Research Article

Formulation and Evaluation of Lovastatin Loaded Proniosomal Powder

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ABSTRACT

The aim of the present research was to develop a proniosomal formulation of Lovastatin and to evaluate the influence of proniosomal systems. Approaches to stabilize niosomal drug delivery system without affecting its properties of merits have resulted in the development of the promising drug carrier "Proniosomes". Proniosomes is a dry formulation using suitable carrier coated with non-ionic surfactants and can be converted into niosomes immediately before use by hydration Proniosomes were prepared by slurry method using molar ratios of nonionic surfactants span60 with cholesterol as membrane stabilizing agent and maltodextrin a water soluble carrier. The proniosome formulations were evaluated for FT-IR study, angle of repose and scanning electron microscopy. The niosomal suspensions were further evaluated for entrapment efficiency, In-vitro release study, kinetic data analysis, stability study. The result from SEM analyses has confirmed the coating of surfactant on the surface of carrier. The formulation F3, which showed higher entrapment efficiency of 72.69% and invitro release of 91.17 % at the end of 24h, was found to be best among the all 7 formulation. The stability study reveals that the proniosome formulations are stable when stored at 4°C.

Keywords: Lovastatin, Maltodexdrin, Proniosomes, Encapsulation.

INTRODUCTION

Vesicular systems have a lot of advantages as a carrier for advanced drug delivery that Encapsulate drug in vesicular structures to reduce the problem of aqueous solubility and toxicity of certain drugs.

Liposomes are colloidal, vesicular structures having concentric phospholipidic bilayers with an aqueous core inside which encloses a wide variety of substances and drug.But liposomes have some stability problems such as sedimentation, aggregation, fusion, phospholipid hydrolysis and oxidation so to overcome the problems associated with Niosomes and proniosomes are better alternatives to liposomes. Niosomes are vesicles composed mainly of hydrated non-ionic surfactants with cholesterol and its derivatives such as lecithin. Niosomes acts as drug carriers with greater chemical stability, entrapment efficiency of both hydrophobic and hydrophilic drugs and are less toxic due to their non-ionic nature. They possess greater stability and lack of many disadvantages associated with liposomes in which high cost and the purity problems of phospholipids.so advantage for this simple method for high scale production of this niosomes without loss of more solvent is to prepare a stabilized drug delivery system known as Proniosomes.Another advantage is simple method for the routine and large scale production of niosomes without the use of acceptable solvents.

Lovastatin is a member of the drug class of statins, used for lowering cholesterol (hypolipidemic agent) in those with hypercholesterolemia and so preventing cardiovascular disease . use of surfactants and change in solid form such as nanocrystals in which preparation of Proniosomes is one of the approaches to increase the dissolution rate of poorly water soluble drugs. The proniosomal formulation of lovastatin helps to sustain the drug release from an vesicles. Sustained release dosage form delivers the drug at a slow release rate over an extended period of time. The short biological half life (about 3-5 hours) and dosing frequency not more than once a day makes lovastatin an ideal candidate for proniosomes. Niosomes suffers from various problems of physical stability (aggregation, fusion, leaking) could be minimized. Reported methods for preparation of proniosomes were the spraying of surfactant on water soluble carrier particles and the slurry method.The dry free flowing granular product upon addition of water, disperses or dissolves to form a multilamellar niosomal suspension suitable for administration by oral or other routes. Nowadays considerable interest has been focused on niosomes based targeted drug delivery.

MATERIALS AND METHODS

Lovastatin obtained as a gift sample from Yarrow pharmaceuticals Pvt.Ltd, Mumbai. Cholesterol obtained from Loba Chemie .Pvt. Ltd. Mumbai (India). Maltodextrin and Span 60 obtained also from Loba Chemie Pvt. Ltd. Mumbai (India) Chloroform from same Loba Chemie .Pvt. Ltd. Mumbai (India). Rotary flash evaporator for the preparation of proniosomes procured from Superfit India. All other materials used and received were of analytical grade.

Table 1: Formulation Codes of various Proniosomal Powder

Batch Code	Drug	Maltodextrin	Span 60	Cholesterol
F1	40mg	100mg	0	200
F2	40mg	100mg	50	150
F3	40mg	100mg	100	100
F4	40mg	100mg	150	50
F5	40mg	100mg	200	0

Method of Development Of Proniosomal Powder

Proniosomal powders were prepared by a slurry method. Precisely weighed amount of drug40mg,surfactant (span 60) and cholesterol were taken in 250 ml round bottom flask and dissolved in mixture of chloroform and methanol (1:1) at room temperature.100mg maltodextrin was added to above solution to from slurry. The flask was attached to a rotary flash evaporator, lowered into a water bath, maintained at temp. 45±2^0 C and organic solvent was evaporated under reduced pressure of 600 mmHg to from thin, dry film on the wall of flask.After ensuring the compete removal of a solvent, the resultant powder were collected and dried overnight in a vacuum oven at room temperature. The resultant dry powder was passed through sieve no. 60 and stored in a tightly closed container for further evaluation.Composition of proniosomal powder formulations are given in table no.1

Evaluation of Proniosomal Powder

Percentage Production yield

The prepared batches were evaluated as per formula using the weight of final product after drying with respect to the initial total weight of the drug and polymer used for preparation.

% production yield = Practical yield / Theoretical yield *100

Microscopical Examination

After the hydration of the proniosomal powder with hot water the noisome dispersion was formed which was seen under the microscope with the attachment of the Magnus camera and photographs of drug and all formulations (F1-F5) were taken which is shown in fig.2

Scanning electron microscopy (SEM)

The morphology of the optimized batch F4 was studied by using Scanning Electron Microscopy (SEM-JEOL Instruments, JSM-6360, and Japan). Samples were mounted on a double-faced adhesive tape, sputtered with gold. Scanning electron photographs were taken at an accelerating voltage of 15 kV of accelerating voltage and obtained micrographs were examined at X500, X1000, X2000 magnifications.

Particle Size Analysis

Proniosome suspension (as directed above) was characterized for average particle size using laser diffraction technique (Beckman Coulter Instruments.) The particle size distribution is given by depends upon intensity Distribution.

Percentage Entrapment Efficiency

Proniosome powder equivalent to 10 mg was taken and 10 ml of aqueous phase i.e PB 7.4 was added. The aqueous suspension was sonicated for 2-3 min. This suspension was centrifuged using ultramicrocentrifuge at 14000 rpm for 45 min at 4^{0}C. The suspernant was taken and suitably diluted with same solvent. Absorbance was measured using UV spectrophotometer at 245nm.

$\% EE = (C_t - C_{f)} \times 100$

Where, C_t = Total amount of drug added,

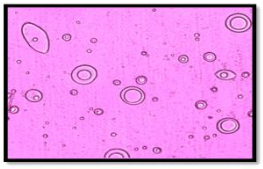
C_f = Unentrapped drug

In Vitro Release Studies

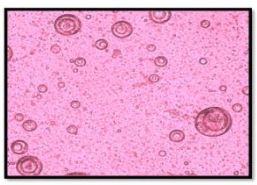
The dissolution studies were performed using USP Type II (Paddle) Apparatus. Formulation Powder equivalent to 40 mg and pure drug 40 mg were compressed and forms the tablet by direct compression method. The dissolution was performed in pH 7.4 Phosphate Buffer. Volume of dissolution media used was 900 ml, maintained at temperature 37 ± 0.5^0 C. The speed of paddle was set at 50 rpm. The individual tablet was placed in individual vessel. The samples were withdrawn at a time intervals from 5 min to 12 hrs. 5 ml of sample was withdrawn and replaced with same media to maintain sink condition. The sample were immediately filtered through 0.45 µm membrane filter, suitably diluted and analyzed spectrophotometrically at 245 nm respectively.

Stability Studies

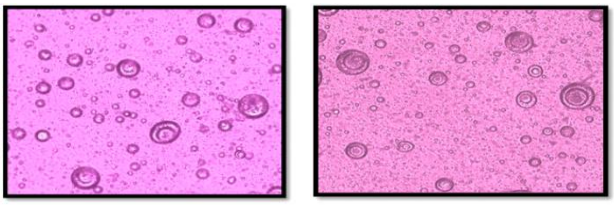
Stability study was ascertained by monitoring the physical appearance and % EE of optimized batch F4 after storage at refrigerated temperature (4±2^{0}C) and room temperature. Formulation was sealed in glass vials and stored at given temperatures. At definite period of time (0, 30 and 60 days), samples were withdrawn and observed.



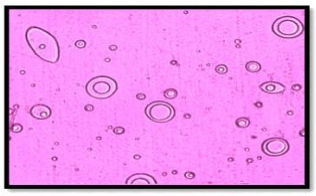
PNG 1



PNG2



PNG3 PNG4



PNG5

Figure 2: Photomicrograph of Formulation PNG1, PNG2, PNG3, PNG4, PNG5 Containing Span 60

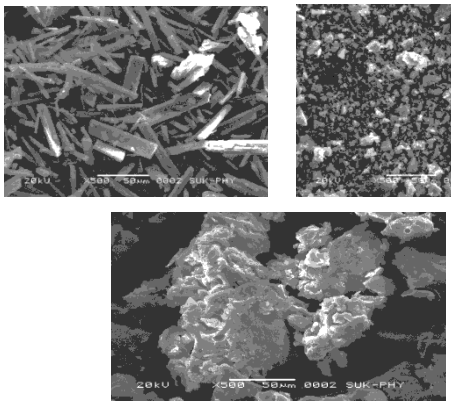


Figure 3: Scnanning Electron Microscopy of Lovastatin, PNG4, Maltodextrin

Table 2: Particle Size Analysis Data For Formulation Batches

Batch no. & Variables	Particle Size (nm)
Pure Drug	304.6nm
F1 [S0 : C200]	248.8nm
F2 [S150 : C200]	227.3nm
F3 [S100 : C100]	267.1nm
F4 [S50: C150]	160.1nm
F5 [S200 : C0]	276.5nm

Table 3: Entrappment Efficiency Data For Formulation

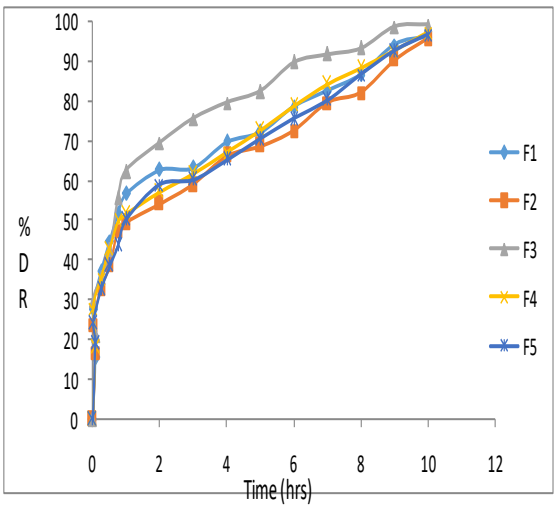
Batch no. & Variables	% EE ± S.D
F1 [S0 : C200]	42.46%±0.513
F2 [S150 : C50]	44.3%±0.577
F3 [S100 : C100]	59.9%±0.671
F4 [S50 : C150]	64.9%±0.578
F5 [S200 : C0]	54.9%±0.515

Table 4: Particle Size (nm) for Formulation Batches:-

Batch no. & Variables	Particle Size (nm)
Pure Drug	304.6nm
F1 [S0 : C200]	248.8nm
F2 [S150 : C50]	227.3nm
F3 [S100 : C100]	267.1nm
F4 [S50: C150]	160.1nm
F5 [S200: C0]	276.5nm

The mean particle sizes of all the hydrated pronisomal formulations are shown in Table 3 which shows that the niosomes composed of span 60 are larger in sizes.Span 60 has longer alkyl and it was reported that surfactants with larger alkyl chains generally give larger vesicles. Increasing cholesterol content content contributed to an increase in hydrophobicity with consequent reduction in vesicle sizes.For niosomes derived metformin hydrochloride proniosomes, entrapment efficiency of formulation PNG4 was found to be approximately 64.9%The length of alkyl chain is higher the permeability and highest entrapment efficiency of drug. As per literature the cholesterol content of formulations decreased and entrapment efficiency of drug is also decreased.

Vesicle size of different proniosomal powder formulations were determined using optical microscopy. It was observed that vesicle size of PNG1 formulation (248.8nm) was largest and vesicle size of PNG4(160.1nm)was smallest because of lesser cholesterol content.From the reported results in literature, [10, 11] it can be concluded that as the concentration of cholesterol increased, hydrophobicity increase which leads to decrease in particle size.As compared to cholesterol, span 60 posses less hydrophobicity due to presence of polar groups. Hence on addition of water, swelling of bilayer takes place which leads to increase in particle size.Increase in concentration of both span 60 and cholesterol results in increasing encapsulation volume which further leads to increase in particle size.



When release rate was compared for all these formulations, the proniosomal formulation exhibits an alkyl chain length- dependent release. Moreover, due to larger vesicle size of span 60 proniosomal formulations PNG4 which acted as barrier in the drug release and the release rate was less in formulations as compare to PNG1, PNG2, PNG3. Also, low release rate for PNG4 high was due to high phase transition of span 60.

CONCLUSION

This study suggests that niosomes formulation can provide consistent and prolonged release of lovastatin from different niosomal formulations. It will lead to sustained action of the entrapped drug that reduce the side effects associated with frequent administration of the drug and potentiate the therapeutic effects of the drug. This may also provide the high absorption inside the lumen and the same may be expected even in blood circulation. The dry granular proniosomes which has been anticipated to provide improved stability as compared to conventional vesicular delivery systems in terms of aggregation, leakage etc. For the better efficacy of the formulation refrigeration of the product is necessary. The future scopes for the work are the microbial as well as in vivo studies.There are different variables which affects on formation of proniosomes that are cholesterol,span 60 which affects on encapsulation efficiency of drug in vesicles so batch PNG4 is gives good results.

Aknowdgement: Every step towards goal needs appreciable extent of self-motivation, inspiration, blessings and support of complimentary factors along with our efforts. Words may be failed to portrait gratefulness of all those, who have been lifted me up to this stage.I take this opportunity to express my heartfelt gratitude to my revered guide. I consider myself most lucky to work under the excellent guidance of **Dr. F. J. Sayyad** Assistance professor of Govt. college of Pharmacy, Karad for her active guidance, innovative ideas, constant inspiration, continuous supervision, valuable suggestions and support to complete this Research work effectively and successfully. I am very much grateful to her for her invaluable guidance.

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