearance	Appearance of dispersion is optically clear to translucent	Appearance of dispersion is optically clear.
Stability	Thermodynamically stable system	Thermodynamically unstable and kinetically stable
Order of mixing	Surfactant should me mixed with oily phase followed by the titration of the obtained mixture with the aqueous phase	The order of mixing the component does not affect formation.
Type of System	In both the system drug is given in solubilized form, but micro system is one phasic with swollen micelles i.e. equilibrium systems	Nano- emulsion is true emulsion i.e. non equilibrium system with spontaneous tendency to separate into the constituent phases.
Concentration	The oil concentration in SMEDDS is less than 20%	The oil concentration in SNEDDS should be less as possible.
Energy Required	Large amount of energy is required for preparation as compared to nano emulsion.	Less energy required for preparation.

CONCLUSION

The aim of above review is to gathered the latest information from review and research articles regarding formulation and evaluation of SNEDDS loaded with natural origin drug for enhancing solubility of poorly water soluble drug and increasing its bioavailability by maintaining drug concentration within therapeutically effective range. It may be involved scientific site-targeting within the body, or it might involve facilitating systemic pharmacokinetics; in any case, it is typically concerned with both quantity and duration of drug presence. The main objective is to improve drug potency, control drug release to give a sustained therapeutic effect, provide greater safety; finally it is to target a drug specifically to a desired tissue and to enhance the solubility and bioavailability of water insoluble natural drug by using SNEDDS. Moreover to perform in-vitro studies of the formulation and to perform the in-vivo study of the optimized formulation.

Consent for publication

Not applicable.

Conflict of interest

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Authors are thankful to Prof. M. P. Pandey, Hon'ble Vice Chancellor, IFTM University for providing the research facility at Central Instrument Facility and School of Pharmaceutical Sciences of IFTM University, Moradabad-244102, U.P, India.

REFERENCES

1. Tiwari G, Tiwari R, Bnnerjee SK: Drug Delivery Systems: An updated review. International Journal of Pharm Investigation, 2012; 2: 2-11.
2. Sachan AK, Gupta A: A Review on Nanotized Herbal Drugs, Internatioal Journal of Pharmaceutical Scinces and Research, 2015; 6: 961-970.
3. Goldberg M, Langer R, Jia X: Nanostructured materials for applications in drug delivery and tissue engineering, Journal of Biomaterial Science, 2007; 18: 241-288.
4. Banifacio BV, Silva PBD, Chorilli M: Nanotechnology- based drug delivery systems and herbal medicines: A review, International Journal of Nanomedicine, 2014; 9: 1-15.
5. Dean DA: Peptide nucleic acids: versatile tools for gene therapy strategies, Advanced drug delivery reviews, 2000; 44: 81-95.
6. Khan I, Saeed K, Khan I: Nanoparticles:Properties, applications and toxicities, Arabian Journal of Chemistry, 2017; 1-24.
7. Patra JK, Das G, Shin HS: Nano based drug delivery systems: recent development and future prospects, Journal of Nano biotechnology, 2018; 16: 1-33.
8. Amarachi CS, Onyishi I: Lipid- based drug delivery system (LDDS): Recent advances and applications of lipids in drug delivery, African journal of pharmacy and pharmacology, 2013; 7: 3034- 3059.
9. Zanchetta B, Chaud MV, Santana MHA: Self- emulsifying Drug delivery Systems in Pharmaceutical Development, Journal of Advanced Chemical Engineering, 2015; 5: 1-7.
10. Gavasane AJ, Pawar HA: Synthetic Biodegradable Polymers Use in Controlled Drug Delivery Systems: An Overview, Clinical Pharmacology and Biopharmaceutics, 2014; 3: 1-7.
11. Syukri Y, Martein R, Lukitaningsih E, Nugroho AE: Novel Self- Nano Emulsifying Drug Delivery System of andrographolide isolated from Andrographis paniculata Nees: characterization, in vitro and in- vivo assessment, Journal of Drug Delivery Science and Technology, 2018; 47: 514-520.
12. Kristic M, Medarevic D, Duris J, Ibric S: Self- nano emulsifying drug delivery systems and self- microemulsifying drug delivery systems as lipid nano carriers for improving

dissolution rate and bioavailability of poorly soluble drugs, Lipid Nanocarriers for Drug Targetting, 2018: 473- 508.

13. Landge A, Krishnamoorthy K: Microemulsion as drug delivery system for peptides and proteins, Journal of Pharmaceutical Sciences & Research, 2018; 10: 16-25.
14. Ujilestari T, Martien R, Ariyadi B, Dono ND: Self-nanoemulsyfying drug delivery system (SNEDDS) of Amomum compactum essential oil: Design, formulation, and characterization Journal of Applied Pharmaceutical Science, 2018; 8: 014-021.
15. Liu C, Lv L, Guo W, Mo L, Huang Y, Li G , Huang X: Self-Nanoemulsifying Drug Delivery System of Tetrandrine for Improved Bioavailability: Physicochemical Characterization and Pharmacokinetic Study, BioMed Research International, 2018; 1-10.
16. Xue X, Cao M, Ren L, Qian Y, Chen G, Preparation and Optimization of Rivaroxabab by Self- Nanoemulsifying Drug Delivery System (SNEDDS) for Enhanced Oral Bioavailability and No Food Effect, AAPS PharmaSci Tech, 2018; 19: 1847- 1859.
17. 17.Kalantari A, Kosa D, Nemes D: Self nano emulsifying drug delivery systems containing plantago lanceolata- an assessment of their antioxidant and anti-inflammatory effects, Molecules, 2017; 2: 1-17.
18. Kumar SR, Artesunate: Loaded Self Nanoemulsifying Drug Delivery System: A preliminary study for Improved Efficacy in the treatment of Malaria: Formulation, Characterization and Bio- distribution Study, Journal of Bioequivalence and Bioavailability, 2017; 9: 364- 371.
19. Andey T, Patel A, Marepally S, Chougule M, Spencer SD, Rishi AK, Sing M: Formulation, Pharmacokinetic, and Efficacy Studies of Mannosylated Self-Emulsifying Solid Dispersions of Noscapine, PLOS one, 2016; 11(1): 1-20.
20. Shukla SN, Modi DC, Shah DP: A Review on solid self-nanoemulsifying Drug Delivery System: An Approach for Bioavailability Enhancement, World Journal of Pharmacy and Pharmaceutical sciences, 2016; 5: 302-316.
21. Bhanse ND, Shah CN: A Review of Research Study on-Self Nanoemulsifying Drug Delivery System, Journal of Pharmaceutical Science and Bioscientific Research, 2016; 6: 621-627.
22. Nasr A, Gardough A, Ghonaim H, Abdelghany E, Ghorab M: Effects of oils, surfactants and co-surfactants on phase behaviour and physicochemical properties of self-nanoemulsifying Drug Delivery System for Irbesartan and Olmesartan, International Journal of Applied Pharmaceutics, 2016; 8(1): 13- 25.

23. Tripathi S, Kushwah V, Thanki K, Jain S: Triple antioxidant SNEDDS formulation with enhanced oral bioavailability: Implication of chemoprevention of Brest cancer, Nanomedicine, 2016; 12(6):1431-1443.
24. Jinyang S, Jianping B, Fei L: Preperation and evaluation of a self- nanoemulsifying drug delivery system loaded with Akebia saponin D- phospholipid complex, International Journal of Nanomedicine, 2016; 11: 4919-4929.
25. Jamshaid T: Pharmaceutics and novel drug delivery systems, Pharmaceutical Regulatory Affairs, 2015; 4: 74.
26. Avachatt AM, Patel VGG: Self nano emulsifying drug delivery system of stabilized ellagic acid – phospholipid complex with improved dissolution and permeability, Saudi Pharmaceutical Journal, 2015; 23: 276- 289.
27. Savale SK: A review - self nano-emulsifying drug delivery system (SNEDDS), International Journal of Research in Pharmaceutical and Nano Sciences, 2015; 4: 385– 397.
28. Sachan AK, Gupta A: A Review on nanotized Herbal Drugs, International Journal of Pharmaceutical Sciences and Research, 2015; 6: 961-970.
29. Pramar K, Patel J, Sheth N: Self nano emulsifying drug delivery system for Embelin: Design, characterization and in-vitro studies, Asian Journal of Pharmaceutical Sciences, 2015; 10: 396-404.
30. Khan AW, Kotta S, Ansari SH, Sharma RK, Ali J: Self- nanoemulsifying drug delivery system (SNEDDS) of the poorly water- soluble grape fruit flavonoid Naringenin design, characterization, in vitro and in vivo evaluation, Drug Delivery, 2015; 22: 552-561.
31. Zhang L, Zhang L, Zhang M: Self emulsifying drug delivery system and the applications in herbal drugs, Drug Delivery, 2015; 22: 475-486.
32. Mahjub R, Dorkoosh FA, Tehrani MR, Schnurch AB: Oral self- nanoemulsifying peptide drug delivery systems: impact of lipase on drug release, Journal of Microencapsulation, 2015; 32(4): 401-407.
33. Cherniakov I, Domb AJ, Hoffman A: Self- nano- emulsifying drug delivery systems: an update of the biopharmaceutical aspects, Expert opinion on Drug Delivery 2015; 12: 1121-1133.
34. Li J, Larreqieu CA, Benet LZ: Classification of natural products as sources of drugs according to the biopharmaceutics drug deposition classification system (BDDCS), Chinese Journal of Natural Medicines, 2014; 14: 888-897.

35. Bonifacio BV, Saliva PB, Ramos MA: Nanotechnology- based drug delivery systems and herbal medicines: A review, International Journal of Nanomedicine, 2014; 9: 1-15.
36. Shambhu S, Joshi AK: Self- microemulsifying drug delivery system (SMEDDS)- challenges and road ahead, Drug Delivery, 2015; 22(6): 675-690.
37. Zhang J, Peng Q, Shi S: Preparation, Characterization, and in vivo evaluation of a self nanoemulsifying drug system (SNEDDS) loaded with morin-phospholipid complex, International journal of Nanomedicine., 2011; 6: 3406- 3414.
38. Obitte NC, of okansi KC, Nzkwe IT, Esimone CO, Okoye IE: Self- nanoemulsifying Drug Delivery Systems based on Melon Oil and its Admixture with a homolipid from Bos indicus for the Delivery of Indomethacin, Tropical Journal ofPharmaceutical Research, 2011; 10: 299-307.
39. Zhao Y, Wang C, Chow AH, Ren K, Gong T, Zhang Z, Zheng Y: Self nanoemulsifying drug delivery system (SNEDDS) for oral delivery of Zedoary essential oil: formulation and bioavailability studies, International Journal of Pharmaceutics, 2010; 383: 170-177.
40. Rao SV, Shao J: Self- nanoemulsifying drug delivery system (SNEDDS) for oral delivery of protein drugs: Formulation development, International Journal of Pharmaceutics, 2008; 362: 2- 9.
41. Kohli K, Chopra S, Dhar D, Arora S: Self- emulsifying drug delivery systems: An approach to enhance oral bioavailability, Drug Discovery Today, 2010; 15(21-22): 958-965.