Unveiling the Potential of SEDDS in Delivering Lipophilic Drugs: Formulating Lulucanzole and Posacunazole Nanoemulsions for Enhanced Therapeutic Impact

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Abstract:

This research paper focuses on the preparation and evaluation of Lulucanzole and Posacunazole nanoemulsions for potential pharmaceutical applications. The preparation process was methodical, including components of the aqueous phase (sodium metabisulfite and aqua bidestilate), the oil phase (oleic acid, lucanzol, and posacunazole), and an emulsifier combination (Tween 80 and PEG 400). Homogenization and sonication techniques were employed to create clear nanoemulsions.

A number of analyses were carried out to evaluate these nanoemulsions' stability and quality. A particle size analyzer (PSA) was used to measure the distribution of particle sizes. organoleptic tests were performed to evaluate visual aspects and clarity, pH measurements were recorded, viscosity was assessed using a Brookfield viscometer, and the type of nanoemulsion was determined using a water-soluble dye (methylene blue) test. Additionally, the nanoemulsions underwent cycling tests and centrifugation tests to assess their stability under various conditions.

The results indicated that all formulations exhibited clear appearance, were odorless, and had a weak yellow color. pH measurements remained within the skin-compatible range throughout the 8-week storage period. Viscosity increased over time, suggesting stability, while the cycling and centrifugation tests showed no phase separation. Particle size measurements demonstrated that higher concentrations of Lulucanzole and Posacunazole resulted in larger particle sizes, but all formulations maintained sizes within the specified nanoemulsion range.

Furthermore, observations from the methylene blue test confirmed that all formulations exhibited an oil-in-water (o/w) emulsion type.

In conclusion, the developed Lulucanzole and Posacunazole nanoemulsions showed promising characteristics in terms of stability, particle size distribution, pH maintenance, and emulsion type. These findings lay the groundwork for potential pharmaceutical applications and further research in drug delivery systems.

Keywords: Preparation, evaluation, nanoemulsion, pharmaceutical, stability, particle size, drug delivery, formulation.

INTRODUCTION

The realm of pharmaceutical research continually seeks innovative strategies to enhance drug delivery systems, aiming for improved therapeutic outcomes, increased drug stability, and enhanced patient compliance. Nanoemulsions have emerged as a promising avenue in this pursuit, offering a versatile platform for delivering hydrophobic drugs effectively.[1,2] However, within this burgeoning field, there exists a noticeable research gap concerning the investigation and characterization of nanoemulsions containing specific drugs like Lulucanzole and Posacunazole. The scarcity of comprehensive studies focusing on these drug-loaded nanoemulsions limits our understanding of their stability, particle size distribution, and pharmaceutical potential.[3,4]

This research paper seeks to address this gap by presenting an in-depth exploration into the formulation, evaluation, and characterization of Lulucanzole and Posacunazole nanoemulsions. The novelty of this study is underscored by its systematic and detailed approach towards understanding the behavior and properties of these drug-loaded nanoemulsions, an area that has received limited attention in existing literature. By examining the stability, particle size distribution, and pharmaceutical applicability of these nanoemulsions, this research endeavors to shed light on their feasibility as effective drug carriers, offering insights that could significantly impact drug delivery systems. [5,6]

The novel contributions of this research paper encompass several aspects. Firstly, it fills a critical void in current literature by providing a comprehensive investigation into the formulation and evaluation of nanoemulsions encapsulating Lulucanzole and Posacunazole. Secondly, this study delves into crucial parameters such as stability, particle size distribution, and pharmaceutical characteristics of these nanoemulsions, offering valuable insights that could steer future research in this domain. Moreover, by focusing on specific drugs within the context of nanoemulsions, this research endeavors to contribute to the understanding of tailored drug delivery systems, potentially paving the way for enhanced therapeutic strategies.

This research aims to bridge the existing gap in nanoemulsion-based drug delivery systems and offer a foundational understanding of the behavior and potential applications of Lulucanzole and Posacunazole nanoemulsions. The insights gained from this study could stimulate further investigations, thereby propelling advancements in pharmaceutical formulations and fostering the development of more effective drug delivery systems with improved therapeutic outcomes.[7-10]

MATERIALS AND METHODS

Preparation of Lulucanzole and Posacunazole nanoemulsion

Table 1: composition of Lulucanzole and Posacunazole nanoemulsion

Ingredients	F1	F2	F3	F4
LULICANAZOLE (%)	1.5	2	-	-
POSACUNAZOLE (%)	-	-	2.0	1.5
Oleic acid (%)	11	11	11	11
Tween 80 (%)	28	28	28	28
PEG 400 (%)	8	8	8	8
Sodium metabisulfite (%)	0.11	0.11	0.11	0.11
Ad-Bidest Aqua (ml)	Q.s	Q.s	Q.s	Q.s

Add oleic acid, lucanzole, and posacunazole to the oil phase and mix well using magnetic stirrers. The sodium metabisulfite and aqua bidestilate were added in the aqueous phase and mixed with a stirring bar until a homogeneous mixture was obtained. To create an emulsifier, blend Tween 80 and PEG 400 in a separate vessel and thoroughly mix them together using a magnetic stirrer until fully integrated. Subsequently, the oil and water phases should be merged, gradually introducing the emulsifier mixture while intermittently stirring using a magnetic stirrer. The clear nanoemulsion was prepared by first combining all the components, followed by homogenization using a

homogenizer set at 1000 rpm for 60 minutes, and then subjecting it to sonication using a sonicator for 30 minutes.[11,12]

Tracking the Size Distribution of Nanoemulsion Particles

On a particle size analyzer (PSA), we took the particle sizes. Administer a nanoemulsion comprising four drops of the lucanzole and Posacunazole formulation to the designated area in the PSA. Subsequently, the PSA closes and exhibits the measurements' outcomes on a computer monitor.[13]

Nanoemulsion of lucanzole and posacunazole evaluated organoleptically

For the organoleptic test, we looked at the nanoemulsion's color, smell, clarity, and the likelihood of phase separation or nanoemulsion rupture.[14]

pH measurement

Using to a pH-meter, we were able to determine the formula's pH. The electrode must first be pre-calibrated using an acidic buffer solution (pH4.01) and a neutral buffer standard (pH 7.01). The next step is to prepare a nanoemulsion and submerge the electrode in it. We make note of the pH value that appears on the device. We measured at room temperature.[15]

Assessing of viscosity

We used a Brookfield viscometer to test the formula's viscosity at room temperature, which is 28°C±20°C. Filling a 100 ml beaker with the mixture, we lowered the spindle until the preparation reached the edge of the glass container. This spindle is number 3. The next step was to push the on button to activate the viscometer. The next step is to adjust the usage rpm to 30 rpm, which is the spindle speed. Once the red needle comes to a halt, you may then determine the reading on the scale (dial reading). To get the viscosity value in centipoise (cps), one may multiply the dial reading by the correction factor. [16]

Examining the nanoemulsion kind

By applying a water-soluble dye, namely methylene blue, onto the surface of the nanoemulsion and then depositing it onto the cleaned glass object, we were able to identify the specific kind of nanoemulsion. If the solution is of the oil-in-water type, methylene blue will readily dissolve in the nanoemulsion and disseminate evenly throughout the water. Nanoemulsions, which combine water and oil, will have methylene blue particles clumped together on their surfaces.[17]

Assessment of cycling performance

The nanoemulsion preparation is put in an oven set at 40°C±2°C for another 24 hours after being held at 4°C±2°C for the first 24 hours. One week is the duration of this program. Six times, we conducted the experiment. Evaluate the nanoemulsion's physical condition both initially and subsequent to cycling.[18]

Test using centrifugation

Centrifugators spin samples at 3800 rpm for 5 hours after inserting them into centrifugation tubes. The effects of the treatment are comparable to a gravitational pull lasting a year. There was a comparison of the preparation's physical state before and after centrifugation.[19,20]

RESULTS AND DISCUSSION

Organoleptic observation

All nanoemulsion formulations were prepared to be transparent, without any odor, and with a faint yellow hue. There is no discernible variation across all formulations when kept in storage.

pH measurement

An appropriate pH range for a topical drug is 4.5-6.5, which is in line with the skin's natural pH. In order to avoid skin irritation, keep the pH level balanced. Excessive acidity may lead to skin irritation, while excessive alkalinity can result in scaly skin. After 8 weeks of pH measurements, modifications were made to all nanoemulsion and cream formulations of Lulucanzole and Posacunazole. Despite this, the pH has not changed much and is still within the skin-safe range.

Measurement of viscosity

After 8 weeks of room temperature storage, the nanoemulsion's viscosity value rose, proving its stability. Due to the comparatively low ambient temperature, the four nanoemulsion formulations saw an increase in viscosity. The connection between viscosity and density is inverse. A decrease in viscosity during storage suggests the presence of kinetically unstable emulsions, where freely moving droplets clash and tend to merge together. The viscosity values are derived by multiplying the dial reading with the correction parameters included in the Brookfield viscometer.

Assessment of cycling performance

The nanoemulsion preparation remained odorless and a pale yellow hue after 6 cycles, whilst the cream preparations remained white and showed no signs of phase separation.



Fig 1: Formula after cycling test

Table 2: pH examination at 0 week and 8th week

Formulation		Nanoemulsion		
	Initial day	56 th day		
Blanko	6.22	6.26		
F1	6.09	6.11		
F2	6.13	6.14		

F3	6.07	6.09
F4	6.01	6.04

Test using centrifugation

Both the nanoemulsion and cream formulations failed to exhibit phase separation after 5 hours of centrifugation at 3800 rpm.

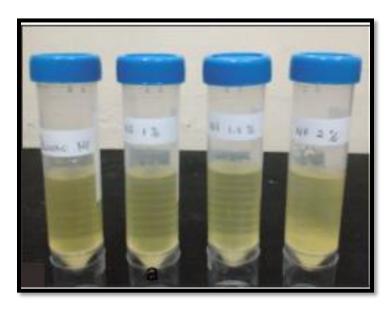


Fig. 3: The formula subsequent to the centrifugation test

Table 3: The viscosity was determined at Initial day and 56 th day

Formulation	Average viscosity (cps)		
	Initial day	56 th day	
Blanko	1100	1700	
F1	1113	1807	
F2	1207	2020	
F3	1260	2087	
F4	1206	1880	

Ascertaining the size of nanoemulsion particles

According to PSA's particle size measurements, the nanoemulsion formulations with 1% lucanzole and posacunazole had the smallest particles before and after storage, measuring 102.36 nm and 177.88 nm, respectively. Lulucanzole and Posacunazole, when added to the mixture at greater concentrations, produce a bigger nanoemulsion. Evidently, the particles were bigger than 100 nm before and after storage, according to the results.

Still, according to reference, their size is still within the nanoemulsion dose-required range of 2-500 nm. According to Shahid and Chowdeswari's study, nanoemulsion may be described as an emulsion where oil is dispersed in water, with droplets ranging in size from 50 to 1000 nm. Typically, the mean droplet size falls within the range of 100 to 500 nanometers.

Table 4: Before and after 56 th days of room temperature storage, the particle size of the Lulucanzole and Posacunazole nanoemulsion

Formula	Before storage	Before storage		After storage	
	Particle	Intensity	Particle	Intensity	
	size		size		
F1	105.16 nm	0.56	177.17 nm	0.59	
F2	103.16 nm	0.52	146.29 nm	0.54	
F3	113.12 nm	0.49	224.34 nm	0.45	
F4	116.92 nm	0.72	315.26 nm	0.54	

Observation of emulsion type

Through the use of nanoemulsion, the observation was conducted by introducing methylene blue onto the formula via a dripping method. The four formulas seem to be oil-in-water emulsion types (m/a) based on the distribution of blue methylene throughout the formula.

CONCLUSION:

In conclusion, the preparation and evaluation of Lulucanzole and Posacunazole nanoemulsions have demonstrated promising outcomes in terms of stability, particle size distribution, and pharmaceutical potential. The findings highlight the successful formulation of stable nanoemulsions with suitable characteristics for drug delivery applications. Future perspectives lie in exploring these nanoemulsions' efficacy in targeted drug delivery systems, enhancing their therapeutic effectiveness, and conducting extensive in vivo studies to ascertain their bioavailability, safety, and clinical applications. Further research should focus on optimizing the formulations, exploring additional drug encapsulation strategies, investigating long-term stability, and elucidating the specific mechanisms underlying their drug release profiles and pharmacological actions. These endeavors can pave the way for the practical utilization of Lulucanzole and Posacunazole nanoemulsions as potential candidates in pharmaceutical formulations with enhanced therapeutic benefits.

REFERENCES:

- [1] Gao, P., Jiang, Z., Luo, Q., Mu, C., Cui, M., & Yang, X. (2021). Preparation and Evaluation of Self-emulsifying Drug Delivery System (SEDDS) of Cepharanthine. *AAPS PharmSciTech*, 22(7), 245. https://doi.org/10.1208/s12249-021-02085-9
- [2] Zupančič, O., Leonaviciute, G., Lam, H. T., Partenhauser, A., Podričnik, S., &Bernkop-Schnürch, A. (2016). Development and in vitro evaluation of an oral SEDDS for desmopressin. *Drug delivery*, 23(6), 2074–2083. https://doi.org/10.3109/10717544.2016.1143056
- [3] Karim, F. T., Kalam, A., Anwar, R., Miah, M. M., Rahman, M. S., & Islam, S. M. (2015). Preparation and evaluation of SEDDS of simvastatin by in vivo, in vitro and ex vivo technique. *Drug development and industrial pharmacy*, 41(8), 1338–1342. https://doi.org/10.3109/03639045.2014.950271

- [4] Wei, L., Sun, P., Nie, S., & Pan, W. (2005). Preparation and evaluation of SEDDS and SMEDDS containing carvedilol. *Drug development and industrial pharmacy*, 31(8), 785–794. https://doi.org/10.1080/03639040500216428
- [5] Liang, X., Hua, Y., Liu, Q., Li, Z., Yu, F., Gao, J., Zhang, H., &Zheng, A. (2021). Solid Self-Emulsifying Drug Delivery System (Solid SEDDS) for Testosterone Undecanoate: In Vitro and In Vivo Evaluation. *Current drug delivery*, 18(5), 620–633. https://doi.org/10.2174/1567201817666200904172626
- [6] Zupančič, O., Grieβinger, J. A., Rohrer, J., Pereira de Sousa, I., Danninger, L., Partenhauser, A., Sündermann, N. E., Laffleur, F., &Bernkop-Schnürch, A. (2016). Development, in vitro and in vivo evaluation of a self-emulsifying drug delivery system (SEDDS) for oral enoxaparin administration. European journal of pharmaceutics and biopharmaceutics: official journal of Arbeitsgemeinschaft fur PharmaceutischeVerfahrenstechnike.V, 109, 113–121. https://doi.org/10.1016/j.ejpb.2016.09.013
- [7] Kale, A. A., &Patravale, V. B. (2008). Design and evaluation of self-emulsifying drug delivery systems (SEDDS) of nimodipine. *AAPS PharmSciTech*, 9(1), 191–196. https://doi.org/10.1208/s12249-008-9037-9
- [8] Zaichik, S., Steinbring, C., Caliskan, C., &Bernkop-Schnürch, A. (2019). Development and in vitro evaluation of a self-emulsifying drug delivery system (SEDDS) for oral vancomycin administration. *International journal of pharmaceutics*, 554, 125–133. https://doi.org/10.1016/j.ijpharm.2018.11.010
- [9] Cai, Y., Liu, L., Xia, M., Tian, C., Wu, W., Dong, B., & Chu, X. (2022). SEDDS facilitate cinnamaldehyde crossing the mucus barrier: The perspective of mucus and Caco-2/HT29 co-culture models. *International journal of pharmaceutics*, 614, 121461. https://doi.org/10.1016/j.ijpharm.2022.121461
- [10] Kubackova, J., Holas, O., Zbytovska, J., Vranikova, B., Zeng, G., Pavek, P., &Mullertz, A. (2021). Oligonucleotide Delivery across the Caco-2 Monolayer: The Design and Evaluation of Self-Emulsifying Drug Delivery Systems (SEDDS). *Pharmaceutics*, *13*(4), 459. https://doi.org/10.3390/pharmaceutics13040459
- [11] Kubackova, J., Holas, O., Zbytovska, J., Vranikova, B., Zeng, G., Pavek, P., &Mullertz, A. (2021). Oligonucleotide Delivery across the Caco-2 Monolayer: The Design and Evaluation of Self-Emulsifying Drug Delivery Systems (SEDDS). *Pharmaceutics*, *13*(4), 459. https://doi.org/10.3390/pharmaceutics13040459
- [12] Liu, M., Zhang, S., Cui, S., Chen, F., Jia, L., Wang, S., Gai, X., Li, P., Yang, F., Pan, W., & Yang, X. (2017). Preparation and evaluation of Vinpocetine self-emulsifying pH gradient release pellets. *Drug delivery*, 24(1), 1598–1604. https://doi.org/10.1080/10717544.2017.1388453
- [13] Menzel, C., Holzeisen, T., Laffleur, F., Zaichik, S., Abdulkarim, M., Gumbleton, M., &Bernkop-Schnürch, A. (2018). In vivo evaluation of an oral self-emulsifying drug delivery system (SEDDS) for exenatide. *Journal of controlled release : official journal of the Controlled Release Society*, 277, 165–172. https://doi.org/10.1016/j.jconrel.2018.03.018
- [14] Khan, M., Nadhman, A., Sehgal, S. A., Siraj, S., &Yasinzai, M. M. (2018). Formulation and Characterization of a Self-Emulsifying Drug Delivery System (SEDDS) of Curcumin for the Topical Application in Cutaneous and MucocutaneousLeishmaniasis. *Current topics in medicinal chemistry*, 18(18), 1603–1609. https://doi.org/10.2174/1568026618666181025104818
- [15] Nipun, T. S., & Ashraful Islam, S. M. (2014). SEDDS of gliclazide: Preparation and characterization by invitro, ex-vivo and in-vivo techniques. *Saudi pharmaceutical journal: SPJ: the official publication of the Saudi Pharmaceutical Society*, 22(4), 343–348. https://doi.org/10.1016/j.jsps.2013.06.001
- [16] Malkawi, A. S., Haddad, R., Malkawi, A., &Alrabadi, N. (2022). Development of Fluorescently Labeled Self-Emulsifying Drug Delivery Systems (SEDDS) for Prolonged Stability, In Vitro Sustained Release, and Cellular Uptake. *Pharmaceutical nanotechnology*, 10(2), 146–161. https://doi.org/10.2174/2211738510666220314103400

- [17] Seo, Y. G., Kim, D. W., Cho, K. H., Yousaf, A. M., Kim, D. S., Kim, J. H., Kim, J. O., Yong, C. S., & Choi, H. G. (2015). Preparation and pharmaceutical evaluation of new tacrolimus-loaded solid self-emulsifying drug delivery system. *Archives of pharmacal research*, *38*(2), 223–228. https://doi.org/10.1007/s12272-014-0459-5
- [18] Srivastava, R., Choudhury, P. K., Dev, S. K., &Rathore, V. (2022). Formulation and Evaluation of α-Pinene Loaded Self-emulsifying Nanoformulation for *In-Vivo* Anti-Parkinson's Activity. *Recent patents on nanotechnology*, *16*(2), 139–159. https://doi.org/10.2174/1872210515666210329161439
- [19] Chintalapudi, R., Murthy, T. E., Lakshmi, K. R., &Manohar, G. G. (2015). Formulation, optimization, and evaluation of self-emulsifying drug delivery systems of nevirapine. *International journal of pharmaceutical investigation*, 5(4), 205–213. https://doi.org/10.4103/2230-973X.167676
- [20] Salimi, A., Sharif MakhmalZadeh, B., Hemati, A. A., &AkbariBirgani, S. (2014). Design and Evaluation of Self-Emulsifying Drug Delivery System (SEDDS) Of Carvedilol to Improve the Oral Absorption. *Jundishapur journal of natural pharmaceutical products*, 9(3), e16125. https://doi.org/10.17795/jjippp-16125