Advances in Bioresearch
Adv. Biores., Vol 15 (3) May 2024: 429-432

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.15.3.429432

Advances in Bioresearch

ORIGINAL ARTICLE

To Study Effect of High-Pressure Homogenizer Techniques for Preparation of Ezetimibe Nanoparticles with Combination of Two Polymers

Amit Agrawal, Sharad Kamble*
Faculty of Pharmacy, Mansarovar Global University, Billkisganj, Sehore, Madhya Pradesh-466001. Mob.
Corresponding Author: Sharad Kamble
Email: sharadkamble5@gmail.com

ABSTRACT
The present study was aimed at to effect of ultra turrex and High Pressure Homogenizer techniques (HPH) to enhance the solubility of Ezetimibe by nanotechnology approaches several attempts were made to develop a nanosuspension. Ezetimibe is a BCS class II drug that is insoluble in low pH solution and soluble in high pH solution. In this study, polymeric NPs formulations of Ezetimibe with Soluplus and Chitosan polymer in different ratios will be prepared by HPH of the resulting dispersions will be compared to those of crystalline Ezetimibe. Further evaluate with determination of entrapment efficiency size particle and zeta potential. We prepared two batches one without HPH (BATCH 1) and another one with HPH (BATCH 2) compared result. The entrapment efficacies were found to be 205 and 82.02 % for BATCH 1 and BATCH 2 respectively. From the result of particles size analysis batch 2 shows minimum particles size 349.5 nm this batch consider for further study. The batch 2 zeta potential found to be 18.3 m v colloidal stability is achieved when voltage is greater than +30mV and lower than -30mV it indicates the BATCH 2 of ezetimibe are stable. On the above result it concluded that the better result shows BATCH 2 prepared by using HPH techniques.
Keywords: *ezetimibe nanoparticles, ultra turrex, High Pressure Homogenizer, zeta potential, entrapment efficacy, solubility, colloidal stability*

Received 24.03.2024 Revised 01.04.2024 Accepted 21.05.2024

How to cite this article:
Amit A, Sharad K. To Study Effect of High Pressure Homogenizer Techniques For Preparation Of Ezetimibe Nanoparticles With Combination Of Two Polymers. Adv. Biores., Vol 15(3) May 2024: 429-432.

INTRODUCTION

Nanotechnology has opened up various opportunities in the field of drug delivery. HPH is a commonly employed method for producing nanosuspensions of poorly soluble drugs. This method involves forcing a suspension, which contains drug and stabilizers, through a valve with a small orifice under pressure (1). Homogenization is a process of achieving homogeneity throughout a product by particle size modification. The ULTRA-TURRAX® UTC is a high-performance dispersing machine used for the production of a variety of emulsions and suspensions in batch operations (2). Using the rotor-stator 3 principle, the UTC is best suited for applications that cannot be accomplished using conventional stirring methods. (3) The goal of this work is to see how a polymeric NPs formulation prepared using HPH effects on ezetimibe solubility. The goal of this research is to increase the solubility, release, and comparability of a poorly soluble drug utilizing the HPH approach and a combination of polymer (Soluplus and chitosan). The soluplus is Hydrophilic polymer which reduces aggregation; improve wet ability, and local solubilization by the carrier in the diffusion layer, resulting in a higher dissolving rate.

MATERIALS AND METHODS

Ezetimibe was obtained as a gift sample from SVK Laboratories Pvt. Ltd, Hydrabad, India. soluplus and Chitosan were purchased from BASF chemicals Ltd, Mumbai, India and Fine Chemicals, Mumbai, India respectively. All the other reagents and solvents used were of analytical grade.

Preparation of ezetimibe NPs Formulation:
Complete Dissolve Ezetimibe in Methanol then Formation of anti-solvent.(Solution A) Mixing of Soluplus in distilled water and use Bath sonicator for complete dissolution of soloplus in distilled water then Formation of aqueous solution.(Solution B) Dropwise addition of solution A into B at 1200 rpm on magnetic stirrer for Removal of organic solvent (methanol) by continuous stirring up to 1-2 hrs. Then Formation of suspension the suspension was stirred with Ultra Turrax 5 min at 8000 rpm. And the other ratios of drug polymer (see table no. 1) using the polymer soluplus and Chitosan were formulated in the similar manner. HPH at 900bar for 25 cycles was used to further homogenize the suspension (Only batch 2). All activities were carried out with a cooling unit to keep the sample temperature between 25 and 35 degrees Celsius nano suspension was formed.(2)(4)

Particle size, Polydispersity index and Zeta potential
Freeze dried nanoparticles were dispersed in double distilled water. Particle size and Zeta potential was measured using a Malvern Zetasizer 3000 (Malvern Instruments, UK). The measurement of particle size was based on photon correlation spectroscopy. Polydispersity index was studied to determine the narrowness of the particle size distribution. Zeta potential was studied to determine the surface charge of NPs. The zeta potential was determined using electrophoretic light scattering (ELS) at 25˚C with electric field strength of 23 V/cm using Zetasizer nano ZS. (5)(6)

Percentage entrapment efficiency (%EE)
Entrapment efficiency is defined as the ration of amount of entrapped drug to the amount of total drug used for preparation of nanoparticles. 2 ml of the NPs dispersion was placed in centrifuge (Remi Instrument Ltd., Mumbai, India) at 10000 rpm for 30 min at 4˚C. Supernatant was suitably diluted with methanol and analysed spectrophotometrically at 233 nm. (7)(8).

$$EE\ (\%) = \frac{Wt.of\ drug\ used\ in\ formulation - \text{Wt. of unbound drug in supernatant}}{Wt.\ of\ drug\ used\ in\ formulation} * 100$$

RESULTS AND DISCUSSION
Pre-formulation study:
Preformulation study to check the purity of given drugs was performed. The drug ezetimibe was found solid, white in colours and having λ max at 234nm. It is practically insoluble in water, soluble in methanol and slightly soluble in acetone, HCl and ethanol.

Entrapment efficacy (%):
Entrapment efficacy (%) found to be 205 and 82.02 % for BATCH 1 and BATCH2 respectively. The drug load for BATCH 2 were found to be 17.28 better than BATCH 1. (See Table No. 2)

Particle size (particle size) and size distribution PDI
A result of analysis is as per below figure No. 2. The sizes of BATCH 1 and BATCH 2 were found in 1141.5 and 394.5 nm respectively; therefore, we could expect better drug release as compared to pure drug. Particle size BATCH 2 reduces due to high pressure homogenization method & its impact. High pressure homogenization method helps to reduce the Particle size from micro to nano, hence improves solubility and rate of dissolution. For PDI see table no. 3. Batch 2 is selected for further characterization. Particle size were found to be 394.5 nm

Zeta Potential:
Zeta Potential Batch (BATCH 2) had Zeta potentials of 18.3mV Colloidal stability is achieved when the voltage is greater than + 30 mV or lower than -30 mV (See Figure No. 3); however, a value approaching zero indicates instability and fast coagulation, Even though the measured Zeta Potential was low, batch BATCH 2 stabilized Ezetimibe nanoparticles were relatively stable in our investigation. Using this standard range of zeta potential. it was determined that all of the manufactured batches were colloidally stable. The Zeta potential of BATCH 2 was found to be 18.3 mV. The above result it concluded that The Polymer, Soluplus was used to prepare the narioparticles with Ezetimibe by high pressure homogenization. The effect of process variable on the solubility and the Particle size was identified. The high-pressure homogenization was proven that to be a simple and efficient Technology for reducing the Particle size. Thus, the current study was aimed to enhance the solubility of Ezetimibe with the combination of polymer and prepared by high pressure homogenization technique.

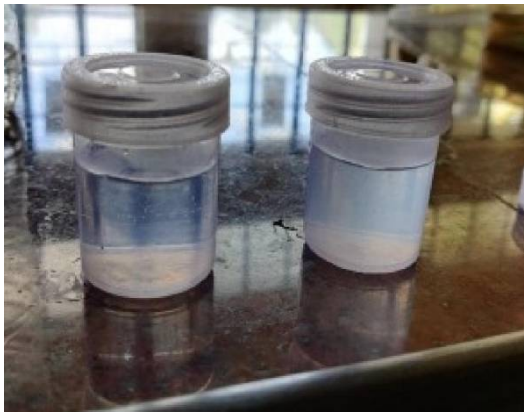

Figure No. 1: formulated batches

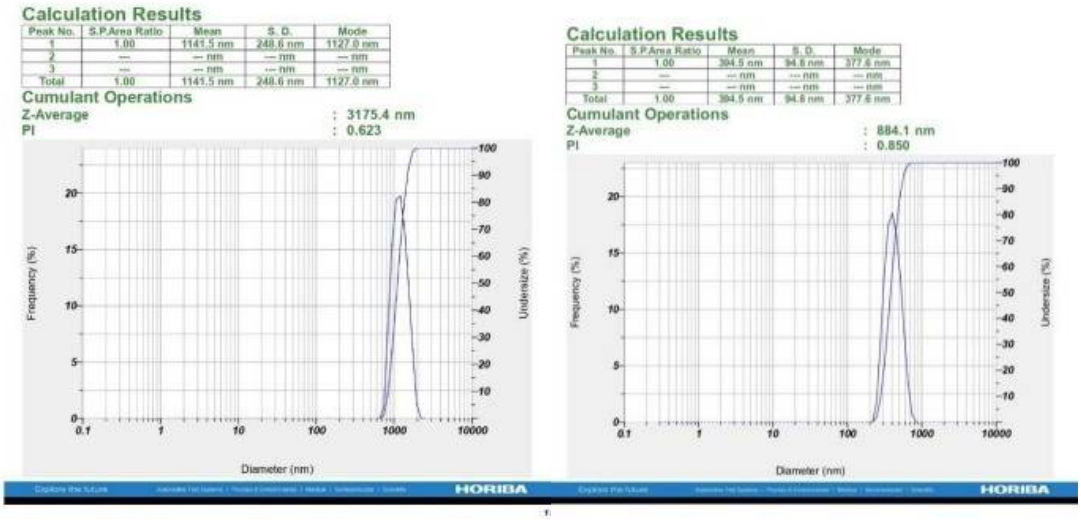

Figure No. 2: Particle Size distribution of BATCH 1 and BATCH2 respectively

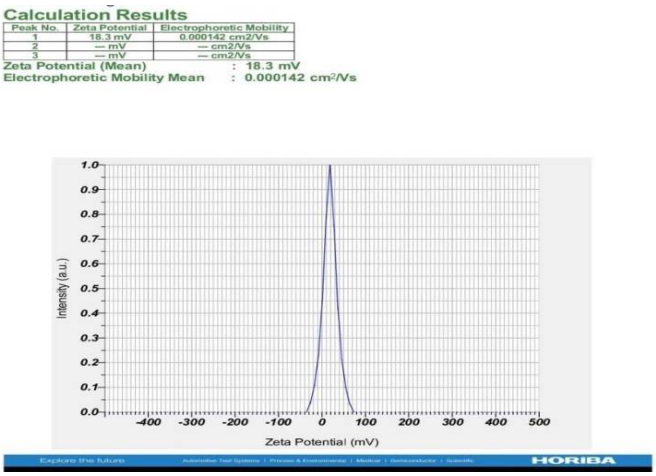

Figure No. 3: Zeta potential of BATCH2

Table No. 1: formulation of batches

Formulation code	Formulation composition			
	DRUG (EZETIMIBE) Mg	SOLUPLUS (mg)	CHITOSAN (mg)	WATER (ml)
BATCH 1	10	2	1.75	20 ml
BATCH 2 (hph)	10	2	1.75	20ml

Table No. 2: Entrapment efficacy (%) of batches

Batch 1	**205.0**
Batch 2	**82.02**

Table No. 3: Particles Sizes and PDI of different Batches

Batches	Particles Size (nm)	PDI
Batch 1	**1141.5**	**0.623**
Batch 2	**394.5**	**0.859**

REFERENCES

1. Libby P., Buring JE., Badimon L., Harisson OK., Deanfield J., Bittencourt MS,, Tokpzoglu L., Lewis EF., (2019). Atherosclerosis. Nat Rev Dis Primers 1, 56. doi: 10.10381s41572-019-0106-z.
2. Govind Soni, Ketaki Kale, Saritha Shetty, M.K. Gupta, Khushwant S. Yadav, 2020. Quality by design (QbD) approach in processing polymeric nanoparticles loading anticancer drugs by high pressure homogenizer, Heliyon, Volume 6, Issue 4. https://doi.org/10.1016/j.heliyon.2020.e03846
3. M.H. Shukr., S. Ismail., S.M. Ahmed., (2019). Development and optimization of ezetimibe nanoparticles with improved antihyperlipidemic activity. J drug delivery science and Technology. doi: https:// doi,org/10,1016/ j.jddst.2018.12.001.
4. Bhargav, Eranti & Barghav, G. & Reddy, Y. & Chintamaneni, Pavan & Peraman, Ramalingam & Chinthaginjala, Haranath. 2020. A Design of Experiment (DoE) based approach for development and optimization of nanosuspensions of telmisartan, a BCS class II antihypertensive drug. Future Journal of Pharmaceutical Sciences. 6. 10.1186/s43094-020-00032-2.
5. Mathur M., Kusurp Devi V., 2016. Potential of novel drug delivery strategies for the treatment of hyperlipidemia. J Drug Target,10, 916-926. doi: 10.310911061186X.2.016.1172586r
6. Phan BA., Dayspring TD., Toth PP., 2012. Ezetimibe therapy: mechanism of action and clinical update. Vasc Health Risk Manag. 415-27. doi: 10.2147NHRIvI.S33664.
7. Wilczewska., A. Z., Niemirowicz., K., Markiewicz., K. H., Car, H., (2012). Nanoparticles as drug delivery systems. Institute of pharmacology policy academy of science 64,1020-1037.https://doi.org/10_1016/s1734-1140(12)70901-5.
8. Pranav Shah et al. (2017). Formulation and Evaluation of Ezetimibe Loaded Solid Lipid Nanoparticles. Indo American Journal of Pharmaceutical Research.:7(08): 100-109