



# Self Emulsifying Drug Delivery System a Tool for Enhancement of Solubility: A Critical Review

Tejaswini A. Dhawale<sup>1</sup>, Shital D. Pande<sup>2</sup>, Madhuri K. Sonawane<sup>3</sup>,  
Ashwini R. Jambhale<sup>4</sup>, Ruchita R. Giri<sup>5</sup>

Yashodeep Institute of Pharmacy, Aurangabad, Maharashtra, India

**Abstract:** Oral drug delivery system is an oldest and most preferable form of drug administration. The main concern regarding oral drugs are most of them are very poorly soluble which may affect directly or indirectly affect the bioavailability. SEDDS is the oldest and most preferable method to enhancing bioavailability. An ideal self-emulsifying SEDDS containing API, emulsification agents like oils and surfactant, polymers and antioxidant etc. the problem arises to researcher that all data are scattered in various places, this has been tried to resolve in this review. This review comprehensively describes literature updates containing composition, factor affecting, various emulsification processes, studied carried out on formulation, recent advancement, bioavailability enhancement, patents and marketed preparation.

**Keywords:** Poorly-soluble, surfactants, lipid-based, SEDDS, bioavailability

## REFERENCES

- [1]. Gursoy R.N., Benita S. Self-emulsifying drug delivery systems for improved oral delivery of lipophilic drugs: Biomedicine and Pharmacotherapy, 2004; 58:173-182.
- [2]. Abdalla A., Klein S., Mader K. A new Self emulsifying drug delivery system for poorly soluble drugs: European Journal of Pharmaceutical Sciences. 2008; 35:357-464.
- [3]. Gershanik T., Benita S. Self-dispersing lipid formulations for improving oral absorption of lipophilic drugs: European Journal of Pharmaceutics and Biopharmaceutics. 2000; 50:179- 188.
- [4]. Tang B., Cheng G., Chun J. Development of solid self emulsifying drug delivery systems, preparation techniques and dosage forms: Drug Discovery Today. 2008; 13:606-611.
- [5]. Craig D.Q.M, Barker S.A., Banning D., Booth S.W. An investigation into the physicochemical properties of self-emulsifying systems using low frequency dielectric spectroscopy: International Journal of Pharmaceutics. 1993; 96:147-155.
- [6]. Tang J.L., Sun J., Guihe Z. Self-Emulsifying Drug Delivery Systems: Strategy for Improving Oral Delivery of Poorly Soluble Drug, Current Drug Therapy. 2007;2:85-93.
- [7]. Patel PA, Chaulang GM. Self Emulsifying Drug Delivery System: A Review. Research J Pharm and Tech 2008; 1(4): 313-323.
- [8]. Hauss DJ, Fogal SE. (1998). Lipid-based delivery systems for improving the bioavailability and lymphatic transport of poorly water soluble LTB4 inhibitors, J Pharm Sci, 87,164-169.
- [9]. Sapraa K, et al: Self Emulsifying Drug Delivery System: A Tool in Solubility Enhancement of Poorly Soluble Drugs; Indo Global Journal of Pharmaceutical Sciences 2012; 2(3): 313-332.
- [10]. Kumar S, Malviya R, and Sharma P K: Solid Dispersion: Pharmaceutical Technology for the Improvement of Various Physical Characteristics of Active Pharmaceutical Ingredient; African Journal of Basic and Applied Science 2011; 3(4): 116- 125.
- [11]. Kumar S, Gupta S and Sharma P K: Self-Emulsifying Drug Delivery Systems (SEDDS) for oral delivery of lipid based formulations. African Journal of Basic & Applied Science 2012; 4 (1): 07-11.
- [12]. Nigade P M, Patil S, Tiwari S S: Self Emulsifying drug delivery system (SEDDS): A review. International Journal of Pharmacy and Biological Sciences 2012; 2(2): 42-52.
- [13]. Sharma V, et al: SMEDDS: A novel approach for lipophilic drugs. International Journal of Pharmaceutical Science and Research 2012; 3(8): 2441-2450.



- [14]. Khedekar and Mittal, SELF EMULSIFYING DRUG DELIVERY SYSTEM: A REVIEW , IJPSR, 2013; Vol. 4(12): 4494-4507
- [15]. BhargavaP, Bhargava S, and Daharwal S J: Self-emulsifying drug delivery System: an approach to improve the solubility of poorly water soluble drugs. Advance Research in Pharmaceuticals and Biologicals 2011; Vol 1(1): 1-9.
- [16]. Christopher Porter J H, et al: Enhancing intestinal drug solubilization using lipid-based delivery systems. Advanced Drug Delivery Reviews 2008; 60: 673–691.
- [17]. Kumar A, Sharma S, Kamble R: Self-emulsifying drug delivery system (SEDDS): future aspects. International Journal of Pharmacy and Pharmaceutical Sciences 2010; 2(4): 7-13.
- [18]. Mittal P, Seth N, Rana AC: Self-microemulsifying drug delivery system (SMEDDS): An alternative approach for hydrophobic drugs. International Journal of Natural Product Science 2012; 1: 80.
- [19]. Sudheer P, et al: Approaches to development of solid- self micron emulsifying drug delivery system: formulation techniques and dosage forms – a review. Asian Journal of Pharmacy and Life Science 2012; 2(2):214-225
- [20]. Patel P A, et al: Self Emulsifying Drug Delivery System: A Review. Research Journal of Pharmacy and Technology 2008; 1(4): 313-323.
- [21]. Revathi S, DhanaRaju MD: Self-emulsifying drug delivery system: A review. World Journal of Pharmacy and Pharmaceutical Sciences 2013; 2(1): 89-107.
- [22]. Singh G, et al: Self-emulsifying drug delivery systems (SEEDS): An approach for delivery of poorly water soluble drug. International Journal of Pharmacy & Life Sciences 2012; 3(9): 1991-1996.
- [23]. Rajinikanth P S, Suyu Y, and Garg S: Development and In-Vitro Characterization of Self-nanoemulsifying Drug Delivery Systems of Valsartan. World Academy of Science, Engineering and Technology 2012; 72: 1418-1423.
- [24]. Sachan R, Khatri K, Kasture S B: Self-Eumlsifying Drug Delivery System A Novel Approach for enhancement of Bioavailability. International Journal of PharmTech Research 2010; 2(3): 1738- 1745.
- [25]. Patil P, Patil V, Paradkar A: Formulation of SEDDS for oral delivery of Simvastatin: In vitro and in vivo evaluation. Actapharma. 2007; 57: 111-122.
- [26]. Kohli K, et al: Self-emulsifying drug delivery systems: an approach to enhance oral Bioavailability. Drug Discovery Today 2010; 15: 958-965
- [27]. Jang D J, et al: Improvement of bioavailability & photo stability of amlodipine using redispersible dry emulsion. European Journal of Pharmaceutical Science 2006; 28: 405-411.
- [28]. Kinesh V P, et al: Novel approaches for oral delivery of insulin and current status for oral insulin product. International Journal of Pharmaceutical Science and Nanotechnology 2010; 3(3): 1057- 1064.
- [29]. Gupta M K, et al: Hydrogen Bonding with Adsorbent during storage governs drug dissolution from solid dispersion granules. Pharmaceutical Research 2002; 19: 1663-1672.
- [30]. Nazzal S, Khan MA: Response Surface Methodology for the Optimization of Ubiquinone Self-Nanoemulsified Drug Delivery System. American Association of Pharmcetical Sciences Pharm Sci Tech 2002; 3 (1) 240: 1-9.
- [31]. Attama AA, et al: The use of solid self-emulsifying system in the delivery of diclofenac. International Journal of Pharmaceutics 2003; 262: 23-28. 27. Attama A, Nkemnele M O: In vitro evaluation of drug release from self-emulsifying drug delivery systems using a biodegradable homolipid from Capra Hircus. International Journal of Pharmaceutics 2005; 304: 4-10.
- [32]. Hu Yunxia, et al: Preparation and evaluation of 5-FU/ PLGA/Gene nanoparticles. Key Engineering Materials 2005; 288- 289: 147-150. 29. Trickler WJ, Nagvekar AA, Dash AK: A novel nanoparticle formulation for sustained Paclitaxel delivery. American Association of Pharmaceutical Scientist Pharm Sci Tech. 2008; 9: 486–493.
- [33]. Nazzal S, Smalyukh II, Lavrentovich OD, Khan MA. Preparation and in vitro characterization of a eutectic based semisolid self-nanoemulsified drug delivery system (SNEDDS) of ubiquinone: mechanism and progress of emulsion formation. International Journal of Pharmaceutics. 2002;235(1-2):247–65.

- [34]. Pouton CW. Lipid formulations for oral administration of drugs: non-emulsifying, self-emulsifying and self-microemulsifying drug delivery systems. *European Journal of Pharmaceutical Sciences*. 2000;11(2):S93–8.
- [35]. Abdalla A, M'ader K. Preparation and characterization of a self-emulsifying pellet formulation. *European Journal of Pharmaceutics and Biopharmaceutics*. 2007;66(2):220–6.
- [36]. Erratoni MS, Newton M, Booth S, Clarke A. Controlled drug release from pellets containing water-insoluble drugs dissolved in a self-emulsifying system. *European Journal of Pharmaceutics and Biopharmaceutics*. 2007;65(1):94–8.
- [37]. Patil P, Paradkar A. Porous polystyrene beads as carriers for self-emulsifying system containing loratadine. *AAPS Pharm SciTech*. 2006;7(1):E199–E205.
- [38]. Sriraksa S, Sermkaew N, Sethacheewakul S. Floating alginate beads as carriers for self-emulsifying system containing tetrahydrocurcumin. *Advanced Materials Research*. 2012;506:517–20.
- [39]. You J, Cui FD, Han X, et al. Study of the preparation of sustained-release microspheres containing zedoary turmeric oil by the emulsion-solvent-diffusion method and evaluation of the Selfemulsification and bioavailability of the oil. *Colloids and Surfaces B*. 2006;48(1):35–41.
- [40]. Attama AA, Nkemnele MO. In vitro evaluation of drug release from self microemulsifying drug delivery systems using a biodegradable homolipid from *Capra hircus*. *International Journal of Pharmaceutics*. 2005;304(1-2):4–10.
- [41]. Patel D, Sawanth KK. Oral bioavailability enhancement of acyclovir by self micro emulsifying drug delivery System (SMEDDS). *Drug DevInd Pharm*. 2007;33(12):1318-26.
- [42]. Jing Q, Shen Y, Ren F, Chen J, Jiang Z, Peng B, et al. HPLC determination of anetholetrithione and its application to pharmacokinetics in rabbits, *J Pharm Biomed Anal*. 2006;42(5):613-7.
- [43]. Shen HR, Li ZD, Zhong MK. Preparation and evaluation of self microemulsifying drug delivery system containing atorvastatin. *Yao XueBao*. 2005;40(11):982-7.
- [44]. Singh AK, Chaurasiya A, Jain JK, Awasthi A, Asati D, Mishra G, et al. HPLC method for the pharmacokinetic study of bicalutamide SMEDDS and suspension formulations after oral administration to rats. *Talanta*. 2009;78(4-5):1310-4.
- [45]. Wei L, Sun P, Nie S, Pan W. Preparation and evaluation of sedds and smedds containing carvedilol. *Drug DevInd Pharm*. 2005;31(8):785-94.
- [46]. Wei L, Li J, Guo L, Nie S, Pan W, Sun P, et al. Investigations of novel self emulsifying osmotic pump tablet containing carvedilol. *Drug DevInd Pharm*. 2007;33(9):990-8.
- [47]. A Singh, AChaurasiya, M Singh, SC Upadhyay, R Mukherjee, RK Khar. *AAPS PharmSciTech*. 2008;9(2): 628-34.
- [48]. R Chouksey, AK Jain, H Pandey ,AMaithil. *International journal of pharmacy & life sciences*. 2011;2(8):982-988.
- [49]. AK Gupta, DK Mishra, SC Mahajan. *Int. J. of Pharm. & Life Sci*. 2011;2(3):633-639.
- [50]. S Sharma, PK Suresh. *International Journal of Innovative Pharmaceutical Research*. 2010;1(4):66-73.
- [51]. B Sharif, M Zadeh, S Dahanzadeh, F Rahim. *International Journal of Advances in Pharmaceutical Sciences*. 2010; 1:239-248.
- [52]. VK Pal, A khan. *Asian Journal of Pharmaceutical and Clinical Research*. 2012;5(1):76-78.
- [53]. JB Shukla, SJ Patel. *International journal of pharmacy and pharmaceutical sciences*. 2010;2(4):143-146.
- [54]. Y Jing, L Yun, PZ Jian. *J Pharm Pharmaceut Sci*. 2008;11 (3): 22-29.
- [55]. X Jia, C Qi, CK Chan, YM Zhao, NW Geng, BS Jia, TW Yi, HYT Henry, Z Ying Zheng. *AAPS PharmSciTech*. 2009;10(1):172-182.
- [56]. L Linjie, P Xiujuan, Z Wei, W Siling. *Asian Journal of Pharmaceutical Sciences*. 2007; 2 (4):150-160.
- [57]. MK Kale, PB Suruse, SP Warke. *American Journal of PharmTech Research*. 2012;2(1):338-348.
- [58]. YM Lin, CC Ying, DS Yu, TK Wen, OH Hsiu, TS Ming. *International Journal of Nanomed*. 2011;6:2445–2457.
- [59]. H Thakkar, J Nangesh, M Parmar, D Patel. *Journal of pharmacy and bioallied sciences*. 2011;3 (3): 442-448.



- [60]. IT Ehab. *Scientiapharmaceutica. Sci Pharm.* 2009;77: 443–451.
- [61]. Z Yi, W Changguang, HL Albert, Chowb, R Ke, G Tao, Z Zhirong, Z Ying. *International Journal of Pharmaceutics.*2010;383:170–177.
- [62]. Tang, J.; Sun, J.; Cui, F.; He, Z. Preparation of self emulsifying drug delivery systems of Ginkgo biloba extracts and in vitro dissolution studies. *Asian J. Traditional Med.*, 2006, 1(3-4) 1-4.
- [63]. Bongkyu, Y.; Hee, Y.J.; Srinivasan,S. Oral pharmaceutical composition containing lutein using self microemulsion system. KR Patent 20110019327(A), February 25, 2011.
- [64]. Kohli, K.; Chopra,S. Self-emulsifying drug delivery system for a curcuminoid based composition. U.S. Patent 2011294900(A1), December 1, 2011.
- [65]. Guo, H.M.T. Rhizoma corydalis totals alkaloids self-emulsifying drug delivery system and preparation method and application thereof. CN Patent 101912447(A), December 15, 2010.
- [66]. Guo, J.W.M. Apogossypolone self-emulsifying drug delivery system and preparation method thereof. CN Patent 102247321(A), November 23, 2011.
- [67]. Yin, X.X. Novel curcuminself emulsifying drug delivery system and preparation thereof. CN Patent 101627969(A), January 20, 2010.
- [68]. Murty, R.B.; Lexington, K.Y.; Murty, S.B. Delivery of tetrahydrocannabinol: A self emulsifying drug delivery system to improve dissolution, stability, and bioavailability of drug compounds of dronabinol or other cannabinoids. EP Patent 1903866(A1), April 2, 2008.
- [69]. Cai, Q.; Liang, L. Hemlock parsley oil self emulsifying oral medicine delivery system and preparing method thereof. CN Patent 101229205(A), July 30, 2008.
- [70]. Nakhat, P.; Mandaogade,P. Self-emulsifying pharmaceutical compositions of Rhein or Diacerein. U.S. Patent 2010303902(A1), December 2, 2010.
- [71]. Li, G.; Chen, Y. Vinpocetine oral self-micro emulsification medicine releasing system and preparation method thereof. CN Patent 10113962(A), January 16, 2008.
- [72]. Hang, C.S.; Young, J.S. Pharmaceutical composition for hyperlipidemia treatment of self emulsifyingphytoconstituent delivery system to increase bioabsorption and improve stability of active ingredient. KR Patent 20050011323(A), January 29, 2005.
- [73]. Christina, H.; Britta, S. Self-emulsifying phytoconstituent delivery system, wherein the fatty agent is optional. HK Patent 1050632 (A1), March 18, 2005.
- [74]. S. Revathi et al SELF EMULSIFYING DRUG DELIVERY SYSTEM: A REVIEW *wjpps* volume 2, Issue 1, 89-107.
- [75]. S. Nazzal and M.A. Khan, *Int. J. Pharm.*, 315, 110 (2006)
- [76]. Y.P. Wang, Y. Gan and X.X. Zhang, *ActaPharmacol. Sin.*, 32, 1294 (2011)
- [77]. E.A. Mahmoud, E.R. Bendas and M.I. Mohamed, *AAPS PharmSciTech*, 10, 183 (2009)
- [78]. V. Nekkanti, P. Karatgi, R. Prabhu and R. Pillai, *AAPS PharmSciTech*, 11, 9 (2010);
- [79]. R. Gandhi, C.L. Kaul and R. Panchangnula, *Pharm. Sci. Technol. Today*, 4, 160 (1999);
- [80]. M. Serraton, M. Newton, S. Booth and A. Clarke, *Eur. J. Pharm. Biopharm.*, 65, 94 (2007);
- [81]. J. Hamdani, A.J. Moës and K. Amighi, *Int. J. Pharm.*, 260, 47 (2003)
- [82]. J. You, F.D. Cui, X. Han, Y.S. Wang, L. Yang, Y.W. Yu and Q.P. Li, *Colloids Surf. B Biointerfaces*, 48, 35 (2006)
- [83]. 83. C. Holmberg and B. Siekmann, *Self-Emulsifying Drug Delivery System*, US Patent US 7736666B2 (2010).
- [84]. G. Shlieout, B. Boedecker, S. Schaefer, B. Thumbeck and P. Gregory, *Pharmaceutical Compositions of Lipase-Containing Products, In Particular of Pancreation*, US Patent 2005/0250817 (2005).
- [85]. S. Nazzal, I.I. Smalyukh, O.D. Lavrentovich and M.A. Khan, *Int. J. Pharm.*, 235, 247 (2002)
- [86]. T. Bekerman, J. Golenser and A. Domb, *J. Pharm. Sci.*, 93, 1264 (2004)
- [87]. P.R. Nepal, H.K. Han and H.K. Choi, *Eur. J. Pharm. Sci.*, 39, 224 (2010);
- [88]. R. Koynova and M. Tihova, *Biochim. Biophys. Acta*, 1798, 646 (2010);
- [89]. P. Patil and A. Paradkar, *AAPS PharmSciTech.*, 7, E199 (2006);



- [90]. A. Sookkasem, S. Chatpun, S. Yuenyongsawad and R. Wiwattanapatapee, *J. Drug Deliv. Sci. Technol.*, 29, 159 (2015)
- [91]. J.Y. Kim and Y.S. Ku, *Int. J. Pharm.*, 194, 81 (2000);
- [92]. K. Takada and M. Murakami. Glycyrrhizin Preparations for Transmucosal Absorption, US Patent 6890547 (2005).
- [93]. B. Whittle and G. Guy, GW Pharma Ltd., Mucoadhesive Pharmaceutical Formulations. World Patent WO 02/064109A2 (2002).
- [94]. G.M. El Maghraby, *Colloids Surf. B Biointerfaces*, 75, 595 (2010)
- [95]. Z. Yu and S. Huth, Stable Ophthalmic Oil-in-Water Emulsions with Sodium Hyaluronate for Alleviating Dry Eye, United States Patent US 2007/0036829 (2007).
- [96]. P.J. Dor, S. Mudumba, T. Nivaggioli and D.A. Weber, Formulations for Ocular Treatment, United States Patent US 2006/0182771 (2006).
- [97]. Q. Wang, H. Zhang, J. Huang, N. Xia, T. Li and Q. Xia, *J. Microencapsul.*, 35, 90 (2018);
- [98]. C. Hu, G. Zhao, Q. Xia and R. Sun, *J. Mater. Sci.*, 50, 6567 (2015);
- [99]. Q. Wang, C. Hu, H. Zhang, Y. Zhang, T. Liu, A. Qian and Q. Xia, *J. Microencapsul.*, 33, 785 (2016);
- [100]. S. Tantarawongsa and T. Phaechamud, *Thai Pharm. Health Sci. J.*, 6, 66 (2011).
- [101]. K.P. Parthasarathi, D. Mudit, R. Prudhvi, D. Lavanya and L.N.V. Krishna, *Int. Res. J. Pharm.*, 2, 82 (2011).
- [102]. L. Zhang, L. Zhang, M. Zhang, Y. Pang, Z. Li, A. Zhao and J. Feng, *Drug Deliv.*, 22, 475 (2015);
- [103]. F.L. Yen, T.H. Wu, L.T. Lin, T.M. Cham and C.C. Lin, *Pharm. Res.*, 26, 893 (2009);
- [104]. J. Cui, B. Yu, Y. Zhao, W. Zhu, H. Li, H. Lou and G. Zhai, *Int. J. Pharm.*, 371, 148 (2009);
- [105]. M. Sierant, P. Paluch, M. Florczak, A. Rozanski and B. Miksa, *Colloids Surf. B Biointerfaces*, 111, 571 (2013)
- [106]. Zhou, X. Zhu, G. Hung, N. Zhang and B. Zhang, *Sheng Wu Yi Xue Gong Cheng XueZaZhi*, 24, 918 (2007)
- [107]. J. Khan, A. Alexander, S. Ajazuddin, Saraf and S. Saraf, *J. Control. Rel.*, 168, 50 (2013)
- [108]. S. Li, Z. Ji, M. Zou, X. Nie, Y. Shi and G. Cheng, *AAPS PharmSciTech*, 12, 1011 (2011);
- [109]. L. Wei, G. Li, Y.D. Yan, R. Pradhan, J.O. Kim and Q. Quan, *Arch. Pharm. Res.*, 35, 1037 (2012);
- [110]. Q. Cai, L. Liang, Y.P. Huang and S.X. Hou, *ZhongguoZhongyaoZazhi*, 32, 2003 (2007).
- [111]. N. Chouhan, V. Mittal, D. Kaushik, A. Khatkar and M. Raina, *Curr. Drug Deliv.*, 12, 244 (2015)