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Design and Evaluation of Fluvoxamine Nanoparticles by Emulsification Method

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ABSTRACT

Nanoparticulate carriers may provide a better therapeutic output by targeting drugs specifically to their site of action and by improving the pharmacokinetic profile of effective drugs low bioavailability and low halflife. In present investigation Nanoparticles were prepared by emulsification method. New Nanoparticulate drug carrier that combines the benefits of polymeric nanoparticles to enhance the bioavailability of drugs, retain the drug in the absorption site more than the half life of the drug, reduce dose frequency, toxicity and patient compliance.Total nine nanoparticles formulations was formulated using Ethyl cellulose, Eudragit RS 100 & Eudragit RL 100.Estimation of Fluvoxamine was carried out spectrophotometrically at 245nm. The Nanoparticles were evaluated for parameters such as drug content uniformity, scanning electron microscopy, particle size analysis, zeta potential, in-vitro release, Drug release kinetics Form the drug excipient compatibility studies we observe that there are no interactions between the pure drug (Fluvoxamine) and optimized formulation (Fluvoxamine+ excipients) which indicates there are no physical changes. Zeta potential value for the optimized formulation (F6) was found to be within the acceptable limits. Average particle size of Nanoparticles of optimized formulations (F6) was found to be 180nm. From the invitro studies we can say that formulation F6 shows best drug release of 98.05% within 12 hrs to release the drug.

Key words: Fluvoxamin, Ethyl cellulose Eudragit RS 100, Eudragit RL 100 were obtained from sigma Aldrich Mumbai.

Introduction

Oral drug delivery is the most favoured manner of drug delivery for achieving mutually systemic and local therapeutic effects. But a variety of problems are also related with the conventional oral dosage forms, that it is frequently essential to take several times per day to retain the concentration of administered drug within the therapeutically effective range which results in a fluctuated drug level and consequently undesirable toxicity and poor efficiency. So to overcome such problems associated with conventional oral dosage form, the idea of controlled drug delivery systems was introduced[1-4].

The real challenge in the development of a controlled drug delivery system is not just to control the drug release, also to extend the existence of the dosage form in the absorption site until all the drug is completely released in the preferred period of time [5-8].

Continuous release of the drug involves polymers that release the drug at a controlled manner due to the degradation of polymer over time and it can be achieved by using drug carrying polymer.

In the present work, our aim was to develop a new nanoparticulate drug carrier that combines the benefits of chitosan nanoparticles and cyclodextrins to enhance the bioavailability of drugs, retain the drug in the absorption site more than the half life of the drug, reduce dose frequency, toxicity and patient compliance.

The prefix "nano" comes from the ancient Greek *vavoc* through the Latin *nanus* meaning *very small*. Nanotechnology defined as design characterization, production and applications of structures, devices and systems by controlling shape and size at nanometer scale. According to International System of Units (SI) nanotechnology is typically measured in nanometers scale of 1 billionth of a meter (1nm corresponding to 10-9 m) referred as the „tiny science". At this small size molecules and atoms work differently, behave as a whole unit in terms of its properties and transport, provide a variety of advantages. Nanoparticles (NPs) are defined as particulate dispersions or solid particles drug carrier that may or may not be biodegradable. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. The term nanoparticle is a combined name for both nanosphares and nanocapsules. Drug is confined to a cavity surrounded by a unique polymer membrane called nanocapsules, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed. Where conventional techniques reaches their limits, nanotechnology provides opportunities for the medical applications [8-12].

MATERIALS AND METHODS

Fluvoxamine were obtained from spectrum labs Mumbai Ethyl cellulose were obtained from Signet Chemical Corp., Mumbai Eudragit RS 100 , Eudragit RL 100 were obtained from sigma Aldrich Mumbai.

Method of Preparation of Nanoparticles:

Fluvoxamine Nanoparticles were prepared by emulsification method. In this method Polymer was dissolved in organic solvent (methanol). Drug is dispersed in this solution. Then this mixuture emulsified in an aqueous phase containing surfactant (polyvinyl alcohol) make an oil in water emulsion by using mechanical stirring, or sonication. After formation of emulsion the organic solvent evaporate by increased the temperature and reduced pressure with continuous stirring.

Formulation code	Drug:polymer	Ratios	Concentartion of PVA (%w/v)
F1	Drug : Ethyl cellulose	1:1	2
F2	Drug : Ethyl cellulose	1:2	2
F3	Drug : Ethyl cellulose	1:3	2
F4	Drug : Eudragit RS 100	1:1	2
F5	Drug : Eudragit RS 100	1:2	2
F6	Drug : Eudragit RS 100	1:3	2
F7	Drug : Eudragit RL 100	1:1	2
F8	Drug : Eudragit RL 100	1:2	2
F9	Drug : Eudragit RL 100	1:3	2

***In vitro* drug release study:** In vitro Release studies Drug release from nanoparticles in-vitro was carried out by dialysis method (Dialysis membrane-60 HI MEDIA, Mumbai). The donor chamber filled with 5ml of nanoparticles suspension, whereas reservoir chamber containing the phosphate buffer pH 7.4. This total setup was placed on a rotary shaker rotating at 50 rpm at 37°C ± 0.5°C. In pre determined time intervals the content of receiver chamber was withdrawn and replaced with equal volume of fresh phosphate buffer, the amount of Fluvoxamine that diffused into the receiver chamber was quantified by UV- spectrophotometer at 232 nm.

Drug and Excipients compactability studies:

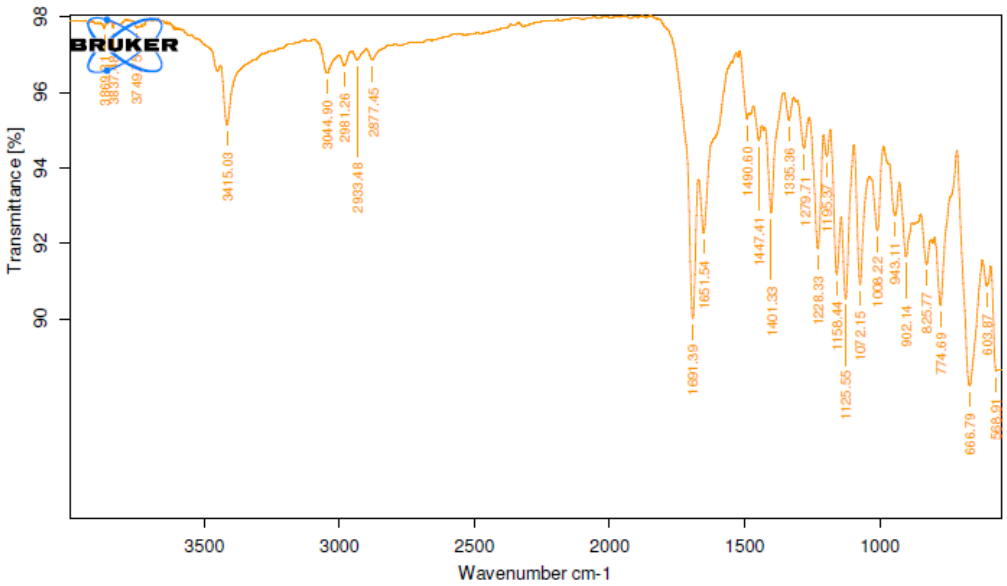


Fig: FTIR of Pure Drug

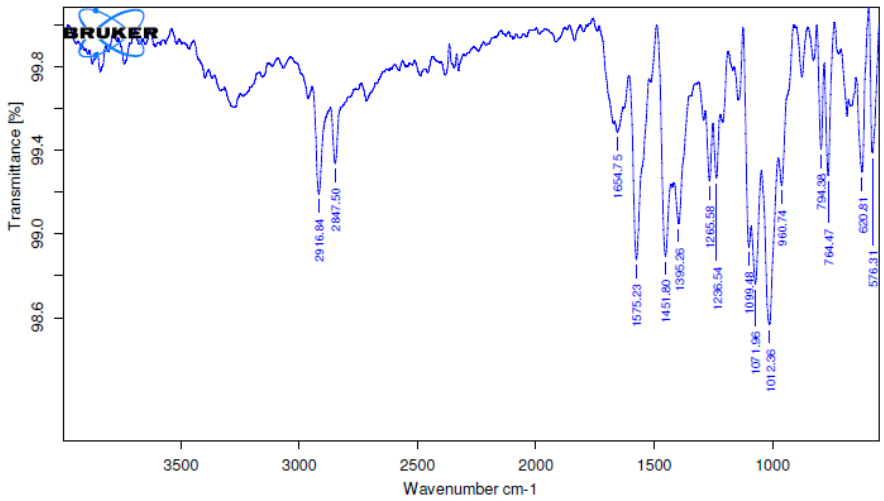


Fig: FTIR of Drug + Excipients

Discussion:

From the compatibility studies it was concluded that the functional groups that were presented in the pure drug were present in the optimized formulation with very minute changes, from this we can concluded that the drug and excipients have no interactions.

Drug entrapment efficacy:

Formulation code	% EE
F1	95.31
F2	96.47
F3	97.23
F4	98.43
F5	96.43
F6	95.08
F7	96.43
F8	95.36
F9	98.13

Discussion: The percentage of drug entrapment efficiency of formulation F1 was found to be 95.31 %formulation F2 was found to be 92.47%formulation F3 was found to be 98.23%, formulation F4 was found to be 97.43%, formulation F5 was found to be 96.43%, formulation F6 was found to be 95.08%, formulation F7 was found to be 97.43%, formulation F8 was found to be 92.36%, formulation F9 was found to be 98.13%.

SCANNING ELECTRON MICROSCOPY:

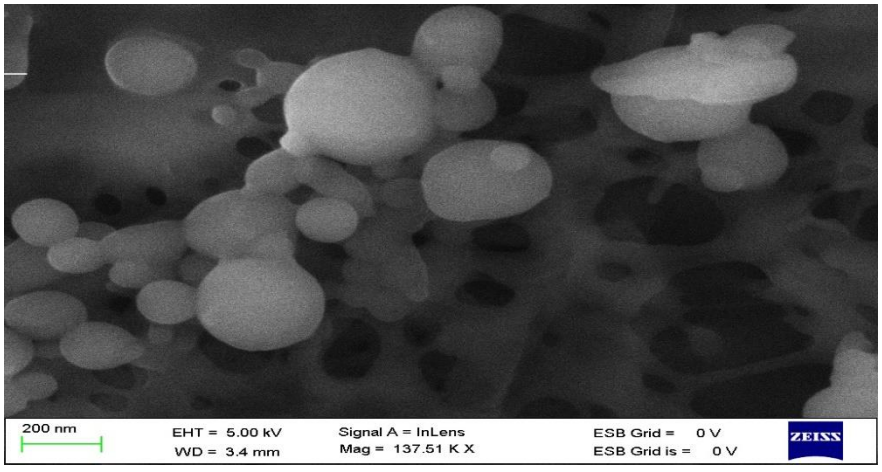
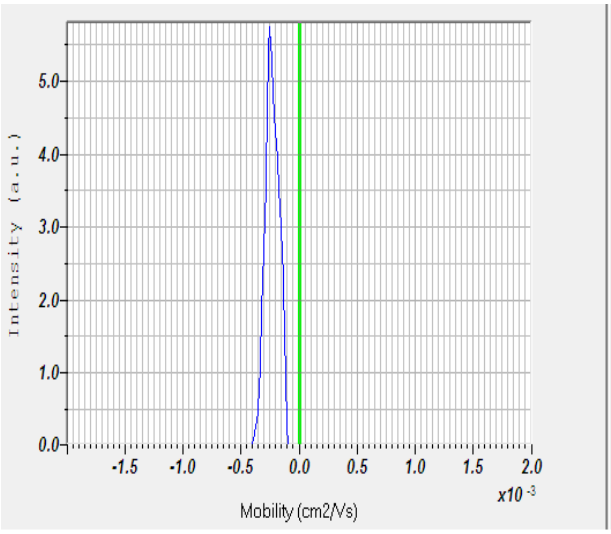


Fig: SEM Image of Optimized Nanoparticle formulation.

Particle size analysis:



Measurement Results

Date	: 29, February 2020
Measurement Type	: Zeta Potential
Sample Name	: np-zeta
Temperature of the Holder	: 25.2 °C
Dispersion Medium Viscosity	: 0.892 mPa·s
Conductivity	: 0.096 mS/cm
Electrode Voltage	: 3.8 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-29.7 mV	-0.000231 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean)	: -29.7 mV
Electrophoretic Mobility Mean	: -0.000231 cm^2/Vs

Zeta Potential: The measurement itself is a particle electrophoresis, the particle velocity is determined via the doppler shift of the laser light scattered by the moving particles. The field strength applied was 20 V/cm. The electrophoretic mobility was converted to the zeta potential in mV using the Helmholtz-Smoluchowski equation. At standard measuring conditions (room temperature of 25 °C, water) this equation can be simplified to the multiplication of the measured electrophoretic mobility (µm/cm per V/cm) by a factor of 12.8, yielding the ZP in mV.

Invitro diffusion studies of fluvoxamine nanoparticles :

Time (hrs)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
1	36.15	40.18	45.46	39.42	34.15	40.81	27.31	22.63	28.49
2	53.16	50.45	57.71	46.98	42.87	46.97	39.52	37.49	36.05
3	67.49	58.08	66.18	58.05	54.98	50.18	51.18	50.02	48.18
4	80.52	70.98	72.31	70.46	66.52	58.51	65.08	62.31	59.17
6	95.75	81.08	85.18	79.32	77.42	65.19	75.98	75.53	65.79
8		97.35	92.21	91.05	83.16	73.94	94.75	91.49	72.43
10			98.42		95.21	82.05		98.61	85.19
12						98.05			96.19

Discussion:

All the 9 formulations of fluvoxamine nanoparticle dispersion were subjected to drug release studies.

Formulations F1, F2, F3 containing the ethyl cellulose as polymer. F1 shows 95.75% drug release at the end of 6hrs. Where as F2 formulation shows 97.35% drug release at the end of 8hrs. While the F3 formulation shows 98.42% drug release at the end of 10hrs. As the concentration of polymer increasing drug release time is increased. So further trails were performed using Eudragit RS 100 with same proportions.

Formulations F4, F5, F6 containing the Eudragit RS 100, F6 formulation shows maximum drug release at the end of 12hrs. while Formulation F7, F8, F9 containing Eudragit RL 100, in which F7 formulation shows 94.75% drug release at the end of 8th hour and F8, F9 shows 98.61% , 96.19% drug release at the end of 10, 12hrs.

Among all the 9 formulations F6 formulation is optimized, as it shows maximum drug release at the end of 12hrs which suits the controlled release drug delivery system criteria as per our studies.Further drug release kinetics were performed to F6 formulation.

Conclusion

From the invitro studies we can say that formulation F6 shows best drug release of 98.05% within 12 hrs to release the drug The drug release from the Nanoparticles was explained by the using mathematical model equations such as zero order, first order, and equation methods. Based on the regression values it was concluded that the optimized formulation F6 follows Zero order drug release with super case II transport mechanism.

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