International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Formulation and Evaluation of Fexofenadine Nanoparticles Loaded in Gel

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Abstract: ***Fexofenadine HCL belonging to class of Anti histaminic is a poorly soluble drug of BCS class II, administered orally as a tablet or a capsule exhibit stomach upset, cough, and fever. Consequently, the present ability heaved to develop nanoparticles to effortlessly consecrate fexofenadine HCL through topical sway to surmount issues. Fexofenadine HCL Nanoparticles through polymer is a tremendous approach used to explore the physiochemical plat of fexofenadine HCL. Nanoparticles of fexofenadine HCL were braced using ionic gelation methods using albumin and carbopol. The braced nanoparticles were guesstimated through solubility, dissolution, differential scanning colorimetry and Fourier transform infrared spectroscopy investigations. Different investigational approach of dissolution and solubility unveiled an increase in solubility among all formulations. The nanoparticles were prepared in 1:1ratio with albumin. Fexofenadine HCL Nanoparticles made known improvement in solubility and dissolution comparatively to authentic fexofenadine HCL. The forming nanoparticles endorsed by alterations in endothermic peaks of DSC and movement infra red spectrum of nanoparticles. Formulation and evaluation of fexofenadine HCL nanoparticles by Ionic gelation to enhance solubility was the major criterion of the present work. From these studies, it can be concluded that nanoparticles enhance solubility of fexofenadine HCL by using ionic gelation method.***

Keywords: fexofenadine, Carbopol, nanoparticles, gel, ionic gelation method, topical gel

1. Introduction

Drugs can be delivered through various common routes such as oral, parenteral, Buccal, nasal, vaginal, rectal etc. Most therapeutic peptides and proteins may not be delivered orally, due to rapid degradation in stomach and size limited transport across the epithelia. Rationally these conventional dosage forms of drug delivery has many limitations, which can be potentially overcome by advanced systems of drug delivery such as transdermal drug delivery systems.

Allergies are chiefly originated by a peculiar counter of the immune system that often reacts to a usually innocuous substance in the environment. This innocuous substance can be a pollen, mold, dust, animal hair/fur, food or stings of insects allude to allergens. Allergies can be treated by two types. They are:-

1) Immunotherapy
2) Medication (antihistaminics and deconge stants)

Nanotechnology has a tremendous potential in pharmaceutical industry where it can improve the therapeutic efficacy and reduce toxicity due to improved sustained/ controlled/ prolonged delivery of drugs. There may be concurrent reduction of the dose of drug with enhanced/sustained bioavailability and lowering toxicity. The selection of appropriate method for the preparation of nanoparticles depends on the physicochemical character of the polymer and the drug to be loaded.

Albumin

Albumin is a family of globular proteins, the most common are the serum albumin. All the proteins of the albumin family are water-soluble, moderately soluble in concentrated salt solutions; and experience heat denaturation. Albumin is the most abundant and long lived serum protein, exhibits novel features as a carrier that can greatly enhance the pharmacological actions of therapeutic payloads. Beyond its long standing role as a half -life extender, albumin is emerging as a versatile drug carrier to aid numerous therapeutic agents that have poor Albumin is primarily considered as a popular building block to create nanoparticles for drug delivery purpose. The performance of albumin as a drug carrier can be enhanced by combining proteins with polymers, which allows the design of carriers to encompass a broader spectrum of drugs while features unique to synthetic polymers such as stimuli- responsiveness are introduced.

Nanoparticles

Nanoparticles based of polymer -albumin hybrids can be divided into two classes: one that carries Albumin as a bioactive surface costing and other that uses albumin as a biocompatible, although non-bioactive building block. Nanoparticles with bioactive albumin surface coating can either be prepared by self -assembly of albumin-polymer conjugates or by post coating of existing nanoparticles with albumin.

Topical delivery

Topical delivery features a number of advantages: the ability to deliver drug substance more selectively to a selected site, avoiding fluctuations in drug levels, inter- and intra-patient variations, improved compliance, and an enhanced suitability for self-medication. It is also possible to avoid systemic adverse effects during this way. Besides, by targeting the drug directly to the affected area, the first-pass effect can be reduced14. The transdermal permeation of API depends

mainly on three factors; the mobility of API within the vehicle, the release of API from the vehicle, and permeation of the drug into the skin. These factors affect the thermodynamic activity which drives the drug into the skin and therefore the permeability of the drug within the skin.

2. Materials and Method

Materials used for the preparation of nanoparticles are Fexofenadine HCl, albumin, Sodium tri polyphosphate .The prepared nanoparticles are loaded in a hydrogel and the ingredients used are carbopol, sodium hydroxide, propylene glycol,methanol, methyl paraben.

Preparation of fexofenadine HCL nanoparticles

Accurately weighed amount of drug was taken and dissolved in methanol solution A , then the polymeric solution was prepared by dissolving albumin in pH 6.8 buffer solutionsolution B, the prepared solution B was added to solution A slowly by continuous stirring. After mixing thoroughly the mixture was stirred magnetically followed by drop wise addition of the cross linker and continued stirring for 2-3 min until the drug and polymer are cross linked.

Table 1: Formulation of Nanoparticles

Ingredients	F1	F2	F3	F4	F5	F6
Fexofenadine HCl	2	2	2	2	2	2
Albumin	2	3	2.5	3.5	1.5	2.5
STPP	2	2.5	2.5	3	2	3

Later, the solution was filtered using grade A whattmans filter paper . The precipitate is dried in hit air oven for 45 min, thus the nanoparticles are obtained and are stored in desiccators

Preparation of fexofenadine HCL nanoparticles loaded gel

Accurately weighed quantity of carbopol 940 was dissolved in 10 ml of distilled water (70°c) in beaker A. In another beaker B, 100 mg of nanoparticles were dissolved in 5ml of Propylene glycol. Then,2ml of 10% NaOH and sufficient quantity of methyl paraben was added to a mixture containing nanoparticles. Finally, beaker B containing solution was added into the beaker A. Properly mixed the above mixture and stirred well using mechanical stirrer to get a homogeneous mixture.

Table 2 : Formulation of Gel Using Nanoparticles

Ingredients	G1	G2	G3	G4	G5	G6
Carbopol	1gms	1.5gms	1.75gms	2gms	2.5gms	2.75gms
Propyl paraben	0.2gms	0.2gms	0.2gms	0.2gms	0.2gms	0.2gms
Methyl paraben	0.2gms	0.2gms	0.2gms	0.2gms	0.2gms	0.2gms
Drug nanoparticles	3of F1	3 of F2	3 of F3	3 of F4	3 of F5	3 of F6
Propylene glycol	5ml	5ml	5ml	5ml	5ml	5ml
NaOH	QS	QS	QS	QS	QS	QS

Characterization of Gel Loaded With Nanoparticles

Physical appearance

The formulated gels were inspected visually for its color, consistency and appearance.

Homogeneity

The formulated gels were checked for its homogeneity by visual inspection after filling into a suitable container . The gels were observed for their appearance and presence of any particulate matter.

pH determination

pH of the formulated gel was determined using pH meter and observed readings were noted.

Spreadability

The spreadability (cm) of the formulated gels was determined by placing accurately weighed 1gm of gel between two horizontal glass plates and 500g of weight was applied over the plate for 1min. Later, the spreadability was determined using by measuring the diameter of gel spread over the plate in 1min.

Viscosity

The Viscosity (cps) of the gels prepared was determined by using Brookfield's viscometer. The spindle was rotated at 10r/min and the sample was allowed to settle for 30min at temperature 25°C before the readings were taken.

***In-vitro*drug release study**

In-vitro drug release % was carried out using fabricated vertical Franz diffusion cell apparatus. The cellophane membrane was used for this study. An accurate amount of gel (0.5g) was applied on the cellophane membrane. Entire surface of the membrane was intact with the receptor compartment filled with 20ml phosphate buffer of pH 6.8 as a media for diffusion. The whole assembly was placed on magnetic stirrer and the solution was stirred continuously at 200rpm with the temperature maintained at 37+/- 1°C . The sample (1ml) was withdrawn at a specific time interval and replaced with the same volume of fresh phosphate buffer to maintain the sink conditions. Further suitable dilution of the sample was made and analyzed using UV – Visible spectrophotometer at 220nm.

Stability studies

Prepared fexofenadine HCL nanoparticles loaded formulation were filled in a suitable container and subjected to stability as per ICH guidelines. Formulations were kept in 40°/75%RH, 25°C/ 60% RH, and room temperature for 1month . Samples were evaluated for pH, physical appearance, viscosity, spreadability and drug release

3. Results and Discussion

The nanoparticles of the drug fexofenadine HCL were prepared successfully using the ionic gelation method. Prepared nanoparticles were subjected to various

physicochemical evaluations and the formulation of the topical gel of the fexofenadine HCL nanoparticles.

Determination of drug content

The drug content of the fxfd nanoparticles were found to be 86.63% . The obtained drug content was satisfactory to the formulation of nanoparticles in a suitable dosage form.

Differential scanning colorimetry

DSC analysis was used to evaluate the phase transformation during the formation of nanoparticles. DSC thermogram of fexofenadine HCL (Fig 4.2) showed an endothermic peak at 142.45° corresponding to its melting point. There was a shift in the thermogram observed in the case of formulation of the gel and the peak was showed at 262.2° . The non covalent interaction between the drug and the co former is an indication of the formation of nanoparticles. This non- covalent interaction between drug and the co former occurs due to the formation of hydrogen bond between the polar functional group. This interaction resulted into the change in the molecular structure of the nanoparticles formed which gives a new crystalline form of drug with altered physical properties such as solubility and melting point.

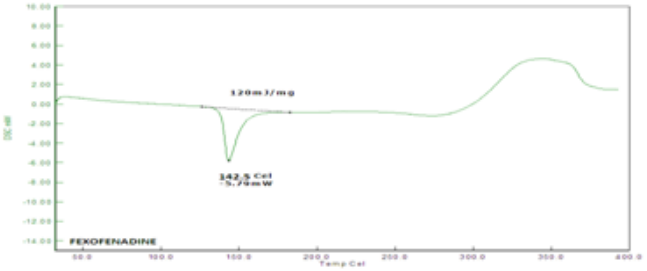


Figure 1: Differential scanning colorimetry of pure fexofenadine HCl

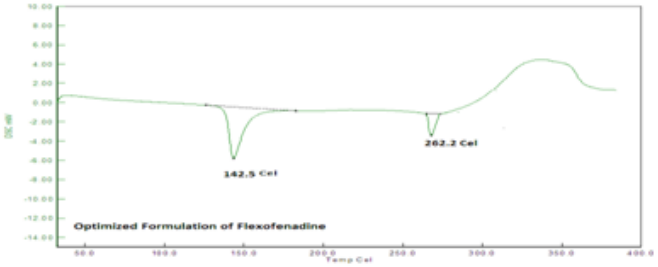


Figure 2: Differential scanning colorimetry of fexofenadine nanoparticles

FTIR spectroscopy study

FTIR is an important medium used for the confirmation of formation of nanoparticles and it showed that the formation of bond between pure durg and polymer. FTIR peaks for pure fexofenadine HCL and fexofenadine HCL nanoparticles was recorded . The principle bands are identified and significant changes were recorded. The pure fexofenadine HCL spectra of IR showed the characteristic peaks which was recorded at 3293.74cm-¹- NH stretching, 2928.84 cm-¹ aromatic, c=0 ketone stretching , 2635cm-¹ ,C= O amide stretching. The IR spectra of the fxfd nanoparticles were showed at the peak at 1703.56Cm-¹ . The change in peak shape , peak intensities , and leak broadening was observed which indicates the formation and confirmation of the fexofenadine HCL nanoparticles with a new crystalline phase4.1.5 In-vitro dissolution study

In-vitro dissolution (%) study of pure fexofenadine HCL and fexofenadine HCL nanoparticles were carried out successfully. The dissolution curve of pure fexofenadine HCL and an fexofenadine HCL nanoparticle in 6.8 pH buffer is shown in figure. It was an evident that the nanoparticles prepared by using albumin clearly showed the improvement in dissolution rate as compared to pure drug.

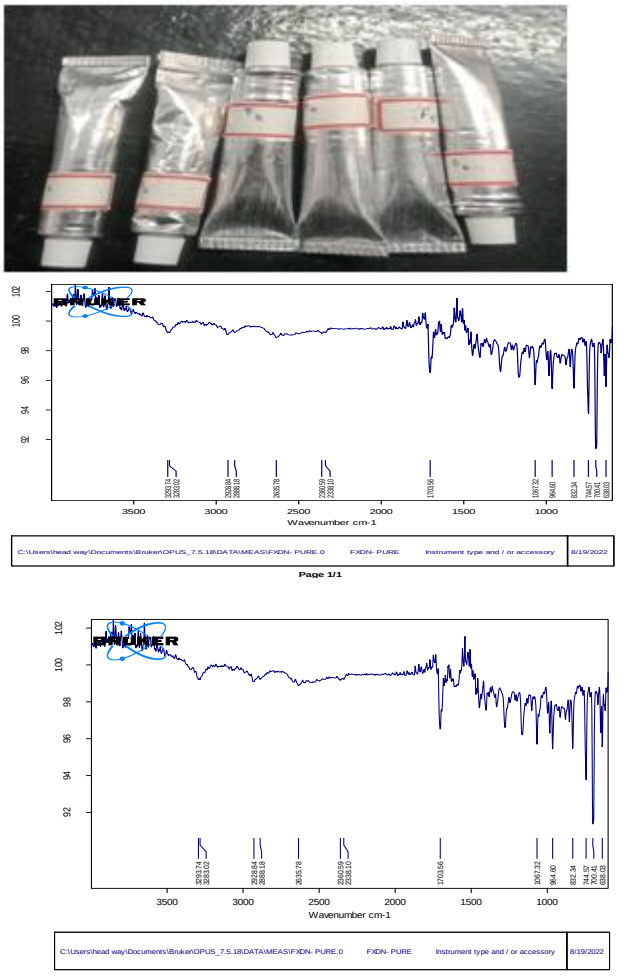


Figure 3, 4: FTIR of fexofenadine HCL and fexofenadine HCl nanoparticles

Evaluation of fexofenadine HCL nanoparticles loaded gel

Physical appearance

The formulated fexofenadine HCL nanoparticles loaded gel were inspected visually. The gel was found to be white in color and smooth appearance.

Figure 5: Formulated nanoparticles gel

Viscosity and pH
The Viscosity and pH of all formulations were determined successfully. The obtained data is given below.

Spreadability (cm)
The spreadability of all the gels was ranging from 4.5cm.to 6.5 cm. It was observed that the formulation F1, F2 and F5 showed higher spreadability, which may be due to an increased concentration of carbopol 940. The spreadability test results are interpreted in the table below

Spreadability of the gel
Result of Viscosity, pH, Spreadability of different preparations

Formulation code	Viscosity (cps)	pH	Spreadability (cm)
F1	571.2	6.4	5.8
F2	563.4	6.9	4.6
F3	390.2	6.3	6.3
F4	456.5	7.0	5.1
F5	525.4	6.7	5.4
F6	516.1	6.5	4.5

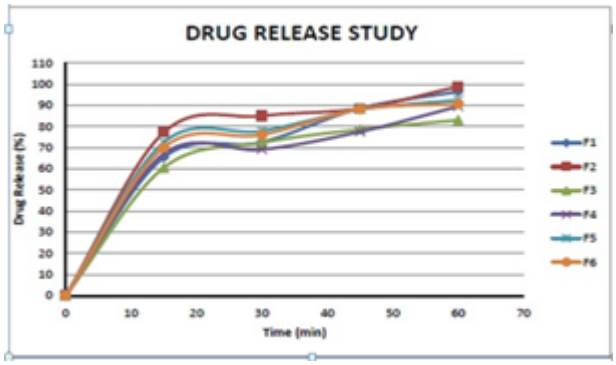
In-vitro drug release (%)
From the drug release study, it was observed that formulation F1, F2 , F5 and F6 showed the drug release from 65 to 98.9 upto 1hour. This might be due to the decrease in the concentration of carbopol 940 from 0.5 to 1.25% .

The gel F3 and F4 showed drug release of 69.5 to 89.5 upto 1hour which is due to the fact that increased concentration of carbopol 940 was led to increasing the viscosity of these formulations which in turn makes the diffusion of drug through the dialysis membrane slower.

Among all the six gels formulated , formulation F2 containing 1.25% of carbopol 940 showed highest drug release of 96.2% and was optimised as the best the drug release profile of fexofenadine HCL is depicted in figure 4.13

Percentage drug release of fexofenadine nanoparticles

Time	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
15	65.4	77.2	60.5	67.05	72.5	70.06
30	72.6	85	72.3	69.08	77.89	76.05
45	88.6	88.5	78.6	77.5	88.06	88.15
60	96.5	98.9	83.02	89.5	92.5	90.6



Stability studies
During the storage of fexofenadine nanoparticles loaded gel, there may be changes in the physicochemical parameters. Hence, the prepared formulations were subjected to the stability studies at room temperature and accelerated condition for a period of 1 month to define the stability. It was found that the fexofenadine nanoparticles loaded gel was stable at both conditions. The obtained data were given in table 4.4

4. Conclusion of Present Work

The fexofenadine HCL shows poor aqueous solubility and oral administration renders low absorption rate and low bioavailability. The aim was to investigate the potential of fexofenadine HCL nanoparticles loaded in gel for topical delivery in order to improve the solubility, thereby increasing the bioavailability of drug. The alternate topical route eliminates oral side effects, skipsfirstpass metabolism and maintains the plasma drug concentration (Cmax) for a longer period of time.

The nanoparticles of fexofenadine HCL and albumin were prepared using ionic gelation method. The prepared nanoparticles exhibit good physicochemical properties such as solubility and dissolution. Solid state characterization of drug and nanoparticles was carried out using DSC and FTIR spectroscopy studies, confirmed the formation of fexofenadine HCL nanoparticles. The altered thermal changes, IR bands along with intensities and change in 20 values in DSC , and FTIR respectively, give the evidence of a new crystalline phase formation. The formulated fxfd nanoparticles were formulated in to topical gel . Carbopol 940 and HPMC were used as a gelling agent as independent variables. F2 formulation was found to be optimised batch and selected variables show a significant effect on the responses such as drug release and spread ability.

From the overall study conducted, we can conclude that the newly developed nanoparticles form of fexofenadine HCL with Albumin showed increased solubility and dissolution rate and it was given in topical formulation to overcome problems pertaining to the oral administration of active pharmaceutical ingredient.

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