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FORMULATION AND EVALUATION OF VESICULAR DRUG DELIVERY SYSTEM OF MEFENAMIC ACID

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ABSTRACT

The objective of the present investigation was to develop niosomal based delivery system for application of mefenamic acid for treatment of inflammatory condition. The idea was to increase the bioavailability of drugs. Niosomes are known to present a solution to these side effects and the study proved that niosomes of mefenamic acid can provide improved drug bioavailability via sustained release of the drug. Among various formulations, CF7 was found to have a good release pattern and controlled release up to 24 hrs it could be suggested that the developed Pluronic P85 modified mefenamic acid niosomes could act as constant released niosomal carrier.

Key words: Niosomes, mefenamic acid, surfactant, sustained release, Vesicular drug delivery.

1 INTRODUCTION

1.1 Vesicular Drug Delivery System

Conventional chemotherapy for the treatment of intracellular infections is not effective, due to limited permeation of drugs into cells. This can be overcome by use of vesicular drug delivery systems. Encapsulation of a drug in vesicular structures can prolong the existence of the drug in systemic circulation, and perhaps, reduces the toxicity if selective uptake can be achieved. The phagocytic uptake of the systemic delivery of the drug-loaded vesicular delivery system provides an efficient method for delivery of drug directly to the site of infection, leading to reduction of drug toxicity with no adverse effects. Vesicular drug delivery reduces the cost of therapy by improved bioavailability of medication, especially in case of poorly soluble drugs. Vesicles can incorporate both hydrophilic and lipophilic drug and delay drug elimination of rapidly metabolizable drugs, and function as sustained release systems. This system solves the problems of drug insolubility, instability, and rapid degradation.[1.,2]

1.1.1 advantages of vesicular systems

- Efficient method for delivery of drug directly to the site of infection.
- Reduction of drug toxicity with no adverse effects.
- Reduces the cost of the therapy by improved bioavailability of the medication,
- Incorporate both hydrophilic and lipophilic drugs.
- Delay drug elimination of rapidly meatbolizable drugs
- Function as sustained release systems.
- Solves the problems of drug insolubility, instability, and rapid degradation[3].

1.2 Niosomal Drug Delivery System

Targeted delivery of drugs is a challenging task with the use of novel drug delivery systems. Different novel approaches used for delivering drugs include liposomes, microspheres, nanotechnology, micro emulsions, antibody-loaded drug delivery, magnetic microcapsules, implantable pumps and niosomes. Niosomes are formations of vesicles by hydrating mixture of cholesterol and nonionic surfactants. These vesicles are called niosomes. These are formed by self-assembly of non-ionic surfactants in aqueous media as spherical, unilamellar, multilamellar system and polyhedral structures in addition to inverse structures which appear only in non-aqueous solvent. Niosomes and liposomes are active in drug delivery potential and both increase drug efficacy as compared with that of free drug. Niosomes are preferred over liposomes because the former exhibit high chemical stability and economy. These types of vesicles were first reported in the cosmetic industries. Non- ionic surfactants used in formation of niosomes are polyglyceryl alkyl ether, glucosyl dialkyl ether, crown ether, polyoxyethylenealkyl ether, ester-linked surfactants, and steroid-linked surfactants and spans, and tweens series. Niosomes preparation is affected by processes variables, nature of surfactants, and presence of membrane additives and nature of drug to be encapsulated[4,5].

1.2.1 Advantages of niosomes

Use of niosomes in cosmetics was first done by L'Oreal as they offered the following advantages

- The vesicle suspension being water based offers greater patient compliance over oil based systems
- Since the structure of the niosome offers place to accommodate hydrophilic, lipophilic as well as amphiphilic drug moieties, they can be used for a variety of drugs.
- The characteristics such as size, lamellarity etc. of the vesicle can be varied depending on the requirement.
- The vesicles can act as a depot to release the drug slowly and offer a controlled release at a particular site.
- They are osmotically active and stable.
- They increase the stability of the entrapped drug.
- Handling and storage of surfactants do not require any special conditions.
- Can increase the oral bioavailability of drugs.
- Can enhance the skin penetration of drugs.
- They can be used for oral, parenteral as well topical use.
- The surfactants are biodegradable, biocompatible, and non- immunogenic.

They improve the therapeutic action of the drug by protecting it from the biological environment and restricting effects to target cells, thereby reducing the clearance of the drug from the circulation[6].

2 METHODS/ TECHNIQUES OF PREPARATION OF NIOSOMES

2.1 Ether Injection Method

In this method a lipid solution in diethyl ether is slowly introduced into warm water typically the lipid mixture is injected into an aqueous solution of the material to be encapsulated (using syringe type infusion pump) at 55-65 oC and under reduced pressure. Vaporization of ether leads to the formation of single layered vesicles (SLVs) depending upon the conditions used, the diameter of vesicles varies. The particle size of the niosomes formed depends on the conditions used, and can range anywhere between 50- 1000μm[7].

2.2 Thin Film Hydration Technique (Hand Shaking Method)

In this method a mixture of the vesicle forming agents such as the surfactant and cholesterol are dissolved in a volatile organic solvent such as diethyl ether or chloroform in a round bottom flask. The organic solvent is removed at room temperature using a rotary evaporator, which leaves a thin film of solid mixture deposited on the walls of the flask. This dried surfactant film can then be rehydrated at room temperature using the aqueous phase, with gentle agitation to yield multilamellar niosomes. The multilamellar vesicles thus formed can further be processed to yield unilamellar niosomes or smaller niosomes using sonication, microfluidization or membrane extrusion techniques[8,9].

2.3 Reverse Phase Evaporation

The novel key in this method is the removal of solvent from an emulsion by evaporation. Water in oil emulsion or inverted micelles are formed by bath sonication of a mixture of two phases, and then the emulsion is dried to a semi-solid gel in a rotary evaporator under reduced pressure. The next step is to bring about the collapse of certain portion of water droplets by vigorous mechanical shaking with a vortex mixture. In these circumstances, the lipid monolayer, which encloses the collapse vesicles, is contributed to adjacent intact vesicles to form the outer leaflet of the bilayer of large unilamellar niosomes. The vesicles formed are unilamellar and have a diameter of 0.5 μm. Briefly, method involves the creation of a solution of cholesterol and surfactant (1:1 ratio) in a mixture of ether and chloroform. An aqueous phase containing the drug to be loaded is added to this, and the resulting two phases are sonicated at 4-5 °C. A clear gel is formed which is further sonicated after the addition of phosphate buffered saline (PBS). After this the temperature is raised to 40 °C and pressure is

niosome suspension which can be diluted with PBS and heated on a water bath at 60 °C for 10 min to yield niosomes[10].

2.4 Trans Membrane Ph Gradient (Inside Acidic) / Drug Uptake Process (Remote Loading)

In this method similar to the hand shaking method, a solution of surfactant and cholesterol is made in chloroform. The solvent is then evaporated under reduced pressure to get a thin film on the wall of the round bottom flask, similar to the hand shaking method. This film is then hydrated using citric acid solution (300mM, pH 4.0) by vortex mixing. The resulting multilamellar vesicles are then treated to three freeze thaw cycles and sonicated. To the niosomal suspension, aqueous solution containing drug is added and vortexed. The pH of the sample is then raised to 7.0-7.2 using 1M disodium phosphate (this causes the drug which is outside the vesicle to become non- ionic and can then cross the niosomal membrane, and once inside it is again ionized thus not allowing it to exit the vesicle). The mixture is later heated at 60 °C for 10 min to give niosomes[11].

2.5 The "Bubble" Method

It is a technique which has only recently been developed and which allows the preparation of niosomes without the use of organic solvents. The bubbling unit consists of a round bottom flask with three necks, and this is positioned in a water bath to maintain the temperature. Water-cooled reflux and thermometer is positioned in the first and second neck, while the third neck is used to supply nitrogen. Cholesterol and surfactant are dispersed together in a buffer (pH 7.4) at 70 °C. This dispersion is mixed for a period of 15 sec with high shear homogenizer and immediately afterwards, it is bubbled at 70 °C using the nitrogen gas to yield niosomes[12,13].

2.6 Formation of Niosomes From Proniosomes

To create proniosomes, a water soluble carrier such as sorbitol or maltodextrin is first coated with the surfactant. The coating is done by preparing a solution of the surfactant with cholesterol in a volatile organic solvent, which is sprayed onto the powder of sorbitol kept in a rotary evaporator. The evaporation of the organic solvent yields a thin coat on the sorbitol particles. The resulting coating is a dry formulation in which a water soluble particle is coated with a thin film of dry surfactant. The niosomes can be prepared from the proniosomes by adding the aqueous phase with the drug to the proniosomes with short agitation at a temperature greater than the mean transition phase temperature of the surfactant[14].

2.7 Microfludization

This is a recent technique to prepare small MLVS. A microfludizer is used to pump the fluid at a very high pressure (10,000 psi) through a 5 µm screen. Hereafter; it is forced along defined micro channels, which direct two streams of fluid to collide together at right angles, thereby affecting a very efficient transfer of energy. The cholesterol can be introduced into the fluidizer. The fluid collected can be recycled through the pump until vesicles of spherical dimensions are obtained. This results in greater uniformity, small size and better reproducible niosomal vesicles are obtained[15].

3 COMPONENTS OF NIOSOMES

3.1 Non-Ionic Surfactants

The non-ionic surfactants orient themselves in bilayer lattices where the polar or hydrophobic heads align facing aqueous bulk (media) while the hydrophobic head or hydrocarbon segments align in such a way that the interaction with the aqueous media would be minimized. To attain thermodynamic stability, every bilayer folds over itself as continuous membrane i.e. forms vesicles so that hydrocarbon /water interface remains no more exposed. Mainly following types of non-ionic surfactants are used for the formation of niosomes:- Alkyl ethers: L'Oreal described some surfactants for the preparation of niosomes containing drugs/chemicals as Surfactant-I (Mol.Wt.473) is C16 monoalkyl glycerol ether with average of three glycerol units. Surfactant-II (Mol.Wt.972) is diglycerol ether with average of the seven glycerol units. Surfactant III (Mol.Wt.393) is ester linked surfactant. Other than alkyl glycerol, alkyl glycosides and alkyl ethers bearing polyhydroxyl head groups are also used in formulation of niosomes. Alkyl esters: Sorbitan esters are most preferred surfactant used for the preparation of niosomes amongst this category of surfactants. Vesicles prepared by the polyoxyethylene sorbitan monolaurate are relatively soluble than other surfactant vesicles. For example polyoxyethylene (polysorbate60) has been utilized for encapsulation of diclofenac sodium. Alkyl amides: Alkyl amide (e.g. galactosides and glucosides) have been utilized to produce niosomal vesicles. Fatty acid and amino acid compounds: Long chain fatty acids and amino acid moieties have also been used in some niosomes preparation[16,17].

3.2 Cholesterol

Sterols are important components of the cell membrane and their presence in membrane affect the bilayer fluidity and permeability. Cholesterol is a sterol derivative, which is mainly used for the formulation of niosomes. Although it may not show any role in the formation of bilayer, its importance in formation of niosomes and manipulation of layer characteristics cannot be discarded. In general, incorporation of cholesterol affect properties of niosomes like membrane permeability, rigidity, encapsulation efficiency, ease of rehydration of freeze dried niosomes and their

toxicity. It prevents the vesicle aggregation by the inclusion of molecules that stabilize the system against the formation of aggregates by repulsive or electrostatic forces that leads to the transition from the gel to the liquid phase in niosome systems. As a result of this, the niosome become less leaky in nature[18,19].

3.3 Charged Inducer

Some charged inducer are added to niosomes to increase stability of niosomes by electrostatic repulsion which prevents coalescence. The negatively charged inducer used are diacetyl phosphate (DCP) and phosphotidic acid. Similarly, stearylamine (STR) and stearyl pyridinium chloride are the well known positively charged inducer used in niosomal preparations. These charged inducer are used mainly to prevent aggregation of niosomes. Only 2.5-5 mol percentage concentration of charge molecules is tolerable because high concentration can inhibit the niosomal formation[20].

4 METHODOLOGY

4.1 Pre-Formulation Studies

Pre-formulation can be defined as an investigation of physical and chemical properties of a drug substance alone. The overall objective of pre-formulation studies is to generate information that are useful to the formulator in developing stable and bio available dosage forms.

4.2 Solubility Studies

An excess of drug is suspended in 100 ml of dissolution medium containing various concentrations of solvents in stopper flask and equilibrated by intermittent shaking for 72 hrs maintained at 37±20C. The solution is filtered through whattman filter paper. A portion of filtrate is diluted suitably and analyzed by UV spectroscopy[21].

4.3 Drug- Excipients Compatibility Studies

4.3.1 FT-IR spectrophotometric analysis

FTIR study was done as a part of preformulation study for the selection of excipients and to check compatibility of the drug with other excipients. The potassium bromide pellets were prepared on KBr press. To prepare the pellets the solid powder sample were grounded together in a mortar with 100 times quantity of KBr. The finely grounded powder was introduced into a stainless steel die. The powder was pressed in the die between polished steel anvils at a pressure of about 10tf/cm^2. For liquid samples thin film of sample liquid is made on pellet. The spectras were recorded over the wave n0 of 4000 cm $^{-1}$ to 400 cm $^{-1}$.

The IR spectra of mefenamic acid and physical mixture of mefenamic acid and polymers (1:1) were taken in the range of 400-4000cm^{-1}.showed the following characteristic features; broad band O-H stretching at 3296.15, C−O stretching at 1268.09 cm^{-1}, N−H deformation at 1587.48 cm^{-1}, CH3 stretching at 2965.71 cm^{-1}. Powder mixture of mefenamic acid and excipients showed that there was no loss of the distinctive functional peaks of metoprolol succinate. Thus, there was not any interaction between the mefenamic acid and excipients.

Table-1: Solubility of prodrugs of mefenamic acid

Pro drug	Dil. HCl	Dil. NaOH	Dil. KOH	Ether	H_2O	MeoH	Chloroform	PBS PH7.4
MA	+++	- -	- -	- -	- -	+++	- -	+++

Insoluble = -- Sparingly soluble = ++ Soluble = +++

4.4 Preparation of Niosomes by Conventional Thin Film Hydration Method

Mefenamic acid loaded niosomes were prepared by thin film hydration technique by using span 60, different grade Pluronic co-polymeric surfactants (L64, P85 and F127), and cholesterol ratios (1 :1:1, 1:2:1 and 1: 3:1). Accurately weighted quantities of drug, surfactants, co-polymeric surfactants and cholesterol were taken to give the desired ratio and were dissolved in 10 ml of chloroform in a round bottom flask and 5 mg of Dicalcium phosphate was added to the above mixture. The solvent mixture was evaporated in a rotary flash evaporator at rotate 100 rpm until a smooth, dry lipid film was obtained followed by introducing it under high vacuum through vacuum pump for at least three hours for removal of residual content of chloroform. Further flask was kept in vacuum desiccators overnight for complete removal of chloroform. Then dry lipid film was hydrated with 5 ml of phosphate buffer saline pH 7.4 at room temperature for a period of 15 min hour until the formation of niosomes[22].

Table-2: Composition of mefenamic acid loaded niosomes

Ingredients	CF1	CF2	CF3	CF4	CF5	CF6	CF7	CF8	CF9
Mefenamic acid (mg)	120	120	120	120	120	120	120	120	120
Span 60 (mg)	50	50	50	50	50	50	50	50	50
Pluronic L64 (mg)	50	100	150	-	-	-	-	-	-
Pluronic F127 (mg)	-	-	-	50	100	150	-	-	-
Pluronic P85 (mg)	-		-	-	-	-	50	100	150
Cholesterol	50	50	50	50	50	50	50	50	50

(mg)									
Dicetyl phosphate (mg)	5	5	5	5	5	5	5	5	5
Chloroform (ml)	10	10	10	10	10	10	10	10	10

5 EVALUATION PARAMETERS OF NIOSOMES

5.1 Estimation of Percentage of Entrapment Efficiency

Entrapment efficiency of the mefenamic acid niosomes were done by separating the unentrapped drug by dialysis method and the drug remained entrapped in niosomes was determined by complete vesicle disruption using 0.1%w/v Triton X- 100 and analyzed UV spectrophotometrically for the drug content after suitable dilution with phosphate buffer saline pH 7.4 and filtered through whatmann filter paper. The filtrate was measured spectrophotometrically using phosphate buffer saline pH 7.4 and triton X-100 mixture as blank. The percentage of drug encapsulation efficiency was calculated by the following equation[23]

% Entrapment efficiency = Amount of entrapped drug/Total amount of drug ×100%

5.2 Estimation of Percentage of Drug Content

The percentage of drug content in the formulation was determined by taking niosomal dispersion equivalent to 5mg in a 10 ml of volumetric flask and made the volume up to required volume using phosphate buffer pH 7.4. After that 1ml of the solution was withdrawn and diluted to 10ml using phosphate buffer saline pH7.4, the absorbance of the solutions were measured in the UV-Visible Spectrophotometer using plain niosomes as a blank and the percentage of drug content was calculated. The drug content is calculated following formula[24]

% Drug content = Sample Absorbance/ Standard Absorbance× 100

Table-3: % of Entrapment efficiency of niosomal formulations (CF1-CF9)

Formulation code	**Span6: Co-polymeric surfactant: Cholesterol ratio**	**% Entrapment efficiency***	**% of Drug Content***
CF1	1:1:1	61.98±0.54	97.99±0.68
CF2	1:2:1	60.90±0.37	98.32±0.21
CF3	1:3:1	45.64±0.32	98.87±0.62
CF4	1:1:1	75.52±0.63	98.53 ±0.32
CF5	1:2:1	71.68±0.72	98.37±0.13
CF6	1:3:1	68.78±0.48	98.67 ±0.41
CF7	1:1:1	90.03±0.31	99.01±0.60
CF8	1:2:1	78.90±0.80	98.12±0.53
CF9	1:3:1	70.54 ±0.43	98.51±0.36

*Mean ± SD, (n=3)

5.3 Vesicle Size Distribution Measurements and Surface Charge

The vesicle size and surface charge of the niosome was determined by measuring the electrophoretic mobility of the niosomal particles using a zeta sizer (Malvern Instruments ltd, UK) equipped with a 5 mW helium neon laser with a wavelength output . Glassware was cleaned of dust by washing with detergent and rinsing twice with water for injections. Measurements of size analysis were made at 25˚C at an angle of 90˚. Polydispersity index (PI) was determined as measures of homogeneity. Values were obtained from the printed report of Malvern zeta sizer which includes the present intensity in terms of size distribution of niosomes and their respective sizes. Small values of PI indicate a homogeneous population while high values indicate heterogeneity The zeta potential of the formulations CF7 was found to -42.01±0.5 mV this is due to higher repulsion, the precipitation was retarded for CF7 formulation. So evenly distributed niosomal suspension were obtained formulation CF7 would yield better stable formulations. The mefenamic acid niosomes size was varied between 240.5±2.13 nm and 318.4±2.32 nm. Results shown that as the amount of co-polymeric surfactant increased from 1:1 to 1:3, the vesicle size also increased by the same ratio. This can be explained that at higher copolymer concentration was increased the viscosity of polymer solution, thereby producing bigger vesicle size, which were later hardened due to the evaporation of chloroform. Among all the nine formulations of Pluronic P85 modified niosomal formulations CF7 to CF9 constantly increased in size. Formulation CF7 containing equal ratio of Span60 and Pluronic P85 produced optimum size of niosomes (240.5±2.13 nm)[25]

Table-4: Vesicle size and Zeta potential analysis of formulations (CF1-CF9)

Formulation code	Vesicle Size (nm)*	PDI*	Zeta Potential (mV)*
CF1	280.4±1.74	0.22±0.1	-29.2±1.8
CF2	295.0±1.50	0.23±0.2	-27.6±0.7
CF3	306.5±2.21	0.18±0.1	-32.5±1.5
CF4	259.0±1.94	0.19±0.2	-27.8±0.4
CF5	280.0±1.18	0.20±0.1	-30.1±0.5
CF6	318.4±2.32	0.21±0.2	-28.5±1.2
CF7	240.5±2.13	0.24±0.2	-42.01±0.5
CF8	269.0±1.94	0.27±0.5	-39.2±0.8
CF9	290.4±3.92	0.23±0.3	-32.5±0.4

5.4 In-Vitro Release Studies of The Formulations

The in-vitro release of mefenamic acid niosomes was carried out using open end cylinder method. One end of the tube is tightly covered with a Himedia dialysis membrane (MW-12,000-14,000 Da). The niosomal suspension (5 ml) was placed over the membrane in the donar chamber. The donar chamber is then lowered to the vessels of the glass beaker containing 100 ml of phosphate buffer saline pH 7.4, which act as a receptor compartment so that the dissolution medium outside and the vesicles preparation inside were adjusted at the same level. The release study was carried out at 37±0.50C, and the stirring shafts were rotated at a speed of 50 rpm. 5ml of samples were withdrawn periodically at predetermined time intervals. Every withdrawal was followed by replacement with fresh medium to maintain the sink condition. The withdrawn samples were diluted and analyzed for the drug content using UV spectrophotometer at 288nm. Phosphate buffer saline was used as blank. The mefenamic acid release pattern was observed for 24hrs[26].

The in-vitro release profile of drug from niosomes clearly indicates that the concentration of co-polymers slows the release of mefenamic acid from niosomes. At the end of 24 hrs, in-vitro drug relased from formulations CF1 to CF9 was found to be 82.27 ± 0.94% to 99.85 ± 1.04%.in phosphate buffer saline pH7.4. The 25 to 34% of drug release was observed upto 4hrs, followed by slowing down and reaching a constant slow drug release observed after 4hrs. The formulation containing both Span 60 and Pluronic P85 ratio of 1:1, 1:2 and 1:3 showed maximum in-vitro release of 99.85 ± 1.04 %, 94.47 ± 0.54 % and 92.11 ± 0.57 % for 24 hrs. The cumulative percentage release at the end of 24 hrs was below 100% for all the dosage forms, this may be due to the relatively slow erosion of the niosomes based on the Pluronic co-polymeric surfactant concentration. Among various formulations, CF7 was found to have a good release pattern and controlled release up to 24 hrs it could be suggested that the developed Pluronic P85 modified mefenamic acid niosomes could act as constant released niosomal carrier it was selected as the optimized formulation and used for the further studies.

Table-5: Cumulative drug release of drug loaded niosomal formulations (CF1-CF9)

Time in hrs	**CF1**	**CF2**	**CF3**	**CF4**	**CF5**	**CF6**	**CF7**	**CF8**	**CF9**
0	0	0	0	0	0	0	0	0	0
0.5	12.65 ±1.10	10.09 ±0.55	8.95± 0.33	14.45 ±0.11	11.30 ±0.08	9.30± 0.46	13.34 ±0.16	15.34 ±0.63	11.14 ±1.04
1	16.82 ±0.84	14.11 ±1.14	11.43 ±0.85	19.81 ±0.26	14.81 ±0.47	13.58 ±0.72	17.72 ±0.50	20.65 ±0.38	15.47 ±0.01
2	21.53 ±0.26	19.71 ±0.72	17.54 ±0.22	26.46 ±0.78	19.62 ±0.35	18.29 ±0.61	25.20 ±1.04	26.70 ±0.49	22.62 ±0.60
3	25.12 ±0.60	23.14 ±1.13	21.80 ±1.26	30.22 ±0.33	24.57 ±0.66	22.74 ±1.33	29.88 ±0.29	30.35 ±0.02	26.79 ±0.73
4	30.33 ±0.85	28.35 ±0.67	25.04 ±1.39	34.36 ±1.41	29.43 ±0.34	26.90 ±0.93	32.49 ±0.38	33.87 ±0.93	30.10 ±0.50
6	36.10 ±0.62	36.13 ±0.75	30.48 ±0.86	40.21 ±1.09	36.20 ±0.73	34.50 ±0.22	40.62 ±0.71	40.92 ±0.72	35.16 ±0.38
8	41.61 ±0.61	39.64 ±1.26	35.62 ±0.73	45.55 ±0.58	41.51 ±1.06	39.39 ±0.70	47.37 ±0.37	46.45 ±0.53	42.06 ±0.90
10	49.37 ±0.30	46.66 ±1.24	41.92 ±0.65	52.03 ±0.11	47.92 ±1.73	45.91 ±0.27	54.91 ±0.64	53.10 ±0.32	49.28 ±0.82
12	55.82 ±0.38	55.87 ±0.08	47.71 ±1.13	58.16 ±0.43	53.48 ±0.63	51.92 ±1.21	62.27 ±0.42	60.37 ±1.41	55.69 ±1.03
18	73.55 ±0.24	71.76 ±0.12	65.03 ±0.37	75.49 ±0.51	71.94 ±0.31	71.08 ±0.35	82.53 ±0.46	79.28 ±0.37	75.52 ±0.02
24	89.18 ±1.2	87.91 ±0.62	82.27 ±0.94	91.29 ±0.18	89.82 ±0.22	86.75 ±0.65	99.85 ±1.04	94.47 ±0.54	92.11 ±0.57

Mean ± SD, (n=3)

6 CONCLUSIONS

The determined parameters concludes that the zeta potential of the formulations CF7 was found to -42.01±0.5 mV this is due to higher repulsion, the precipitation was retarded for CF7 formulation. So evenly distributed niosomal suspension were obtained formulation CF7 would yield better stable formulations. The mefenamic acid niosomes size was varied between 240.5±2.13 nm and 318.4±2.32 nm. The cumulative percentage release at the end of 24 hrs was below 100% for all the dosage forms, this may be due to the relatively slow erosion of the niosomes based on the Pluronic co-polymeric surfactant concentration.Among various formulations, CF7 was found to have a good release pattern and controlled release up to 24 hrs it could be suggested that the developed Pluronic P85 modified mefenamic acid niosomes could act as constant released niosomal carrier. The niosomal delivery systems provides solubility and sustain release of drugs.

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