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PREPARATION, EVALUATION AND OPTIMIZATION OF SOLID LIPID NANOPARTICLE COMPOSED OF FEMOTIDINE

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Abstract: - Posaconazole, lecithin, and stearic acid were used as excipients in the solvent injection method used to create famotidine-containing nanoparticles. Famotidine showed solubility in methanol and chloroform. The phase separation method and the open capillary method were used to determine its partition coefficient and melting point, respectively. At a maximum wavelength of 286 nm, the UV absorbance measurements of standard solutions with drug doses ranging from 15 to 30 µg/mL in methanol showed linearity.

The F4 formulation, which outperformed the other six formulations in terms of drug encapsulation efficiency (80%), was chosen for additional in-vitro drug release investigation and release kinetics research. Over the course of 24 hours, the medication release rate for the F4 formulation was 95%.
Keywords: - Nanoparticles, Famotidine, Solvent injection method, Drug encapsulation efficiency. In-vitro drug release

Introduction

Drug delivery systems (DDSs) are pharmaceutical formulations or devices that help in achieving targeted delivery and/or controlled release (CR) of therapeutic agents in our body. Following administration, the DDSs liberate the active ingredients, and subsequently, the bioactive molecules are transported across various biological barriers to reach the site of action. The drug concentration at the appropriate site should remain in the therapeutic window, that is, between minimal effective concentration (MEC) and minimal toxic concentration (MTC).[1] The dosage form may be gaseous (e.g., anaesthetics), liquid (e.g., solutions, emulsions, and suspensions), semisolid (e.g., creams, ointments, and gels), and solid dosage (e.g., tablets and capsules). Drugs can be administered directly into the body through injection or infusion termed parenteral drug delivery.[2] Depending on the site of administration, one can differentiate among intravenous, intramuscular, subcutaneous, intradermal, and intraperitoneal administration. Mostly semisolid dosage forms including creams, ointments, and gels are applied onto the skin to enter into the body. However, the liquid dosage forms, such as emulsions, or solid dosage forms, such as transdermal patches, can also be used. [3]

In the past few decades, considerable attention has been concentrated on the evolution of a novel drug delivery system (NDDS) for herbal drugs. Conventional dosage forms, including prolonged-release dosage forms, are unable to satisfy for both holding the drug component at a distinct rate as per directed by the requirements of the body, all through the period of treatment, as well as directing the phytoconstituents to their desired target site to obtain an utmost therapeutic response. [4] Thus, the nano-sized NDDSs of herbal drugs have a potential future for enhancing the activity and overcoming problems associated with the plant medicines. Liposomes, which are biodegradable and essentially nontoxic vehicles, can encapsulate both hydrophilic and hydrophobic materials.[5] With the progress in all domains of science and engineering, the dosage forms have developed from simple mixtures and pills to highly sophisticated technology, intensive drug delivery systems, which are known as NDDSs. Transdermal drug delivery is a non-invasive, user-friendly delivery method for therapeutics. The use of lipid vesicles in a delivery system for skin treatment has attracted increasing attention in

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recent years, but it remains controversial.[6]

Use of turmeric in TDDS for the local action of the drug at the site of administration can also be regarded as a young version of Ayurvedic turmeric poultice or leap,[8]

Nanotechnology refers to an emerging field of science that includes synthesis and development of various nano-materials. Nanoparticles can be defined as objects ranging in size from 1- 100 nm that due to their size may differ from the bulk material. Presently, different metallic nano-materials are being produced using copper, zinc, titanium, magnesium, gold, alginate and silver. Nanoparticles are being used for diverse purposes, from medical treatments, using in various branches of industry production such as solar and oxide fuel batteries for energy storage, to wide incorporation into diverse materials of everyday use such as cosmetics or clothes.[9] The HLB scale divides drugs into two categories: hydrophilic and lipophilic compounds. Lipophilic compounds have a low solubility, making it difficult to build safe, effective, and cost-effective drug delivery systems. This has long been a source of frustration for pharmaceutical scientists. Traditionally, lipid-based novel drug delivery systems have focused on the delivery of lipophilic molecules; however, due to inherent properties such as biocompatibility, self-assembly capabilities, ability to cross the blood-brain barrier, particle size variability, and finally cost effectiveness, lipid-based delivery systems have become much more appealing. Lipid-based nanoparticles can also be subcategorized and shown in figure 1.

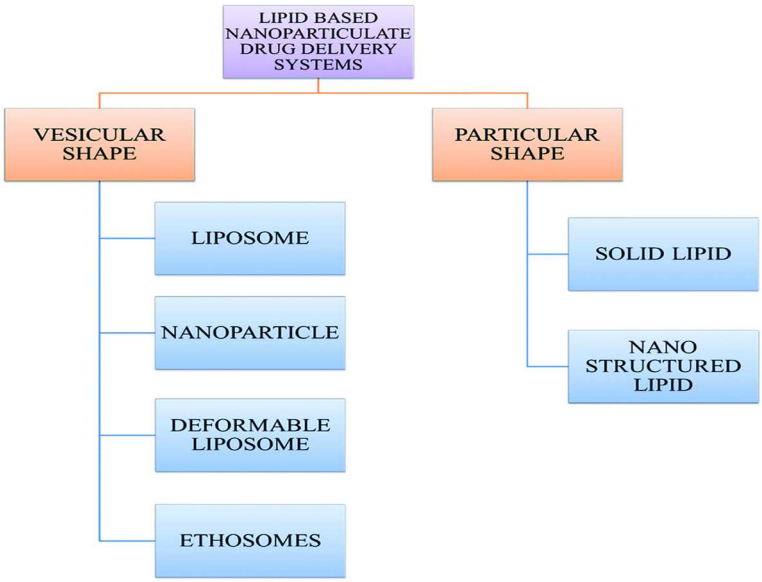

Figure1: classification of lipid-based nanoparticle

Classification of nanoparticles

There are various approaches for classification of nano-materials. Nanoparticles are classified based on one, two and three dimensions.[10]

One-dimension nanoparticles

One dimensional system, such as thin film or manufactured surfaces, has been used for decades in electronics, chemistry and engineering. Production of thin films (sizes1-100 nm) or monolayer is now common place in the field of solar cells or catalysis.

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Two-dimension nanoparticles

Carbon nano-tubes (CNTs)

Carbon nano-tubes are hexagonal network of carbon atoms, 1 nm in diameter and 100 nm in length, as a layer of graphite rolled up into cylinder. CNTs are of two types, single walled carbon nano-tubes (SWCNTs) and multi-walled carbon nano-tubes (MWCNTs). The small dimensions of carbon nano-tubes, combined with their remarkable physical, mechanical and electrical properties, make them unique materials.

Three-dimension nanoparticles

Fullerenes (Carbon 60): Fullerenes are spherical cages containing from 28 to more than 100 carbon atoms, contain C60. This is a hollow ball composed of interconnected carbon pentagons and hexagons, resembling a soccer ball. These molecules do not combine with each other, thus giving them major potential for application as lubricants.[11]

Characterization of Nanoparticles

Particle size:

Particle size distribution and morphology are the most important parameters of characterization of nanoparticles. Morphology and size are measured by electron microscopy. Smaller particles offer larger surface area. As a result, most of the drug loaded onto them will be exposed to the particle surface leading to fast drug release. On the contrary, drugs slowly diffuse inside larger particle**.**

Dynamic light scattering (DLS):

Currently, the fastest and most popular method of determining particle size is photon-correlation spectroscopy (PCS) or dynamic light scattering (DLS). DLS is widely used to determine the size of Brownian nanoparticles in colloidal suspensions in the nano and submicron ranges.

Scanning Electron microscopy:

Scanning electron microscopy (SEM) is giving morphological examination with direct visualization. For SEM characterization, nanoparticles solution should be first converted into a dry powder, which is then mounted on a sample holder followed by coating with a conductive metal, such as gold, using a sputter coater. The sample is then scanned with a focused fine beam of electrons.

Transmission electron microscope:

TEM operates on different principle than SEM, yet it often brings same type of data. The sample preparation for TEM is complex and time consuming because of its requirement to be ultrathin for the electron transmittance.[12]

Atomic force microscopy:

Atomic force microscopy (AFM) offers ultra-high resolution in particle size measurement and is based on a physical scanning of samples at sub-micron level using a probe tip of atomic scale. Instrument provides a topographical map of sample based on forces between the tip and the sample surface.

Surface Charge:

The nature and intensity of the surface charge of nanoparticles is very important as it determines their interaction with the biological environment as well as their electrostatic interaction with bioactive

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compounds. The colloidal stability is analysed through zeta potential of nanoparticles.[13]

Surface hydrophobicity:

Surface hydrophobicity can be determined by several techniques such as hydrophobic interaction chromatography, biphasic partitioning, adsorption of probes, contact angle measurements etc. [14]

Application of Nanoparticles

Table 1: Application of nanotechnology in the different field is summarised

Applied field	Application
Nano-medicines	Nano drugs, medical devices, Tissue engineering
Chemical and Cosmetics	Nano-scale chemicals and compounds, paints, coatings etc
Materials	Nanoparticles, carbon nano-tubes, biopolymers, points, coatings
Food Sciences	Processing, nutraceutical food, nano-capsules.
Environment and Energy	Water and air purification filters, fuel cells, photovoltaic
Military and Energy	Biosensors, weapons, sensory enhancement
Electronics	Semiconductors chips, memory storage, photonic, optoelectronics
Scientific Tools	Atomic force, microscopic and scanning tunnelling microscope
Agriculture	Atomic force, microscopic and scanning tunnelling microscope.

Preparation of nanoparticles [15]

The selection of appropriate method for the preparation of nanoparticles depends on the physicochemical character of the polymer and the drug to be loaded. The primary manufacturing methods of nanoparticles from preformed polymer includes:

Emulsion-Solvent Evaporation Method: This is one of the most frequently used methods for the preparation of nanoparticles. The nano particles are collected by ultracentrifugation and washed with distilled water to remove stabilizer residue or any free drug and lyophilized for storage. Modification of this method is known as high pressure emulsification and solvent evaporation method.

Double Emulsion and Evaporation Method

The emulsion and evaporation method suffer from the limitation of poor entrapment of hydrophilic drugs. Therefore, to encapsulate hydrophilic drug the double emulsion technique is employed, which involves the addition of aqueous drug solutions to organic polymer solution under vigorous stirring to form w/o emulsions.

Salting Out Method

Salting out based on the separation of a water-miscible solvent from aqueous solution via a salting-out effect. Salting-out is based on the separation of a water miscible solvent from aqueous solution via a salting-out effect.

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Emulsions

Diffusion Method: This is another widely used method to prepare nanoparticles. The encapsulating polymer is dissolved in a partially water-miscible solvent (such as propylene carbonate, benzyl alcohol), and saturated with water to ensure the initial thermodynamic equilibrium of both liquids. Several drug- loaded nano particles were produced by the technique, including mesentera (hydroxyphenyl) porphyrin-loaded PLGA (p-THPP) nano particles [13], doxorubicin-loaded PLGA nano particles [14]and cyclosporine (cy-A-); loaded sodium glycolate nanoparticles.[15]

Solvent Displacement / Precipitation method

Solvent displacement involves the precipitation of a preformed polymer from an organic solution and the diffusion of the organic solvent in the aqueous medium in the presence or absence of surfactant. Polymers, drug, and or lipophilic surfactant are dissolved in a semipolar water miscible solvent such as acetone or ethanol. The solution is then poured or injected into an aqueous solution containing stabilizer under magnetic stirring. Nano particles are formed instantaneously by the rapid solvent diffusion.[17]

The morphology of NPs and nano-composites

The morphological characteristics to be taken into account are the flatness, aspect ratio and spatial position of each element in the case of hybrid NPs (HNPs). A general classification exists between high and low aspect ratio particles. These NPs were designed and synthesized using the hydrothermal process for purification of histidine-tagged proteins [18]

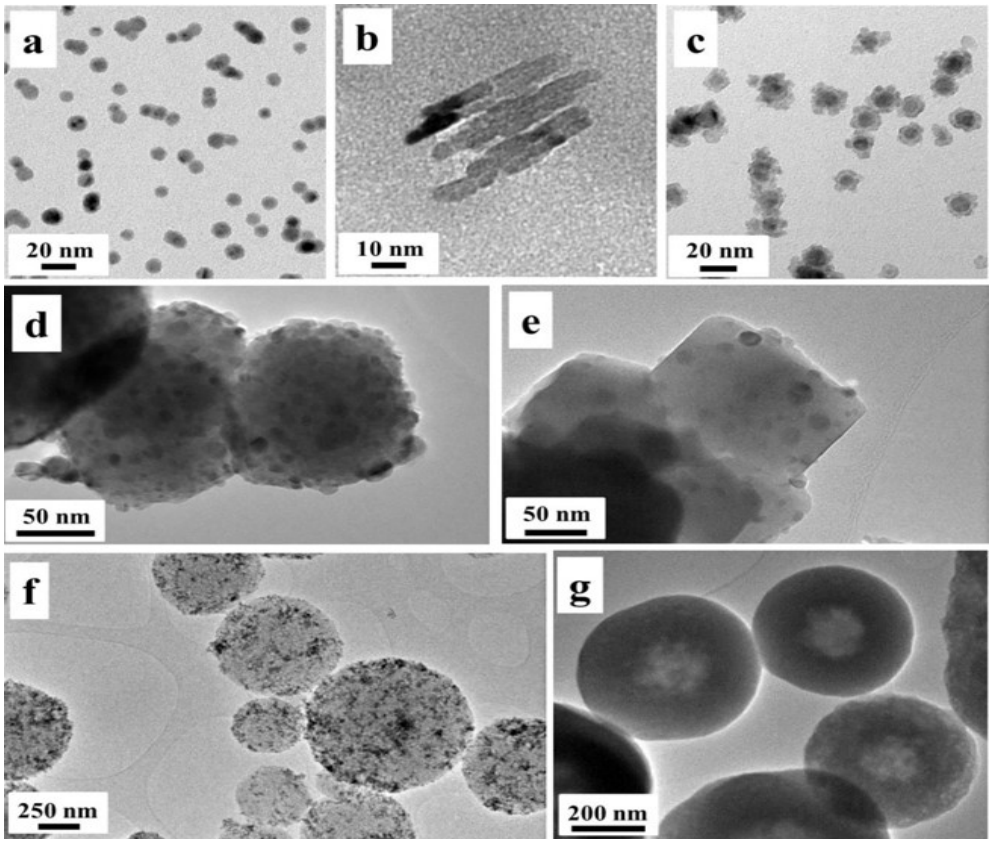

Figure 2: TEM images of examples of NPs with different morphologies and compositions. (a) Monodispersed Cu NPs, (b) Fe nanorods, (c) Cu–Si core–shell NPs, (d) porous Fe_3O_4 NPs, (e) Fe_3O_4 cubes decorated with Ni NPs, (f) porous silica spheres with γ-

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Fe_2O_3 NPs adsorbed on their surfaces and (g) γ-Fe_2O_3 NPs embedded in porous silica spheres.

Nanoparticles chemical composition

NPs can be composed of a single constituent material or be a composite of several materials. There are three main types of chemical ordering in HNPs that describe the way in which the atoms of the elements are arranged within the same NP.[19]

Mixed NPs: can be either random or ordered. Randomly mixed alloys correspond to solutions of solids, whereas ordered nano-alloys correspond to ordered arrangements of A and B atoms.

Core–shell NPs: consist of a shell of one type of atom (B) surrounding a core of another type of atom (A). This pattern is generally denoted by A@B and is common for a large class of NPs. These NPs have alternating A–B–A shells, or A–B–C in the case of ternary NPs as depicted in figure.

Layered NPs: They are commonly referred to in the literature as Janus (or' dumbbell-like') NPs. They consist of two types of NPs (A and B) sharing a common interface. These types of NPs tend to minimize the number of bonds between elements A and B. This heterojunction structure facilitates phase separation.

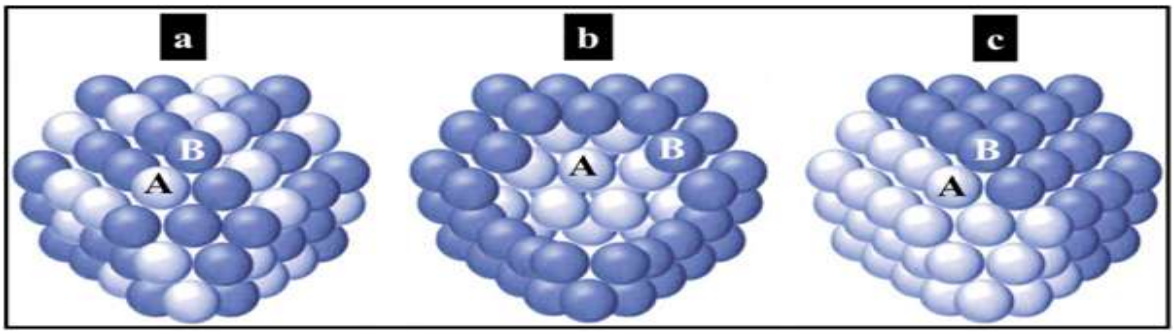

Figure 3: Schematic images of binary NPs: a mixed structure (a), a core–shell structure (b) and a layered structure (c) of A and B elements.

Because of the increasing need for multifunctional NPs, other complex structures of NPs such as multicore–shell structures in which the cores can present either 'dumbbell-like' or 'onion-like' structures have been reported in the literature. Another multifunctional subset of the core–shell arrangement is an alloyed single core NP encapsulated in an inert shell.[20]

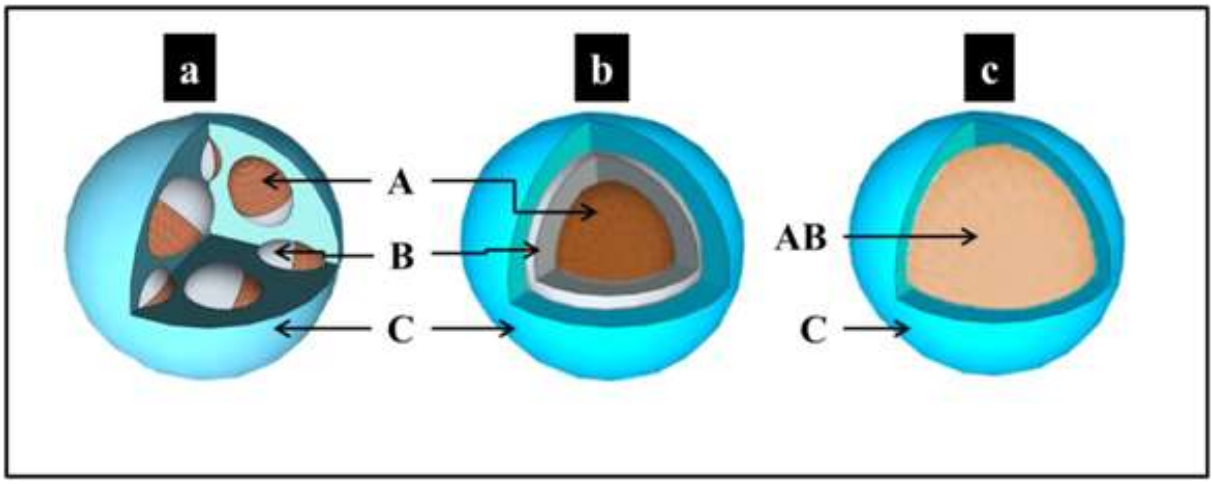

Figure 4: Schematic images of ternary NPs formed of elements A, B and C: (a) a multicore–shell morphology (the cores present a

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dumbbell-like morphology), (b) a core–multishell morphology and (c) an alloyed-core–shell morphology.

Solid lipid nanoparticle

Solid lipid nanoparticles (SLN) introduced in 1991 represent an alternative carrier system to tradition colloidal carriers such as - emulsions, liposomes and polymeric micro – and nanoparticles. They have many advantages such as good biocompatibility, low toxicity and lipophilic drugs are better delivered by solid lipid nanoparticles and the system is physically stable.

Preparation of solid lipid nanoparticles

High pressure homogenization

It is a reliable and powerful technique, which is used for the production of SLNs. High pressure homogenizers push a liquid with high pressure (100–2000 bar) through a narrow gap (in the range of a few microns). Very high shear stress and cavitation forces disrupt the particles down to the submicron range.

Ultrasonication/high speed homogenization

SLNs are also prepared by ultrasonication or high-speed homogenization techniques. For smaller particle size combination of both ultrasonication and high-speed homogenization is required.[21]

Solvent evaporation

SLNs can also prepared by solvent evaporation method. The lipophilic material is dissolved in a water-immiscible organic solvent (e.g. cyclohexane) that is emulsified in an aqueous phase. Upon evaporation of the solvent, nanoparticles dispersion is formed by precipitation of the lipid in the aqueous medium by giving the nanoparticles of 25 nm mean size. The solution was emulsified in an aqueous phase by high pressure homogenization. The organic solvent was removed from the emulsion by evaporation under reduced pressure.[22]

Material and methods

Material used for nanoparticle

Table 2: List of Chemicals Used

S.No.	Materials	Manufacturer
1	Femotidine	Mylan, Hyderabad.
2	ES 100	Gift sample from Degussa Pharma, India.
3	HCl	SD Fine Chemicals
4	Poly vinyl alcohol	Pharmafabrikon, Madurai, India.
5	Dichloromethane	Central Drug House (P) Ltd, New Delhi, India.
6	Ethanol	Central Drug House (P) Ltd, New Delhi, India.
7	DMSO	Central Drug House (P) Ltd, New Delhi, India.

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Table 3: List of Instrument

S.No	Equipment's	Company
1	Electronic Weighing Balance	A&D Company HR 200, Japan.
2	Mechanical Stirrer	Remi Motors, India.
3	Magnetic Stirrer	MC Dalal& Co India
4	UV Visible Spectrophotometer	Shimadzu, Japan.
5	Malvern Zetasizer and Particle size analyser	Malvern instruments
6	SEM Analyzer	Hitachi, Japan
8	Ultracentrifuge	Eppendorf centrifuge, Germany
9	Stability Chamber	Inlab Equipment's Madras PVT (LTD)

Organoleptic parameter

It is the initial evaluation during preformulation studies which assess the colour, odor and taste of the substance. The appearance was checked visually for color, homogeneity and transparency. The appearance was checked visually for color, homogeneity and transparency.[23]

Solubility

Solubility is an important physicochemical property of drug substance, which determines its systemic absorption and in turns its therapeutic efficacy. Solubility of drug was determined in different solvents.

Melting point determination

Melting point of drug was determined by Open capillary method. The melting point of a drug is one of the first and more reliable physical properties measured

Determination of partition coefficient

50 mg of drug was taken in three separating funnels. The separating funnels were shaken for 2 hrs in a wrist action shaker for equilibration. Two phases were separated and the amount of the drug in aqueous phase was analysed spectrophotometrically. The partition coefficient of the drug in phases was calculated by using formula:

K_{PC} = Concentration of Drug in Oil Phase/ Concentration of Drug in Water Phase [24]

Standard calibration curve of famotidine

Determination of absorption maximum (λmax)

From the above stock solution 0.3 ml sample was transferred into a 5 ml volumetric flask and the volume was made up to mark with methanol to prepare a concentration of 6µg/ml. The sample was scanned by UV-VIS Spectrophotometer in the range of 200- 400 nm, using methanol as a blank. The wavelength corresponding to the maximum absorbance (max) was found to be 286nm.

Preparation of calibration curve

Aliquots of 5, 10, 15, 20, 25 and 30µg/ml were prepared utilizing 100 µg/mL famotidine standard stock solution were accurately transferred into a series of 10 mL calibrated flask and made up to the mark with methanol. The absorbance of the resulting solution was measured at 286nm against methanol

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blank. Calibration curve was prepared by plotting the absorbance vs concentration of drug.[25]

Compatibility Study of drug and excipient

Drug excipient compatibility was determining by the FTIR. In this work we are using FTIR for compatibility studies.[26]

FTIR

Fourier Transform Infrared (FTIR) spectral analysis: The pure drug femotidine and polymers used in this experimental work were studied for compatibility studies. We carried out these studies by taking 2 mg of sample in 200 mg of potassium bromide (PerkinElmer, Spectrum100, Japan). The range of scanning was 400-4000cm-1 and resolution was 1cm-1.

Formulation of solid lipid nanoparticle

Famotidin -SLNs were prepared using the solvent injection method. Briefly, Famotidin (150 mg), stearic acid (200 mg), and lecithin (100 mg) were dissolved in 10 mL chloroform in a glass flask (as organic phase). Ethylene glycol was dissolved in 30 mL distilled water and heated to 75°C in a water bath (as aqueous phase). The organic phase was injected into the hot aqueous phase under mechanical agitation at 1000 rpm, and the resulting solution was kept at 75°C with the same agitation speed to remove the organic solvent. The condensed solvent (approximately 5 mL) was then transferred into an equivalent amount of cold water (0°C–2°C) under continuous mechanical stirring (1000 rpm) for 1.5 hours. The resultant suspension was centrifuged at 20,000 rpm to remove the supernatant. The pellet was resuspended in ultrapure water, refrigerated at −80°C for 2 hours, and lyophilized in a lyophilized.[27]

Table 4: Composition of famotidine solid lipid nanoparticle

Ingredients (mg)	Formulations					
	F1	F2	F3	F4	F5	F6
Famotidine	40	40	40	40	40	40
Lecithin	80	100	120	150	180	200
Stearic acid	200	180	150	120	100	80
Water	qs	qs	qs	qs	qs	qs

Characterization of nanoparticles

Determination of Entrapment Efficiency (EE) [28]

UV spectrophotometric method was used to estimate entrapment efficiency of famotidine nanoparticle. A calibration curve was plotted for famotidine in methanolic HCl in the range of 3-18 µg/mL (Beer's Lambert's range) at 286 nm. A good linear relationship was observed between the concentration of famotidine and its absorbance. 100 mg of famotidine solid lipid nanoparticle of each batch were selected, powdered in a mortar and placed in 100 mL of methanolic HCl. Famotidine was extracted by centrifuging at 1000 rpm for 30 min, filtered and analyzed concentration from calibration curve data after necessary dilution. Percentage entrapment was calculated as follows:

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$$\% \text{ Entrapment efficiency} = \frac{Actual\ drug\ content\ in\ nanosponges}{Theoritical\ drug\ content} \times 100$$

Particle size determination

The mean size of the nanoparticle preparations was measured by laser diffraction analyzer (Malvern). Each sample was diluted with water until the appropriate concentration of particles was achieved and measured. All measurements were performed at 25°C

Scanning electron microscopy

Scanning electron microscopy (SEM) was also conducted to characterize the surface morphology of the nanoparticles for which a drop of nanoparticle system was mounted on clear glass stub, air dried and coated with Polaron E 5100 Sputter coater (Polaron,) and visualized under Scanning Electron Microscope (SEM Leo 430,).

Zeta potential

Zeta potential is a measure of surface charge. The surface charge of nanoparticle can be determined by using Zeta sizer. Zeta potential is a measurement of the overall charge of the particles in media and it indicates the stability of the particles in the sense that the higher the zeta potential the more stable the particles.[29]

In vitro drug release from the formulation

The release of famotidine from optimized nanoparticle was determined by membrane diffusion technique using Franz diffusion cell. The nanoparticle equivalent to 5%w/w of nanoparticle was taken in donor compartment. The donor and receptor compartment were separated by synthetic cellophane membrane. The synthetic cellophane membrane was mounted between donor and receptor compartment of cell. The receptor medium was filled with phosphate buffer pH 7.4. The assembly was stirred at 200 rpm and receptor compartment was replenished with equal volume of phosphate buffer. Aliquots each of 1 ml was withdrawn periodically at an interval of 2, 4, 6, 8, 10, 12 and 24 hrs and replaced by an equal volume of receptor medium. The aliquots were suitably diluted with receptor medium and analyzed by UV visible spectrophotometer.[30]

Release kinetics

To analyze the *in vitro* release data various kinetic models were use to describe the release kinetics. The zero order rate Eq. (2) describes the systems where the drug release rate is independent of its concentration. The first order Eq. (3).[31]

The results of *in vitro* release profile obtained for all the formulations were plotted in modes of data treatment as follows:

- Zero - order kinetic model – Cumulative % drug released versus time
- First – order kinetic model – Log cumulative percent drug remaining versustime.
- Higuchi's model – Cumulative percent drug released versus square root of time.

Zero order kinetics

$$A_t = A_0 - K_0 t$$

Zero order release would be predicted by the following equation:

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Where

A_t = Drug release at time 't'

A_0 = Initial drug concentration.

K_0 = Zero- order rate constant (hr^{-1})

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys Zero – order kinetics and its slope is equal to Zero order release constant K_0.

First order kinetics

$$\text{Log } C = \log C_0 - K_t / 2.303$$

When the data plotted as log cumulative percent drug remaining versus time, yields a straight line, indicating that the release follow first order kinetics. The constant 'K1' can be obtained When the data plotted as log cumulative percent drug remaining versustime, yields a straight line, indicating that the release follow first order kinetics. The constant 'K1' can be obtained by multiplying 2.303 with the slope value.[32]

Result and discussion

Organoleptic evaluation: -In organoleptic evaluation of drug, colour, odour, and appearance were evaluated.

Table 5: Organoleptic evaluation of famotidine

Drug	**Organoleptic properties**		**Observation**
Famotidin	Color		White
	Odor		Odorless
	Appearance		Crystalline powder

Discussion: - The above table is depicted that the drug famotidine is white in colour, odourless and crystalline powder.

Solubility study

Table 6: Solubility of famotidine

Drug	**Solvents**	**Observation/Inference**
Famotidin	Dimethyl sulfoxide	Freely soluble
	Water	Slightly soluble
	Chloroform	Soluble
	Methanol	Soluble
	Glacial acetic acid	Freely soluble

Discussion: - The drug is found to be soluble in chloroform and methanol, freely soluble in dimethyl sulfoxide and glacialacetic acid and slightly soluble in water.

Melting point determination

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Table 7: Melting point of femotidine

S. No.	Drug	Observed	Reference
1	Famotidine	162°C	160-165° C

- **Discussion: -** Melting point of famotidine was found to be 162˚C.

Partition Coefficient

Table 8: Partition Coefficient of Femotidine

S. No.	Medium	Log P
1	Octanol: Water	-0.56

Discussion: - Partition coefficient of the drug was found to be -0.56 in n-octanol: water.

Determination of λ max: - Solution was scanned under UV-Vis Spectrophotometer and λ max was determined. It was found to be as per the monograph.

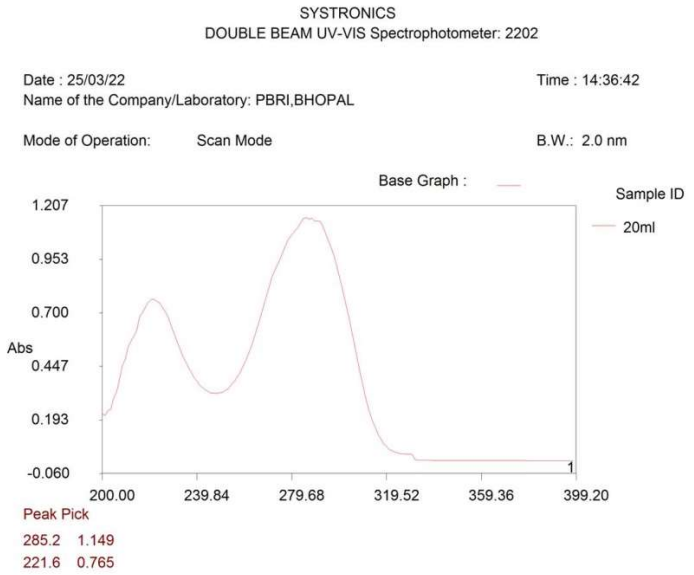

Figure5: λmax of famotidine

Standard calibration curve of famotidine

Table 9: Calibration curve of famotidine

Concentration (µg/ml)	Absorbance (286 nm)
5	0.425
10	0.506
15	0.664
20	0.749
25	0.95
30	1.075

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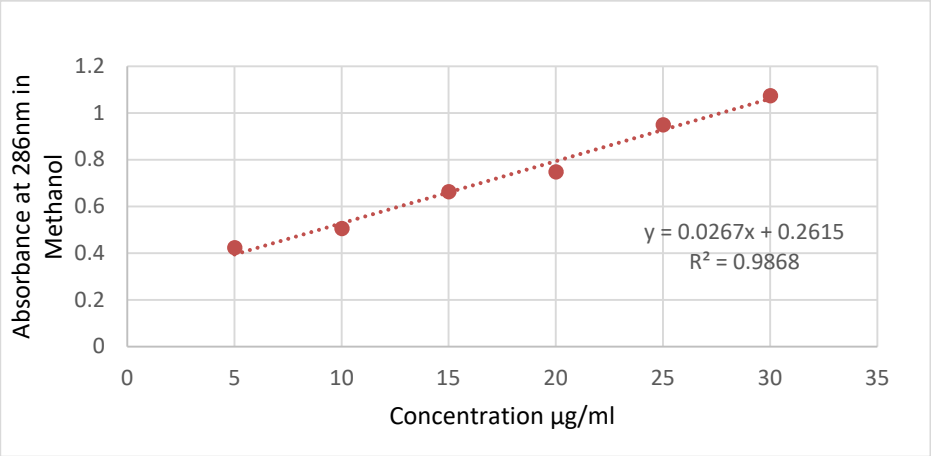

Figure 6: Calibration curve of famotidine

Discussion: - Seven points calibration curve were obtained in a concentration range from 5-30 µg/ml for drug. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = 0.026x + 0.261with correlation coefficient $R^2 = 0.986$.

Drug and excipients compatibility studies

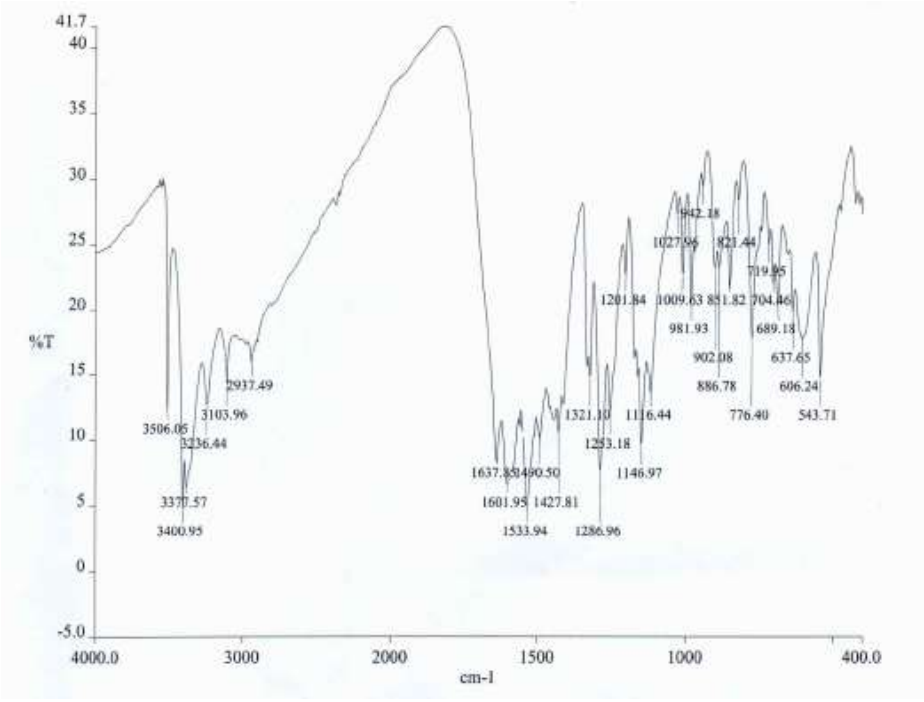

Figure7: FTIR graph of femotidine

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Table 10: Interpretation of FTIR of famotidine

S. No.	Wave number	Reference range	Functional groups
1	3506.05	3550 – 3250	N-H stretching
2	3400.95	3500–3200	O-H stretching
3	3103.96	3100 – 3000	C-H stretching
4	1637.85	1690-1640	Imine stretching
5	1601.95	1625 – 1440	C=C stretching
6	1490.50	1450	Alkane C-H bending
7	1427.81	1415-1380	S=O stretching

Characterization of nanoparticle

Determination of Entrapment Efficiency (EE)

Entrapment efficiency of all the batches of famotidine solid lipid nanoparticle was evaluated and the best formulation was selected on the basis of entrapment efficiency of the formulation.

Table 11: Entrapment efficiency of famotidine solid lipid nanoparticle

S. No.	Formulation batch	% Entrapment efficiency
1	F1	58.23
2	F2	72.85
3	F3	63.65
4	F4	81.45
5	F5	76.46
6	F6	65.28

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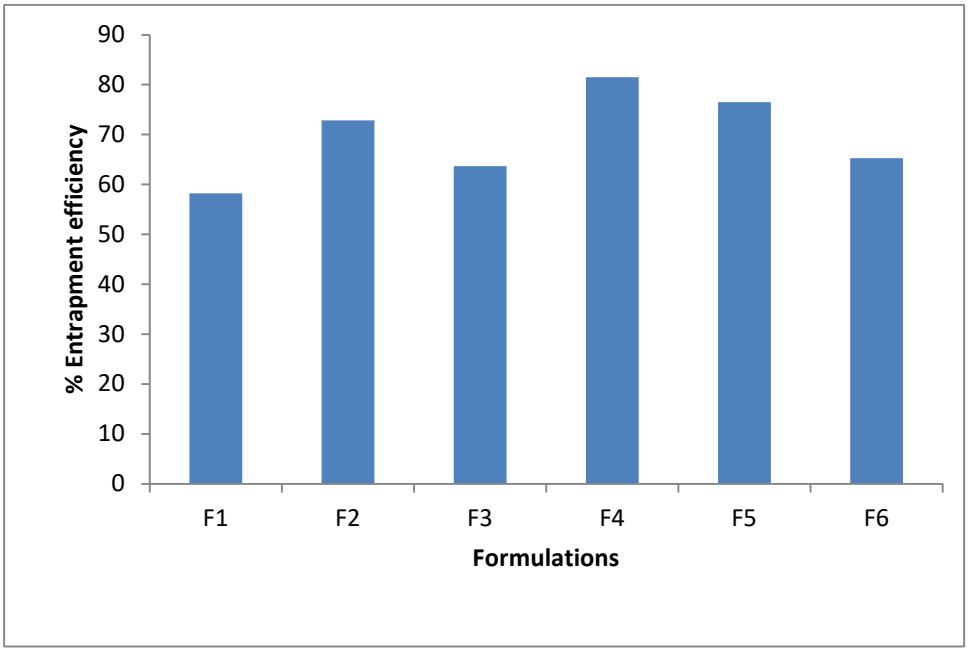

Figure 8: Entrapment efficiency of different formulations

Discussion: - From the entrapment efficiency studies of famotidine nanoparticle, it was observed that formulation F4 showed better entrapment of drug into the nnanoparticle. So it was selected for further in-vitro drug release.

Particle size determination

Average particle size of solid lipid nanoparticle was calculated by sum of all particles size/number of particles. Maximum particle size of famotidine formulation was found to be 263.74nm.

Table 12: Particle size of famotidine solid lipid nanoparticle

S. No	Formulation	Particle size (nm)
1.	F1	230.46
2.	F2	260.57
3.	F3	245.57
4.	F4	247.87
5.	F5	263.74
6.	F6	250.47

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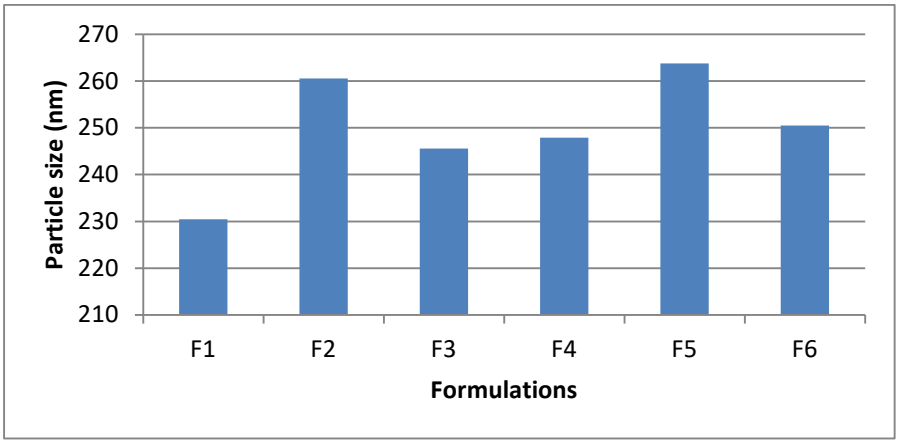

Figure9: Particle size of different formulations

Discussion: - From the particle size determination of famotidine nanoparticle, it was observed that the formulations showed the particle size from 230.46 – 263.74nm.

Scanning electron microscopy

Scanning electron microscopy (SEM) was used to analyze the solid lipid nanoparticle.

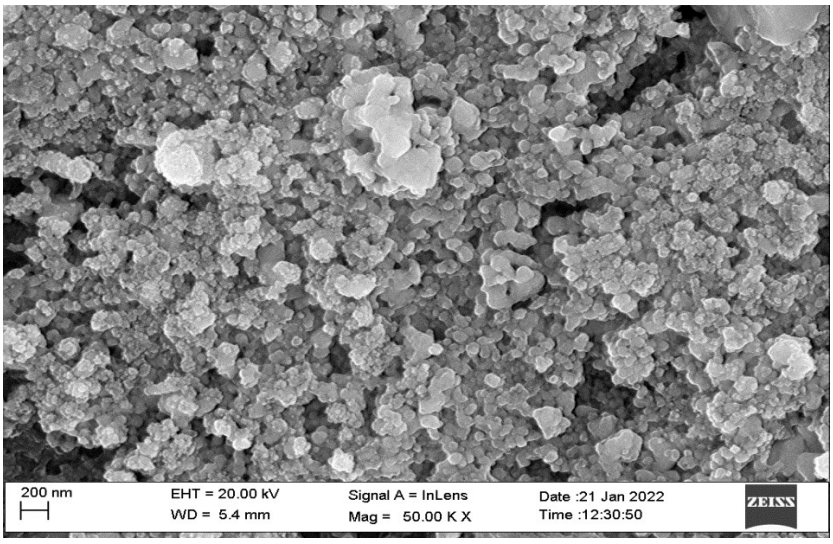

Figure 10: SEM of F4 formulation

Zeta potential :- Formulation showed highest zeta potential (495.1) and was calculated in nm.

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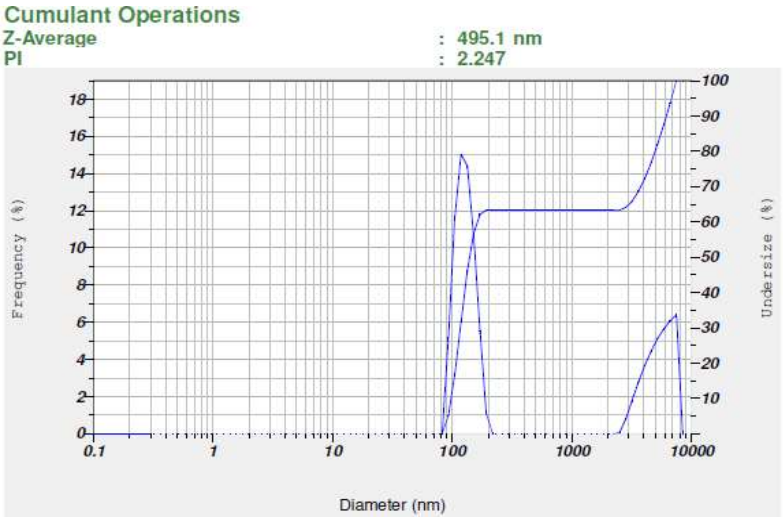

Figure 11: Zeta potential of F4 formulation

In vitro drug release from the formulation

The In-vitro diffusion study was taken by using franz diffusion cell which shows cumulative % drug release of famotidine nanoparticle formulation. Among all the formulations, F4 was selected for in-vitro drug release study because it showed highest drug content.

Table 13: In vitro drug release of F4 formulation of famotidine nanoparticle

S. No.	Time in hours	% cumulative drug release
1	2	17.46
2	4	32.03
3	6	48.67
4	8	55.70
5	10	63.45
6	12	75.47
7	16	88.46
8	24	94.56

Release kinetic studies: - Kinetics studies of the F4 formulation were performed. The results are given below.

Table 14. Release kinetics study of F4 formulation.

Formulation	Model	Kinetic parameter values
F4	Zero Order	$y = 3.512x + 23.47$ $R^2 = 0.878$
	First Order	$y = -0.056x + 2.057$ $R^2 = 0.985$
	Higuchi	$y = 21.64x - 5.375$ $R^2 = 0.969$

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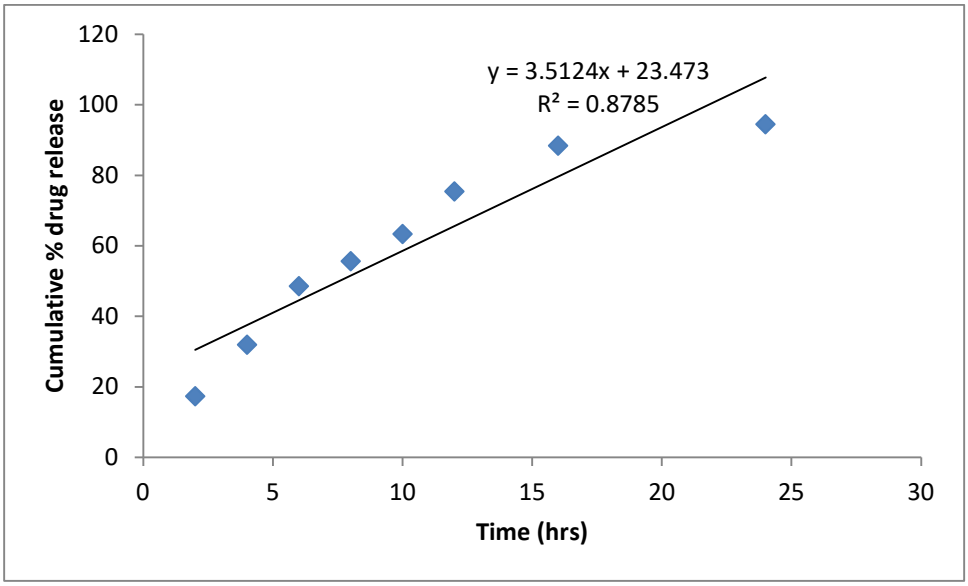

Figure 12: Zero order model of G3 formulation

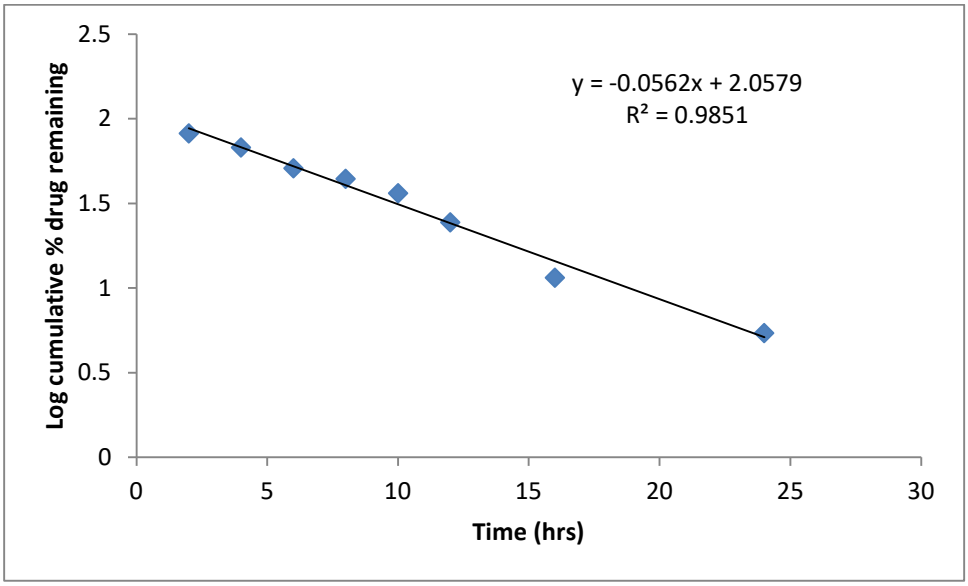

Figure 13: First order model of G3 formulation

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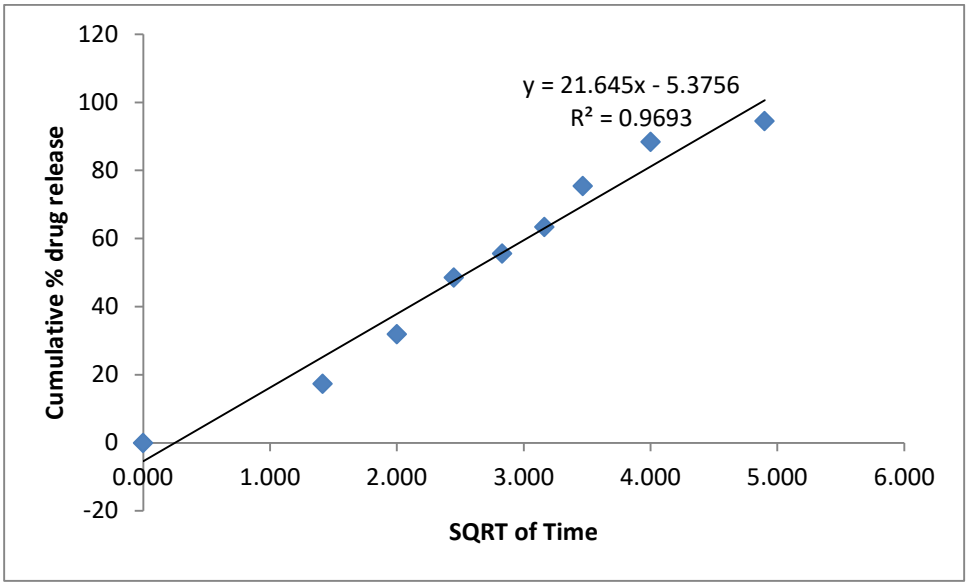

Figure 14: Higuchi model of G3 formulation

Discussion

Zero order kinetic model refers to the process of constant drug release from a drug delivery device independent of the concentration. The zero order graph of F4 formulation showed the constant drug release from the solid lipid nanoparticle, the results of the zero order model was found to be y = 3.512x + 23.47, R^2 = 0.878. The first order kinetic model describes the release from system where

$$Q = Kt^{1/2}$$

release rate is concentration dependent. The results of first order kinetic model was found to be y = -0.056x + 2.057, R^2 = 0.985. The Higuchi model is used to describe the limits for transport and drug release. The Higuchi model of patches was found to be 21.64x - 5.375, R^2 = 0.969.

Summary

Solid lipid nanoparticle of famotidine was successfully prepared by solvent injection method with drug famotidine and excepient like lecithin and stearic acid. Lecithin was used as lipid carrier and stearic acid was used as. Preformulation studies of the drug were performed first and the results were found to be the drug is white in colour, odourless and crystalline powder. The solubility of the drug was found to be soluble in chloroform and methanol, freely soluble in dimethyl sulfoxide and glacialacetic acid and slightly soluble in water.The melting point and partition cov efficient were determined by open capillary method and phase separation method. The melting point and partition coefficient of the drug were found to be 162˚ C and -0.56. The UV absorbance's of famotidine standard solution in the range of 15-30 µg/ml of drug in Methanol showed linearity at λ max 286nm. The linearity was plotted for absorbance against concentration with R^2 value 0.986 and with the slope equation = 0.026x + 0.261. The compatibility between the drug and other Excipient was evaluated using FTIR peak matching method. There was no appearance or disappearance of peaks in the drug excipient mixture, which confirmed the absence of any chemical interaction between the drug, and other chemicals. Famotidine solid lipid nanoparticle were prepared in six batches with varying the excipient and its amount and evaluated for different evaluating parameters.Entrapment efficiency of all the formulations of nanoparticle was evaluated and it was observed that formulation F4 showed

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better entrapment of drug into the formulation. So it was selected for further in-vitro drug release evaluation.Particle size determination of famotidine nanoparticles F4 were perfomed, and it was observed that the formulations showed the particle size range from 230.46 – 263.74nm. Zeta potential and SEM of the nanoparticle F4 formulation were performed.From all the evaluating parameters performed it is concluded that the formulation F4 was found to be the best formulation and it was chosen for drug release analysis and release kinetics studies.In-vitro drug release of F4 formulation was performed by franz diffusion cell for 24 hours duration, so the formulation showed 94% drug release within 24 hours. The nanoparticle formulation F4 was subjected to in vitro release studies using Franz diffusion cell. In general, F4 formulation showed a prolonged release and no burst effect was observed. The drug release from nanoparticle data were fitted into drug release kinetic models such as zero order, first order and higuchi.

Conclusion: -The main objective of this designed work was to prepare and evaluate famotidine loaded solid lipid nanoparticle. This formulation will deliver therapeutically effective amount of drug by oral administration. Nanoparticle was prepared and evaluated for entrapment efficiency, particle size, Zeta potential and SEM. From evaluation results, it was observed that among six formulations, F4 formulation showed better entrapment of drugwith 80% entrapment efficiency, so it was further used for in-vitro drug release. In-vitro drug release of the drug was performed by Franz diffusion cell and the F4 formulation showed 95% drug release within 24 hours. F4 formulation was subjected to release kinetic study. This study concluded that famotidine can be successfully prepared and evaluated in the form of solid lipid nanoparticle.

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