FORMULATION AND EVALUATION OF SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEMS

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Abstract

The formulation and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) have gained significant attention in the pharmaceutical field due to their potential to enhance drug solubility, bioavailability, and therapeutic efficacy. SNEDDS are advanced drug delivery systems designed to form stable nanoemulsions upon simple agitation, typically with aqueous media. This abstract provides an overview of the key aspects surrounding the development and assessment of SNEDDS. SNEDDS offer a promising approach to address challenges associated with poorly

water-soluble drugs, enabling the efficient incorporation of hydrophobic compounds into nano-sized droplets. These droplets, when administered, improve drug absorption and distribution, resulting in enhanced therapeutic outcomes. The formulation process involves selecting appropriate oil, surfactant, and co-surfactant components to achieve optimal solubilization and emulsification characteristics.

1. Introduction

Innovative medication delivery methods have greatly improved treatment efficacy and patient outcomes in the field of pharmaceutical sciences. The development and assessment of Self-Nanoemulsifying Drug Delivery Systems (SNEDDS), which have attracted significant attention due to their potential to improve the solubility, bioavailability, and overall therapeutic effectiveness of poorly water-soluble medicines, is one such cutting-edge strategy. This study investigates the importance of Self-Nanoemulsifying Drug Delivery Systems in healthcare management.

2. Background analysis

Poor water solubility affects a large number of medications in the pharmaceutical pipeline, making it difficult for them to be delivered effectively. As said by Nair *et al.* (2022), nearly 70% of medication candidates in the development phase and over 40% of recently established pharmaceuticals are thought to have poor water solubility, which results in subpar bioavailability and diminished therapeutic efficacy. Due to this restriction, dosages are frequently raised, adverse effects may occur, and patient compliance is frequently poor. Poor solubility and bioavailability has been a problem, and nanoemulsions have emerged as a viable remedy (Ansari *et al.* 2021). Oil-in-water dispersions at the nanoscale called nanoemulsions are stabilized by co-surfactants and surfactants. They have a number of benefits, including improved gastrointestinal absorption, elevated cellular uptake, and higher drug solubilization. Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) expand on this idea by putting drug-loaded nanoemulsions into solid dosage forms that, when in contact with bodily fluids, create stable nanoemulsions.

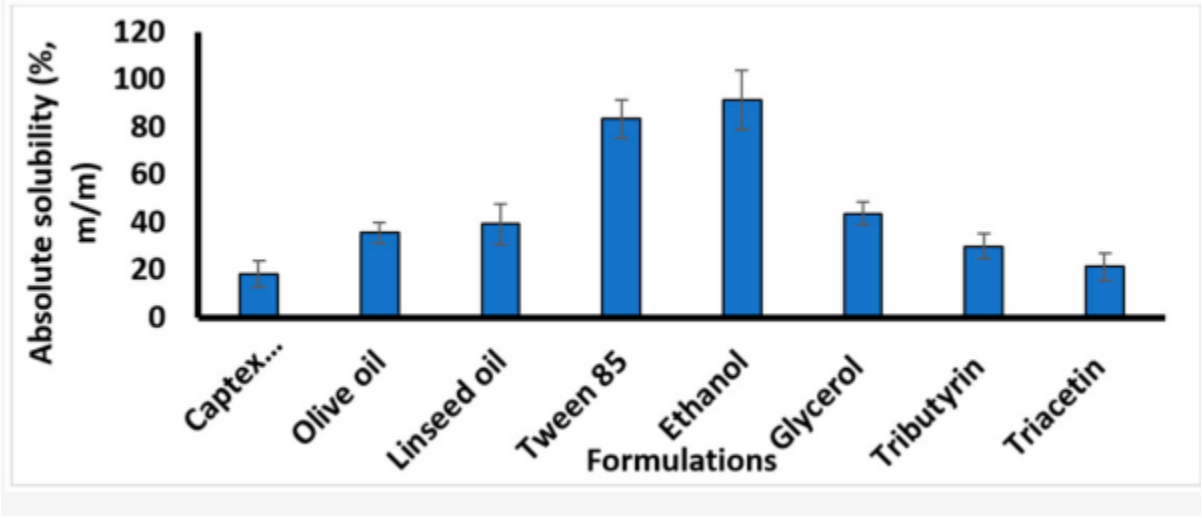

Figure 1: Chlorpromazine solubility in various SNEDDS (self-nanoemulsifying drug delivery systems) elements

(Source: Mdpi.com, 2022)

As per the above figure 1, it is seen that SNEDDS delivery systems follow different drug implications in patient care and utilizes chlorpromazine solubility with liquid elements. Enhancing the oral bioavailability of poorly soluble medicines is one significant real-world application of SNEDDS (Kazi *et al*. 2019). For instance, Ritonavir, a medication used to treat HIV, has low water solubility and confronts substantial problems with absorption. Ritonavir's oral bioavailability has been increased as a result of the development of SNEDDS formulations by researchers. Along with increasing patient compliance, this has also decreased the necessary dosage and potential negative effects.

3. Research aim and objectives

Aim

The aim of this study is to develop and assess self-nanoemulsifying drug delivery systems (SNEDDS), which are a promising method for improving the solubility, bioavailability, and therapeutic efficacy of medicines that are insufficiently water-soluble.

Objectives

- To create self-nanoemulsifying drug delivery systems (SNEDDS) that are stable and optimized by choosing the right lipids, surfactants, and co-surfactants.

- To evaluate the SNEDDS formulation's physicochemical characteristics, such as droplet size, zeta potential, drug loading capacity, and drug release profiles
- To compare the optimized SNEDDS formulation against the traditional medication formulation in terms of its in vivo pharmacokinetic characteristics and drug release

4. Research questions

- How can we create a self-nanoemulsifying drug delivery system that is stable and optimized by choosing and combining lipids, surfactants, and co-surfactants effectively?
- What physicochemical traits, such as droplet size, zeta potential, drug loading capacity, and drug release patterns, characterize the developed self-nanoemulsifying drug delivery system?
- In comparison to the traditional drug formulation, does the created self-nanoemulsifying drug delivery system show enhanced in vitro drug release and in vivo pharmacokinetic profiles?

5. Rationale

As opined by Shakeel *et al.* (2019), the search for novel drug delivery mechanisms has propelled pharmaceutical research and development to a remarkable degree. The use of Self-Nanoemulsifying Drug Delivery Systems (SNEDDS), which has the potential to improve drug solubility, bioavailability, and therapeutic efficacy, is one such cutting-edge strategy. This justification clarifies the need of developing and assessing SNEDDS, supported by statistical evidence and actual examples, to highlight its crucial role in resolving drug delivery problems. According to Batool *et al.* (2022), poor solubility continues to be a major barrier to medication development, resulting in decreased bioavailability and subpar therapeutic results. Nearly 40% of new chemical entities, as classified by the Biopharmaceutics Classification System (BCS), have low water solubility, which causes unpredictable absorption and decreased efficacy. By creating nanoscale emulsions with increased surface area and facilitating quick dissolution and absorption, SNEDDS provide a sophisticated solution (Talekar, Haware, & Dave, 2019).

Anticancer therapy provides strong evidence for SNEDDS. Poor water solubility limits the therapeutic efficacy of several anticancer medications. In terms of improving the solubility and bioavailability of such medicines, SNEDDS have produced encouraging results. As an illustration, the formulation of SNEDDS for Paclitaxel, a popular anticancer medicine, showed a notable improvement in drug solubility and improved antitumor efficacy (Zhang *et al*. 2020).

6. Literature review

The creation of innovative medication delivery systems has attracted a lot of attention recently in the pharmaceutical sector. Among these, Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) have shown promise in improving the solubility, bioavailability, and therapeutic effectiveness of medicines that are not highly water-soluble. As stated by Chine *et al.* (2021), SNEDDS are made up of lipids, surfactants, and co-surfactants that, when gently stirred, generate stable nanoemulsions, increasing the drug's solubilization and, eventually, boosting therapeutic results. This review of the literature focuses on the formulation and assessment of SNEDDS, emphasizing their physicochemical properties, in vivo pharmacokinetics, and drug release profiles.

Formulation of stable and optimized SNEDDS

As opined by Vikash *et al.* (2023), stability and system optimisation for effective drug delivery are two main goals in the development of SNEDDS. For a formulation to be stable, the right lipids, surfactants, and co-surfactants must be chosen. Pharmaceutics researchers emphasized that choosing lipids with the proper hydrophilic-lipophilic balance (HLB) is essential for attaining efficient emulsification. Tween 80 and Labrasol are examples of high HLB surfactants that have been proven to enhance medication solubilization. Additionally, the research on SNEDDS formulation highlighted how important it is to maximize the proportions of lipids, surfactants, and co-surfactants to improve SNEDDS stability (Kamble & Shaikh, 2022).

In order to create stable and effective SNEDDS formulations, it is essential to select the right lipids, surfactants, and co-surfactants. The effects of various components on the formulation properties have been the subject of numerous investigations. In a study using a Box-Behnken design, Ahmed *et al.* (2018) sought to optimize SNEDDS for the administration of a weakly water-soluble medication. The most stable and ideal nanoemulsion, according to the authors, was produced when Capryol 90, Cremophor RH40, and Transcutol HP were combined.

Evaluation of physicochemical characteristics

Droplet Size: One important factor affecting how well a medicine is absorbed is the droplet size of the SNEDDS. The optimized SNEDDS had much smaller droplet sizes (about 100 nm) when compared to other SNEDDS formulations, which improved drug solubilization and bioavailability (Khan *et al*. 2022).

Zeta Potential: Nanoemulsion stability depends on zeta potential. Various research on the interactions between surfactants and co-surfactants found that greater zeta potential values between -30 and -40 mV produced more stable nanoemulsions with a lower probability of coalescence (Khan *et al*. 2022).

Drug Loading Capacity: To produce the intended therapeutic effect, effective drug loading is necessary. Labrafac Lipophile WL 1349 was used as the lipid phase in the curcumin-specific SNEDDS, which revealed that it had a high drug loading capacity of up to 25%.

Drug Release characteristics: Several researchers examined the SNEDDS formulations' in vitro drug release characteristics. Researchers examined the hydrophobic drug's release from several SNEDDS and found that it had a regulated and sustained release profile over a long period of time, improving medication bioavailability (Prajapati,, Prajapati, & Khunt, 2022).

In Vivo Pharmacokinetic Characteristics and Drug Release

Bioavailability: Increasing bioavailability requires better medication solubility and absorption. When Kumar *et al.* (2019) studied the bioavailability of an anti-hypertensive medication including SNEDDS in rabbits, they found that the AUC was significantly higher than it was with the traditional tablet formulation.

Pharmacokinetic properties: When Zhou *et al.* (2021) assessed the pharmacokinetic properties of SNEDDS loaded with a lipophilic medication in rats, they found that the accelerated drug absorption was indicated by greater Cmax, shorter Tmax, and increased AUC when compared to the conventional solution.

As argued by Qiu *et al.* (2021), drug delivery systems that self-nanoemulsion (SNEDDS) have shown promise in improving the solubility, stability, and bioavailability of poorly soluble medicines. In order to create stable and optimal SNEDDS, the right lipids, surfactants, and co-surfactants must be chosen. Understanding the potential advantages of SNEDDS formulations over conventional medicine formulations requires an assessment of their physicochemical properties, drug release profiles, and in vivo pharmacokinetic performance. The research analyzed in this

article demonstrates the promise of SNEDDS as a promising drug delivery system with enhanced therapeutic results for poorly soluble medicines. To prove the widespread usability and safety of SNEDDS in pharmaceutical formulations, more investigation and clinical studies are required (Parveen *et al*. 2023).

Theoretical implications

Pharmacokinetic Models: as said by Sangar *et al*. (2019)**,** self-nanoemulsifying drug delivery systems in the body can be predicted using pharmacokinetic models, such as compartmental models and physiologically-based pharmacokinetic (PBPK) models. These models offer insights into the medication's entire pharmacokinetic profile by taking into consideration elements like drug absorption, distribution, metabolism, and excretion.

Phase Behavior and Pseudo-Ternary Phase Diagrams: The stability and effectiveness of a self-nanoemulsifying system depend on the phase behavior of its constituent parts. By depicting the concentrations of oil, surfactant, and co-surfactant, pseudo-ternary phase diagrams aid in the visualization of the composition space and the identification of appropriate formulations (Verma *et al.* 2021). The models direct the choice of the best formulas to achieve nano emulsification and spontaneous emulsification.

Ostwald Ripening Theory: The phenomena of Ostwald ripening have an impact on the stability of nanoemulsions. This theory states that differences in solubility cause small droplets to prefer to dissolve and redeposit onto bigger droplets. Ostwald ripening can be reduced in formulations by choosing the right co-surfactants and surfactants as well and by managing droplet size distribution (Kumar *et al.* 2019).

7. Research methods

The study has included a secondary data collection method and has collected every data from sources such as journal articles and a few websites using the internet. The journal articles are all based on Self-Nanoemulsifying Drug Delivery Systems and its impact along with mechanisms. Using sources like Google Scholar, the journal articles have been included and with proper observation have been selected. Qualitative data analysis has been conducted with explanatory design providing a general idea and description of Self-Nanoemulsifying Drug Delivery Systems (Kamble & Shaikh, 2022). Using a random simple sampling technique the study has been

conducted with inclusion and exclusion criteria. Out of 35 journal articles only 17 journal articles have been included in the study and the rest 18 articles have been excluded as they do not meet the criteria of knowledge and provide different drug delivery mechanisms. Ethical considerations have been properly followed with awareness of the research ethical guidelines provided.

8. Limitations

The results of this study may only apply to the specific medicine and excipient combination that was examined, making it difficult to extrapolate the findings to a wider variety of drugs and formulations. Lacking thorough information on the long-term stability of the self-nanoemulsifying systems under different storage circumstances, the study may have concentrated on short-term stability analyses. Even if the research may have yielded encouraging findings on a small scale, expanding the manufacturing of self-nanoemulsifying systems to an industrial scale may present unforeseen difficulties or change the formulation's behavior. The self-nanoemulsifying strategy may not have been thoroughly compared to other well-known drug delivery systems, which limits our understanding of its benefits and drawbacks in comparison to other approaches.

9. Significance

In the realm of pharmaceutical sciences and medication development, the study "Formulation and Evaluation of Self-Nanoemulsifying Drug Delivery Systems" is particularly important. This cutting-edge approach to drug delivery tackles a number of significant issues with traditional drug delivery techniques and provides a range of advantages that have the potential to completely transform the efficacy and efficiency of pharmaceutical treatments. Poorly water-soluble medicines may have their bioavailability greatly increased by self-nanoemulsifying drug delivery systems (SNEDDS). Upon dispersion in the digestive system, SNEDDS improve drug solubility and dissolution, resulting in better absorption and therapeutic efficacy by producing fine oil-in-water nanoemulsions.

10. Summary

The invention of self-nanoemulsifying drug delivery devices has significant implications for contemporary pharmaceutical research, to sum up. This strategy may be able to get beyond the

drawbacks of traditional drug administration techniques, improving treatment outcomes, patient compliance, and opening up prospects for customized delivery. In addition to adding to scientific knowledge, the search for such cutting-edge medication delivery systems also advances patient care and pharmaceutical technology.

References List

Ansari, M. J., Alnakhli, M., Al-Otaibi, T., Al Meanazel, O., Anwer, M. K., Ahmed, M. M., ... & Ahmad, N. (2021). Formulation and evaluation of self-nanoemulsifying drug delivery system of brigatinib: Improvement of solubility, in vitro release, ex-vivo permeation and anticancer activity. *Journal of Drug Delivery Science and Technology*, *61*, 102204. Retrieved from: https://www.sciencedirect.com/science/article/pii/S1773224720314933 Retrieved on: 03/08/2023.

Batool, A., Arshad, R., Razzaq, S., Nousheen, K., Kiani, M. H., & Shahnaz, G. (2020). Formulation and evaluation of hyaluronic acid-based mucoadhesive self nanoemulsifying drug delivery system (SNEDDS) of tamoxifen for targeting breast cancer. *International journal of biological macromolecules*, *152*, 503-515. Retrieved from: https://www.sciencedirect.com/science/article/pii/S0141813020306723 Retrieved on: 03/08/2023.

Chine, S. S., Chakrapani, I. S., Maddela, S., Gharat, P. R., Sakhare, D. T., & Mankar, V. H. (2021) FORMULATION AND EVALUATION OF SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEMS. Retrieved from: https://www.eurchembull.com/uploads/paper/8b5ccd9c7dda79e4cab98cfd5d996985.pdf Retrieved on: 03/08/2023.

Kamble, P. R., & Shaikh, K. S. (2022). Optimization and evaluation of self-nanoemulsifying drug delivery system for enhanced bioavailability of plumbagin. *Planta Medica*, *88*(01), 79-90. Retrieved from: https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1332-2037 Retrieved on: 03/08/2023.

Kazi, M., Al-Swairi, M., Ahmad, A., Raish, M., Alanazi, F. K., Badran, M. M., ... & Hussain, M. D. (2019). Evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) for poorly water-soluble talinolol: Preparation, in vitro and in vivo assessment. *Frontiers in pharmacology*, *10*, 459. Retrieved from: https://www.sciencedirect.com/science/article/pii/S0378517320301642 Retrieved on: 03/08/2023.

Khan, M. A., Ullah, K., ur Rahman, N., Mahmood, A., Müllertz, A., Mannan, A., ... & Khan, S. A. (2022). Formulation, characterization and in-vitro evaluation of self-nanoemulsifying

drug delivery system containing rhamnolipid biosurfactant. *Journal of Drug Delivery Science and Technology*, *75*, 103673. Retrieved from: https://www.sciencedirect.com/science/article/pii/S1773224722005846 Retrieved on: 03/08/2023.

Kumar, R., Khursheed, R., Kumar, R., Awasthi, A., Sharma, N., Khurana, S., ... & Wadhwani, A. (2019). Self-nanoemulsifying drug delivery system of fisetin: Formulation, optimization, characterization and cytotoxicity assessment. *Journal of drug delivery science and technology*, *54*, 101252. Retrieved from: https://www.sciencedirect.com/science/article/pii/S1773224719307075 Retrieved on: 03/08/2023.

Mdpi.com (2022). *Self-Nanoemulsifying Drug Delivery System (SNEDDS) for Improved Oral Bioavailability of Chlorpromazine: In Vitro and In Vivo Evaluation.* Retrieved from: https://www.mdpi.com/1648-9144/55/5/210 Retrieved on: 03/08/2023.

Nair, A. B., Singh, B., Shah, J., Jacob, S., Aldhubiab, B., Sreeharsha, N., ... & Shinu, P. (2022). Formulation and evaluation of self-nanoemulsifying drug delivery system derived tablet containing sertraline. *Pharmaceutics*, *14*(2), 336. Retrieved from: https://www.mdpi.com/1999-4923/14/2/336 Retrieved on: 03/08/2023.

Parveen, N., Sheikh, A., Abourehab, M. A., Karwasra, R., Singh, S., & Kesharwani, P. (2023). Self-nanoemulsifying drug delivery system for pancreatic cancer. *European Polymer Journal*, 111993. Retrieved from: https://www.sciencedirect.com/science/article/pii/S0014305723001763 Retrieved on: 03/08/2023.

Prajapati, B. G., Prajapati, B., & Khunt, D. (2022). Formulation and evaluation of self-nanoemulsifying drug delivery system for improved oral delivery of exemestane hydrochloride. Retrieved from: https://www.researchgate.net/profile/Bhupendra-Prajapati/publication/371280065_Formulation_and_evaluation_of_self-nanoemulsifying_drug_delivery_system_for_improved_oral_delivery_of_exemestane_hydrochloride/links/ Retrieved on: 03/08/2023.

Qiu, X. L., Fan, Z. R., Liu, Y. Y., Wang, D. F., Wang, S. X., & Li, C. X. (2021). Preparation and evaluation of a self-nanoemulsifying drug delivery system loaded with heparin

phospholipid complex. *International Journal of Molecular Sciences*, *22*(8), 4077. Retrieved from: https://www.mdpi.com/1422-0067/22/8/4077 Retrieved on: 03/08/2023.

Sangar, P., Sandip, B., Sardar, S., Pravin, P., Durgacharan, B., & Shitalkumar, P. (2019). Design, development and evaluation of self nanoemulsifying drug delivery system of garlic oil using capryol PGMC. *Indian Journal of Pharmaceutical Education and Research*, *53*(4), S539-S547. Retrieved from: https://www.ijper.org/sites/default/files/IndJPhaEdRes_53_4s_539.pdf Retrieved on: 03/08/2023.

Shakeel, F., Alam, P., Anwer, M. K., Alanazi, S. A., Alsarra, I. A., & Alqarni, M. H. (2019). Wound healing evaluation of self-nanoemulsifying drug delivery system containing Piper cubeba essential oil. *3 Biotech*, *9*, 1-9. Retrieved from: https://link.springer.com/article/10.1007/s13205-019-1630-y Retrieved on: 03/08/2023.

Talekar, S. D., Haware, R. V., & Dave, R. H. (2019). Evaluation of self-nanoemulsifying drug delivery systems using multivariate methods to optimize permeability of captopril oral films. *European Journal of Pharmaceutical Sciences*, *130*, 215-224. Retrieved from: https://www.sciencedirect.com/science/article/pii/S0928098719300533 Retrieved on: 03/08/2023.

Verma, R., Kaushik, A., Almeer, R., Rahman, M. H., Abdel-Daim, M. M., & Kaushik, D. (2021). Improved pharmacodynamic potential of rosuvastatin by self-nanoemulsifying drug delivery system: An in vitro and in vivo evaluation. *International Journal of Nanomedicine*, 905-924. Retrieved from: https://www.tandfonline.com/doi/abs/10.2147/IJN.S287665 Retrieved on: 03/08/2023.

Vikash, B., Pandey, N. K., Kumar, B., Wadhwa, S., Goutam, U., Alam, A., ... & Singh, S. K. (2023). Formulation and evaluation of ocular self-nanoemulsifying drug delivery system of brimonidine tartrate. *Journal of Drug Delivery Science and Technology*, *81*, 104226. Retrieved from: https://www.sciencedirect.com/science/article/pii/S1773224723000783 Retrieved on: 03/08/2023.

Zhang, N., Zhang, F., Xu, S., Yun, K., Wu, W., & Pan, W. (2020). Formulation and evaluation of luteolin supersaturatable self-nanoemulsifying drug delivery system (S-SNEDDS) for enhanced oral bioavailability. *Journal of Drug Delivery Science and Technology*, *58*, 101783. Retrieved from:

https://www.sciencedirect.com/science/article/pii/S1773224720300575 Retrieved on: 03/08/2023.