

# Investigation Of Nifedipine And Piperine Loaded Bio-SNEDDS For The Treatment Of Hypertension

Mohsin Kazi, Abdulaziz Almuhanha, Bandar Alyousef

Department of Pharmaceutics, College of Pharmacy, POBOX-2457, King Saud University, Riyadh-11451, KSA

CONTACT INFORMATION: Mohsin Kazi, Tel: +966114677372 | Fax: +966114676295; Email: mkazi@ksu.edu.sa.

## Background

Hypertension, commonly known as high blood pressure, is a chronic medical condition in which the blood pressure in the arteries is consistently elevate. This condition affects millions of people worldwide and is a major risk factor for heart disease, stroke, and other cardiovascular diseases. Combination therapy with two or more antihypertensive drugs aims to reduce blood pressure levels and prevent the development of associated complications. There is limited research on the combination of nifedipine and piperine. The current studies discuss the potential therapeutic benefits of combining nifedipine and piperine for the treatment of hypertension. The aim of this study is to utilize a cutting-edge bioactive self-nanoemulsifying drug delivery systems (Bio-SNEDDS) technology to develop a novel combination therapy of nifedipine and piperine for the treatment of hypertension.

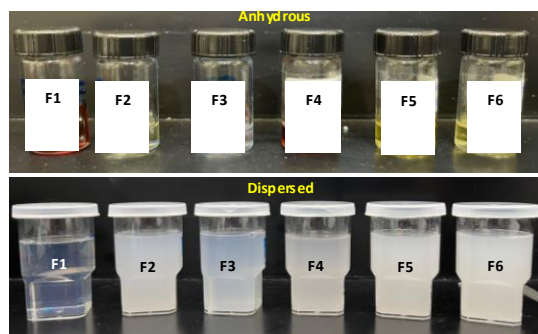
## Methods

Bio-SNEDDS nanoformulations were developed by incorporating black seed oil (BSO), Moringa seed oil and grape seed oil as excipients with non-ionic surfactant in the formulations. Characterization studies were performed of the self-nanoemulsifying systems in terms of their appearance, particle size, polydispersity index (PDI) zeta potential, anti-oxidant tests [by the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assay] and transmission electron microscopic (TEM) analysis. Equilibrium solubility studies were conducted to estimate the drug encapsulation and oral absorption. The optimized Bio-SNEDDS were investigated for the antihypertensive effects (behavioral Y-Maze Test) of combining nifedipine and piperine using mice model.

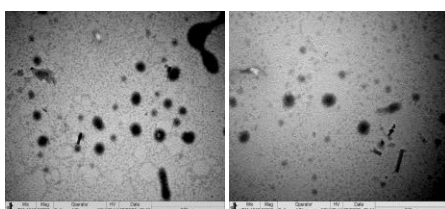
## Results

**Table 1:** The mean particle size, polydispersity index (PDI) and zeta potential of Bio-SNEDDS formulations

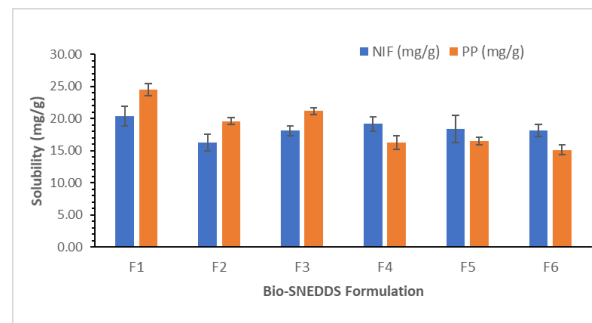
F. No.	Compositions (% W/W)	Particle size (nm)	PDI	Zeta potential (mV)
F1	BSO/1988/PEG400/KHS15. (25/20/15/40)	35.12±0.17	0.23±0.01	-3.55±0.25
F2	MSO/1988/PEG400/KHS15. (25/20/15/40)	205.90±3.95	0.39±0.01	-14.1±0.91
F3	GSO/1988/PEG400/KHS15. (25/20/15/40)	158.63±20.40	0.32±0.05	-5.69±0.30
F4	BSO/1988/T85. (35/15/50)	355.23±48.57	0.55±0.13	-46.4±3.10
F5	MSO/1988/T85. (35/15/50)	424.43±77.90	0.70±0.10	-33.4±2.22
F6	GSO/1988/T85. (35/15/50)	363.07±23.63	0.61±0.07	-34.7±0.88



**Figure 1:** Appearance of the drug-loaded anhydrous Bio-SNEDDS Formulations (Top) and dispersed in water at 1 in 1000 dilution (Bottom) [F1 produced transparent and low viscous solution].



**Figure 2:** TEM images of F1 (BSO/1988/PEG400/KHS15) Bio-SNEDDS formulation



**Figure 3:** Equilibrium solubility of Nifedipine (NIF) and Piperine (PP) in Bio-SNEDDS formulations

**Table 2:** DPPH Scavenging activities (Antioxidant) of the representative Bio-SNEDDS formulations [The results showed that F1 (drug free) & F1D (drug loaded) had the smallest IC50 values and highest antioxidant activities compared to the other samples]

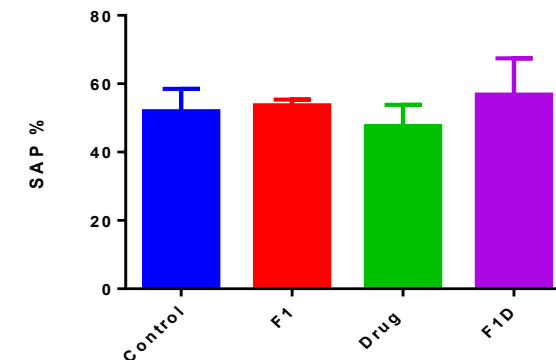
Sample	% of Inhibition	IC <sub>50</sub>
NIF	23.68%	2221.59 ± 673.78 µg/ml
PP	50.66%	13.17 ± 2.35 µg/ml
F1	52.85%	5.25 ± 0.44 µl/ml
F1D	58.33%	8.63 ± 0.13 µl/ml
Ascorbic Acid	73.90%	6.92 ± 0.53 µg/ml

## References

- [1]. Mohsin et al. Pharmaceutics 12 (8), p. 749, 2020
- [2]. Mohsin et al. Drug Delivery 28 (1), P. 100-114, 2021

## Acknowledgement

The author would like to extend their sincere appreciation to the Deanship of Scientific Research at King Saud University, Riyadh, KSA, for its funding.



**Figure 4:** A quantitative analysis of spontaneous alternation behaviors (%SAP) on a Y-maze reveals adverse effects of acute social isolation on spatial working memory

## Discussion & Conclusion

Bio-SNEDDS formulations were successfully prepared and the optimized formulation comprised BSO, Imwitor 988 (mixed mono & diglycerides), PEG 400 (refined) and Kolliphor HS15 (Non-ionic surfactant). Bio-SNEDDS produced around 35.12 nm droplet size with 0.23 PDI upon aqueous dispersion. The zeta potential value of Nifedipine (NIF) and piperine (PP) loaded Bio-SNEDDS suggest that the formulation was stable in anhydrous form. TEM images also confirmed the droplet size of 35.12 nm which was obtained from the particle size analysis. The anti-hypertensive studies in mice model further confirmed the efficacy of the combined NIF and PP loaded Bio-SNEDDS for the effective treatment for hypertension.