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FORMULATION AND EVALUATION OF LACIDIPINE POLYMERIC MICELLES

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ABSTRACT

The Objective of the study was to formulate and evaluate Polymeric micelles (PMs) containing Lacidipine, an Antihypertensive agent by Thin Film Hydration Technique. Historical data design Suggested that the amounts of 4mg of Lacidipine and 60mg of pluronic F127 and particle size DL and EE obtained for the optimized formulation was 15nm, 20.23% and 94.01% respectively. Scanning Electron Microscopy image showed uniform sized spherical micelles. Percentage cumulative Drug release from the Optimum formulation (F7) was 98.24% for 12hrs. The Release kinetics for most of the formulations followed korsmeyer peppas model and followed Non Fickian diffusion mechanism and the optimsed formulation F7 was stable for 3 months. It can be concluded that Lacidipine PMs formulation has significantly showed prolonged release of the drug up to 12hrs and the Drug was formulated successfully into Polymeric micelle forms by Thin film hydration technique.

KEYWORDS

Lacidipine, Encapsulation efficiency and Thin Film Hydration Technique.

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INTRODUCTION

One of the most challenging aspects of the drug development is its drug solubility and oral bioavailability various approaches are available, Apart from those, there are several other Nanotechnology approaches among them one is polymeric micelles (PMs). Polymeric micelles are nanocarriers (10nm-100nm) which possess a hydrophobic core entrapping the hydrophobic drug and not exposing the drug to aqueous environment and hydrophilic shell is present which increases solubility and stability. Polymeric micelles (PMs) are main used for increasing the solubility of poorly

soluble drugs and they are having excellent properties like low toxicity, stability in plasma, increase solubility of poorly soluble drugs and controlled release. The drug used in the present study was Lacidipine belonging to the category of calcium channel blockers drugs. It is a recent and highly visa selective third generation dihydropyridine calcium antagonist. That can be administered once daily. It possess one of the highest known membrane partition coefficient, which allows it to position more deeply within the vascular cell membrane lipid bilayer. Lacidipine decreases arterial smooth muscle contractility and subsequent vasoconstriction by inhibiting the influx of calcium ions through L-type calcium channels.

MATERIALS

Lacidipine was obtained from KP Labs and PF127 (Polaxomer 407) was obtained from Sigma Aldrich, Bengaluru and were used as received. All other chemicals used were of Laboratory grade.

Preparation of Lacidipine (LCDP) Loaded PMs

Lacidipine Loaded PMs were prepared by thin-Film hydration method. The Drug and the block polymer were taken in the ratio 1:20, 1:10 and 1:5 were dissolved in acetone. It was rotate for about 30min. in rotary evaporator at 50^{o}C. Vacuum was applied until a thin film was formed Required volume of pH 7.4 phosphate buffer was added to the film to form drug loaded polymeric micelle at 60°C for 30 min. Un incorporated drug was filtered using 0.2µm cellulose Nitrate membrane, followed by Lyophilization.

Evaluation of LCDP micelles

Particle size determination

The particle size, poly dispersity index (PDI) and zeta potential of diluted formulation were determined using a Zetasizer 3000 (Malvern Instruments Ltd, Japan).

Determination of Encapsulation Efficiency

Lyophilised micelles were taken and diluted with 10ml of methanol: water (1:1) and sonicated for 30min. to promote swelling and drug to be encapsulated. The solution was filtered using 0.2µm filter and absorbance was measured at 232nm.

***In vitro* Release studies**

The Drug release studies were performed by Dialysis method. After Dialysis method the filtrate was taken and UV-absorbance was measured at 232nm.

Kinetic analysis of *In vitro* drug release data

In order to determine drug release pattern the *in vitro* drug release data were fitted into Zero order, First order, Higuchi and Korsmeyer peppas model and the release exponent ‘n’ to describe the drug release mechanism.

RESULTS AND DISCUSSION

Fourier Transform Infrared spectroscopy (FTIR) Studies

The FTIR studies were conducted for Drug and Pluronic F127 to check the compatibilities between them. From the FTIR studies no new peaks were observed apart from the peaks of the existing formulation indicating that there are no in compatibilities among them.

Differential scanning Colorimetry (DSC) studies

From the DSC studies the thermo gram of Drug was found to be 174^{o} - 175^{o}C which is equal to melting point of Lacidipine indicating the purity of the drug.

Evaluation of LCDP PMs

Particle size, PDI and Zeta potential Determination

The Particle size, PDI will be determined by zetasizer 3000 and the results are tabulated in the table among 9 formulations F7 shows lowest particle size of 15.0nm and highest zeta potential of about -25.68mV indicating higher stability when compared to other formulations. The polydispersity value was less than 1 in all the formulations indicating narrow distribution of particles. Therefore it can be concluded that LCDP Polymeric micelles have shown homogenous size distribution.

Determination of DL and EE

Drug loading efficiency decreased as the concentration increases which may be due to aggregation and EE of micelles also increases with increase in concentration and vice versa.

Scanning Electron Microscopy

SEM photographs revealed that there are spherical without any deformations indicating that the polymeric micelles were uniform in size.

***In vitro* Drug release studies**

Drug Release studies were extended up to 12 hours for all the formulations among them F7 showed maximum drug release i.e., 98.24% at the end of 12th hour when compared to other Formulations. The drug release showed sustained release in polymeric micelle form when compared to pure form (1hr).

Kinetic analysis data of polymeric LCDP Micelles

The drug release mechanism showed korsmeyer peppas model and the 'n' value was greater than 0.45 indicating that the release mechanism follows non-fickian diffusion mechanism for most of the formulations.

Stability studies

Stability studies were performed for optimized formulation F7 according to ICH guidelines by storing at 30°C/65% RH, 40°C/75% RH and 25°C/60% RH for 90 days. These samples were analysed for any changes in physical appearance and dug content by UV method at 232nm during this time interval.

Table No.1: Formulation chart of LCDP Polymeric micelles

S.No	Formulation code	LCDP(mg)	Pluronic F127 (mg)	Acetone (ml)	pH 7.4 PBS (ml)
1	F1	4	40	5	10
2	F2	6	40	5	10
3	F3	8	40	5	10
4	F4	4	50	5	10
5	F5	6	50	5	10
6	F6	8	50	5	10
7	F7	4	60	5	10
8	F8	6	60	5	10
9	F9	8	60	5	10

Table No.2: Evaluation Parameters

S.No	Formulation code	Particle size (nm)	Zeta potential (mV)	PDI	DL(%)±SD*	EE(%)±SD*
1	F1	23.25	-15.73	0.537	13.62±0.22	81.21±2.17
2	F2	24.13	-14.21	0.638	12.54±0.26	74.51±1.15
3	F3	24.37	-13.18	0.691	10.31±0.24	66.07 ±0.98
4	F4	16.31	-16.51	0.312	15.98±0.19	85.93±2.23
5	F5	16.53	-18.81	0.387	14.04±0.15	79.63±1.23
6	F6	16.75	-19.13	0.411	13.51±0.25	73.23±1.11
7	F7	15.0	-25.68	0.171	20.23±0.20	94.01±3.83
8	F8	15.63	-23.13	0.191	19.17±0.18	91.27±3.21
9	F9	16.03	-20.01	0.213	16.72±0.19	88.31±2.95

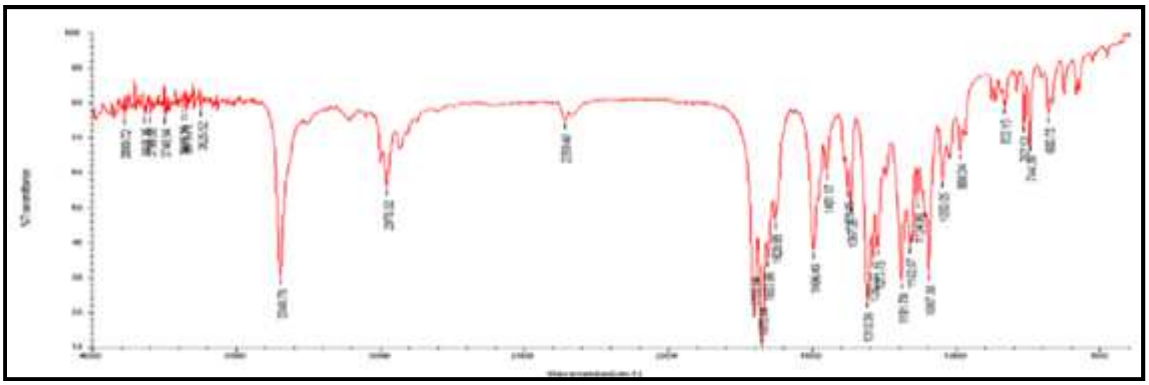

Figure No.1: Fourier transform infrared spectrum of pure drug LCDP and with Pluronic F127

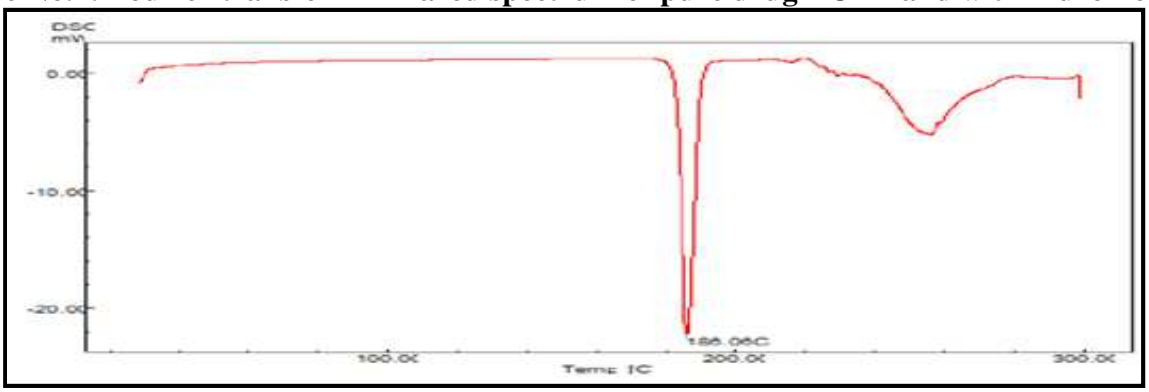

Figure No.2: Differential scanning colorimetric thermogram of LCDP Polymeric micelles

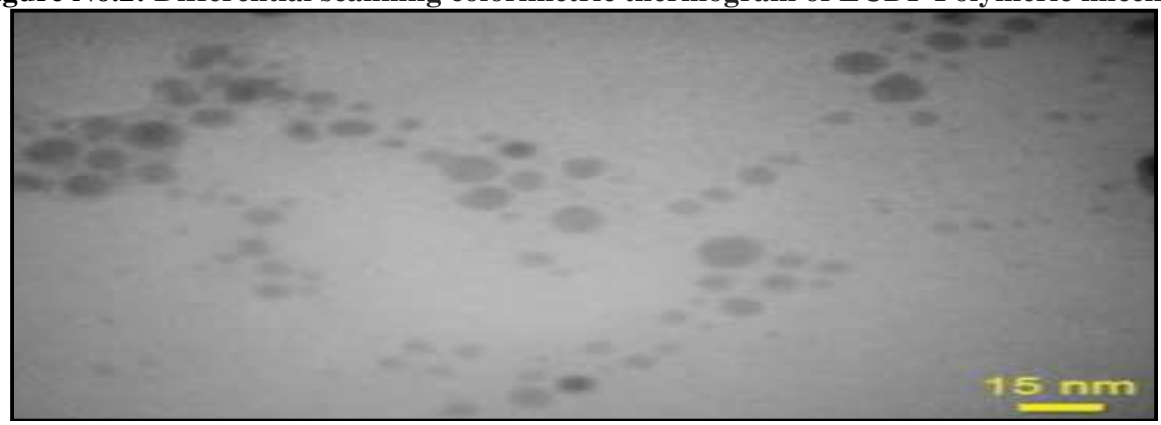

Figure No.3: SEM analysis of Optimized formulation

CONCLUSION

The FTIR spectra and DSC thermogram indicated that drug and polymer used were compatible. Thin film hydration technique was successfully used for the preparation of LCDP PMs. LCDPS, PF127 and their ratios have a great influence on particle size, DL and EE as indicated by historical data. The experimental values were in close agreement with the predicted response, indicating adequate fitting, and validation of formula generated by constrained optimization.

Particle size, Zeta potential, DL and EE of all the formulations within the range of 15.0,-24.37, -15.73 - 25.68, 10.31±0.24 - 20.23±0.20, 66.07 ±0.98 - 94.01±3.83 respectively. The release kinetics revealed that the drug release follows korsmeyer peppas model and non-Fickian diffusion mechanism. Optimized formulation showed no significant changes after 90 days indicating that the product is stable.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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