DEVELOPMENT AND CHARACTERIZATION OF SELF-EMULSIFYING SYSTEMS CONTAINING LINSEED OIL

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Introduction

The use of lipid-based systems has been the alternative to increase the bioavailability of hydrophobic compounds. They are a diverse group of formulations and properties that can be used through different routes, such as oral, transdermal, ocular and rectal. Among these techniques, self-emulsifying systems can be included [1]. Self-Emulsifying Drug Delivery Systems (SEDDS) are liquid and anhydrous mixtures formed by lipids, surfactants, drug and/or co-solvents and co-surfactants, whose original objective is to improve the bioavailability of orally administered drugs. Once in the gastrointestinal tract, the gentle agitation promoted by digestive motility forms a translucent emulsion, providing an extensive surface area to release and absorb bioactive substances [2]. Bioactive oils are often used for their pharmaceutical and functional properties. Linseed oil is obtained by pressing flax seed and is composed of fatty acids, mainly α-Linolenic polyunsaturated fatty acid (ALA). Generally, the amount of oil can vary from 30 to 44%, depending on factors such as environmental conditions and growing location. Its fatty acid composition is peculiar due to the high content of ALA, about 55%. It also has linoleic, oleic, stearic and palmitic acids [3]. This work aimed to develop and characterize a liquid self-emulsifying system containing linseed oil to increase the bioaccessibility of its bioactive components.

Material and Methods

The base formulation consists of PEG-40 (FAGRON) as a surfactant, Span© 80 (VETEC) as a co-surfactant and Linseed Oil (LAZLO) as a bioactive compound. Initially, the required HLB (Hydrophilic-Lipophilic Balance) was evaluated. Ten formulations with different ratios of PEG-40 and Span© 80 were prepared to obtain HLB values from 5.17 to 13 (F1 to F10). The formulations were produced by the phase inversion method and titration: after weighing the materials, the components were homogenized in a magnetic stirrer for 30 minutes at 1000 rpm. Still, distilled water was slowly added through a burette in pre-defined volumes under agitation. Finally, the formulations were stored for 24 hours at room temperature and evaluated for visual appearance (color, consistency and stability) [4].

A new batch, with 15 formulations, was prepared using different ratios of surfactant and oil (A – 1:1; B – 3:2, C – 2:3, D – 4:1 and E – 1:4). The method and the evaluated parameters were the same as the first batch. Then, the approved samples of the second batch were used to develop the SEDDS: each component of the formulation was weighed, vortexed for 2 minutes, and stored for 24 hours. Each sample was produced in triplicate. After the proposed time, the visual aspect was evaluated and those with no changes were centrifuged for 15 minutes at 6000 rpm. Subsequently, the samples were reconstituted in water and analyzed under different conditions: 0.5g of each SEDDS was slowly stirred in 50 mL of water and analyzed by different tests, such as centrifugation for 15 minutes at 6000 rpm; stability evaluation at room temperature and immersion in a water bath for 120 minutes at 37°C. Particle Size (Z-Ave), Zeta Potential

(PZ) and Polydispersion Index (PDI) were evaluated for nanoemulsions and SEEDS by *Direct Light Scattering* (DLS) [5].

Results and Discussion

A consistency change was detected in the first water additions, hardening the first batch of samples. As the volume of water increased, the nanoemulsions became liquid. The stable formulations with nanoemulsions characteristics (liquid, translucent and bluish reflection) (F7, F8 and F9, HLB value 10.39, 11.26 and 12.13, respectively) were selected in the first evaluation. The second nanoemulsions batch showed some samples with yellowish tones and bluish reflexes. Two samples showed instability after 24 hours and Z-Ave, PDI and PZ could not be analyzed (F2-E and F3-E). Six nanoemulsions were selected for the SEDDS production stage (Table 1). All SEDDS were stable after 24 hours according to visual aspects. Two samples were unstable after centrifugation and water bath immersion test (F2-E and F3-E). The DLS analysis showed an increase in particle size lower PDI values and a decrease in the Zeta Potential when compared with the nanoemulsions of the second batch (Table 1).

Table 1: Nanoemulsions e SEEDS Particle Size (Z-Ave), Zeta Potential (PZ) and Polydispersion Index (PDI) values.

	Formulations					
	Nanoemulsions					
	F1-A	**F1-B**	**F1-C**	**F2-A**	**F2-B**	**F3-C**
Z-Ave	147.2	116	183,9	135	136.6	192.7
PDI	0.2765	0.2829	0,2447	0.2548	0.7196	0.1134
PZ	- 20.9033	-25.46	-27,5	-18.2467	-11.1457	-22.7033
	SEEDS					
	F1-A	**F1-B**	**F1-C**	**F2-A**	**F2-B**	**F3-C**
Z-Ave	269.8	214.6	253.1	193.2	201.8	416.9
PDI	0.3269	0.3046	0.3987	0.2439	0.2732	0.1166
PZ	- 20.98	- 18.75	- 22.76	- 13.01	- 12.01	- 20.65

Conclusion

The present study was able to develop nanoemulsions and SEDDS with stability, bluish visual appearance and particle size at the nanometer scale. The results should allow the optimization of formulations on the technological and biopharmaceutical aspects, providing an improved system to release bioactive compounds.

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