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FORMULATION AND *IN VITRO* EVALUATION OF FESOTERODINE FUMARATE SUSTAINED RELEASE TABLETS

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Abstract:

The aim of the present study was to develop Sustained release formulation of Fesoterodine Fumarate to maintain constant therapeutic levels of the drug for over 12 hrs. Here different types of polymers (Locust Bean Gum, Gum Cyamposis, Corn Sugar Gum) were used. Fesoterodine Fumarate dose was fixed as 8 mg. Total weight of the tablet was considered as 100 mg. Polymers were used in the concentration of 10, 20 and 30 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that Among all formulations F2 formulation was considered as optimised formulation. It was shown 99.65% drug release at 12hrs. The optimised formulation F2 was followed Higuchi release kinetics.

Keywords: *Fesoterodine Fumarate, Locust Bean Gum, Gum Cyamposis, Corn Sugar Gum, Sustained release tablets, Natural Polymers.*

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INTRODUCTION:

Sustained release tablets are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect. The advantage of administering a single dose of a drug that is released over an extended period of time to maintain a near-constant or uniform blood level of a drug often translates into better patient compliance, as well as enhanced clinical efficacy of the drug for its intended use.

The first sustained release tablets were made by Howard Press in New Jersy in the early 1950's. The first tablets released under his process patent were called 'Nitroglyn' and made under license by Key Corp. in Florida.

Sustained release, prolonged release, modified release, extended release or depot formulations are terms used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.

The goal in designing sustained or sustained delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, sustained release dosage form is a dosage form that release one or more drugs continuously in predetermined pattern for a fixed period of time, either systemically or to a specified target organ.

Sustained release dosage forms provide a better control of plasma drug levels, less dosage frequency, less side effect, increased efficacy and constant delivery. There are certain considerations for the preparation of extended release formulations:

- If the active compound has a long half-life, it is sustained on its own,
- If the pharmacological activity of the active is not directly related to its blood levels,
- If the absorption of the drug involves an active transport and
- If the active compound has very short half-life then it would require a large amount of drug to maintain a prolonged effective dose.

The above factors need serious review prior to design [1-9]

Sustained release:

During the last two decades there has been remarkable increase in interest in sustained release drug delivery system. This has been due to various factor viz. the prohibitive cost of developing new drug entities, expiration of existing international patents, discovery of new polymeric materials suitable for prolonging the drug release, and the improvement in therapeutic efficiency and safety achieved by these delivery systems. Now-a-days the technology of sustained release is also being applied to veterinary products. These systems also provide a slow release of drug over an extended period of time and also can provide some control, whether this be of a temporal or spatial nature, or both, of drug release in the body, or in other words, the system is successful at maintaining constant drug levels in the target tissue or cells [10,11].

Basic Principle of Drug Release:

In solution, drug diffusion will occur from a region of high concentration to the region of low concentration. This concentration gradient is the driving force for the drug diffusion, out of a system. Water diffuses into the system in analogous manner. There is an abundance of water in the surrounding medium and system should allow water penetration. The inside of the system has low water content initially than the surrounding medium [12].

Fesoterodine, once converted to its active metabolite, 5-hydroxymethyltolterodine, acts as a competitive antagonists at muscarinic receptors. This results in the inhibition of bladder contraction, decrease in detrusor pressure, and an incomplete emptying of the bladder.

For the treatment of overactive bladder (with symptoms of urinary frequency, urgency, or urge incontinence).

MATERIALS AND METHODS:

List of Materials

Fesoterodine Fumarate was a gift sample Provided by Sura Labs, Dilsukhnagar. Locust Bean Gum ,Gum Cyamposis ,Corn Sugar Gum ,PVP K 30 ,Sodium Stearyl Fumarate ,Mannitol were obtained from Merck Specialities Pvt Ltd, Mumbai, India. Aerosil were obtained from Merck Specialities Pvt Ltd, Mumbai, India.

Methodology:

Preparations of Buffers:

Hydrochloric acid solution (0.1N HCL): 8.5 ml of concentrated hydrochloride acid was diluted with distilled water and volume was made up to 1000 ml with distilled water.

Phosphate buffer (6.8 pH): 6.8 grams of potassium di hydrogen phosphate and 10 grams of sodium hydroxide was placed in a 1000 mL volumetric flask. Volume was made up to 1000ml with distilled water. pH was adjusted to 6.8 with dilute sodium hydroxide.

Analytical method development:

a) Determination of absorption maxima:

100 mg of Fesoterodine Fumarate pure drug was dissolved in 100 ml of Methanol (stock solution)10 ml of above solution was taken and make up with 100 ml by using 0.1 N HCL (100 µg/ml).From this 10ml was taken and make up with 100 ml of 0.1 N HCL (10 µg/ml) and pH 6.8 Phosphate buffer UV spectrums was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400 nm.

b)Preparation calibration curve:

100 mg of Fesoterodine Fumarate pure drug was dissolved in 100ml of Methanol (stock solution)10ml of above solution was taken and make up with100ml by using 0.1 N HCL (100µg/ml).From this 10ml was taken and make up with 100 ml of 0.1 N HCL (10µg/ml). The above solution was subsequently diluted with 0.1N HCL to obtain series of dilutions Containing 5,10,15,20 and 25 µg/ml of Fesoterodine Fumarate per ml of solution. The absorbance of the above dilutions was measured at 220nm by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R2) which determined by least-square linear regression analysis. The above procedure was repeated by using pH 6.8 phosphate buffer solutions at 222 nm.

Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy:

The infrared spectrum of the pure drug sample was recorded and the spectral analysis was done. The dry sample of drug was directly placed. The optimised formula was subjected to FT-IR studies, to study the interference of excipients for drug analysis.

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany (Alpha T). The spectra were recorded over the wave number of 4000 cm-1 to 550 cm-1.

Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose:

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$$\mathbf{Tan\ \theta = h / r}$$

Tan θ = Angle of repose
h = Height of the cone ,
r = Radius of the cone base

Table 1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density:

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.

The bulk density was calculated using the formula:

$$\mathbf{Bulk\ Density = M / Vo}$$

Where, M = weight of sample
Vo = apparent volume of powder

Tapped density:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula:

Tap = M / V

Where,

Tap= Tapped Density
M = Weight of sample
V= Tapped volume of powder

Measures of powder compressibility:

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value.

For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

Carr's Index = [(tap - b) / tap] × 100

Where,

b = Bulk Density
Tap = Tapped Density

Table 2: Carr's index value (as per USP)

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Formulation development of Tablets:

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table. The tablets were prepared as per the procedure given below and aim is to prolong the release of Fesoterodine Fumarate. Total weight of the tablet was considered as 100 mg.

Procedure:

1)Fesoterodine Fumarate and all other ingredients were individually passed through sieve no ≠ 60.
2)All the ingredients were mixed thoroughly by triturating up to 15 min.
3)The powder mixture was lubricated with talc.
4)The tablets were prepared by using direct compression method.

Table 3: Formulation composition for tablets

Evaluation of post compression parameters for prepared Tablets

S.NO	USED INGREDIENTS	CATEGORY
1	Fesoterodine Fumarate	DRUG (API)
2	Locust Bean Gum	Natural Polymer
3	Gum Cyamposis	Natural Polymer
4	Corn Sugar Gum	Natural Polymer
5	Mannitol	Diluent
6	Sodium Stearyl Fumarate	Lubricant
7	Aerosil	Glidant
8	PVP K 30	Dry Binder

The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Table 4: Pharmacopoeial specifications for tablet weight variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

Hardness:
Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness:
Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability:
It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = **[(W1-W2) / W] × 100**

Where,

W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

Determination of drug content:
Tablets were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of drug were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with media. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***In vitro* drug release studies Dissolution parameters:**
Apparatus --USP-II, Paddle Method
Dissolution Medium -- 0.1 N HCL, pH 6.8 Phophate buffer
RPM --50
Samplingintervals(hrs)--0.5,1,2,3,4,5,6,7,8,10,11,12
Temperature --37°c + 0.5°c

Procedure:
900 ml 0f 0.1 HCL was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c + 0.5°c. Tablet was placed in the vessel and apparatus was operated for 2 hours and then the media 0.1 N HCL was removed and pH 6.8 phosphate buffer was added process was continued from upto 12 hrs at 50 rpm. At definite time intervals withdrawn 5 ml of sample, filtered and again 5mL media was replaced. Suitable dilutions were done with media and analyzed by spectrophotometrically at respective wavelength using UV-spectrophotometer.

Application of Release Rate Kinetics to Dissolution Data:
Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics: To study the zero–order release kinetics the release rate data ar e fitted to the following equation.

F = Ko t

Where, 'F' is the drug release at time't', and 'Ko' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

Log (100-F) = kt

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

F = k t1/2

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$Mt/ M\infty = K\ tn$$

Where, Mt/ M∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (Mt/ M∞) versus log (time) is linear.

Hixson-Crowell release model:

$$(100-Qt)1/3 = 1001/3– KHC.t$$

Where,

k is the Hixson-Crowell rate constant.

Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).[13,14]

The present study was aimed to developing Sustained release tablets of Fesoterodine Fumarate using various Natural polymers. All the formulations were evaluated for physicochemical properties and in vitro drug release studies.

Analytical Method

Graphs of Fesoterodine Fumarate were taken in Simulated Gastric fluid (pH 1.2) and in p H 6.8 phosphate buffer at 220 nm and 222 nm respectively.

Table 5: Observations for graph of Fesoterodine Fumarate in 0.1N HCl (220nm)

Concentration [µg/ml]	Absorbance
0	0
5	0.12
10	0.248
15	0.361
20	0.482
25	0.61

It was found that the estimation of Fesoterodine Fumarate by UV spectrophotometric method at λmax 220 nm in 0.1N Hydrochloric acid had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 5-25µg/ml. The regression equation generated was y = 0.024x+0.00

RESULTS AND DISCUSSION:

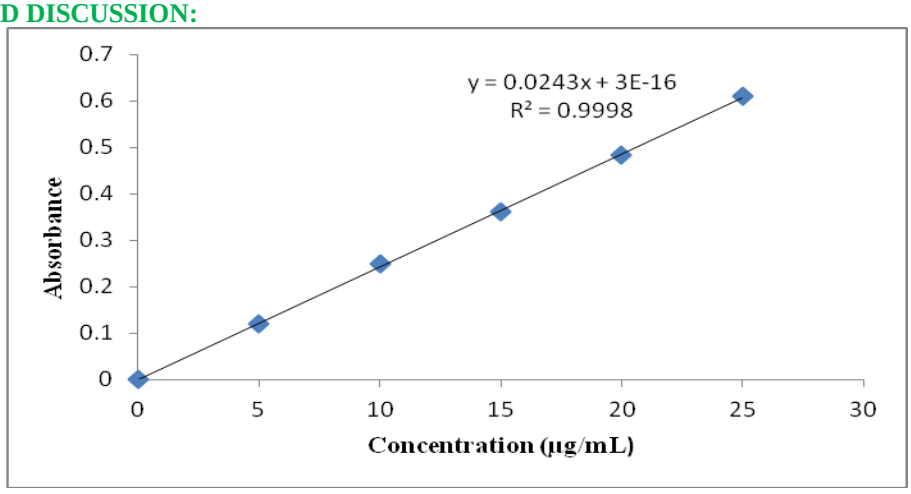

Fig. 1: Standard graph of Fesoterodine Fumarate in 0.1N HCl

Table 6: Observations for graph of Fesoterodine Fumarate in p H 6.8 phosphate buffer (222nm)

Concentration [µg/ml]	Absorbance
0	0
5	0.181
10	0.362
15	0.543
20	0.712
25	0.867

It was found that the estimation of Fesoterodine Fumarate by UV spectrophotometric method at λmax222 nm in pH 6.8 Phosphate buffer. had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 5-25µg/ml. The regression equation generated was y = 0.035x + 0.007.

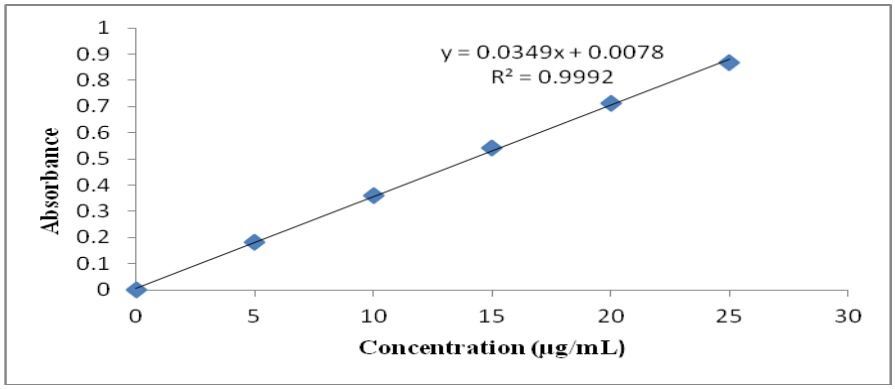

Fig.2: Standard graph of Fesoterodine Fumarate pH 6.8 phosphate buffer (222nm)

Drug – Excipient compatability studies
Fourier Transform-Infrared Spectroscopy:

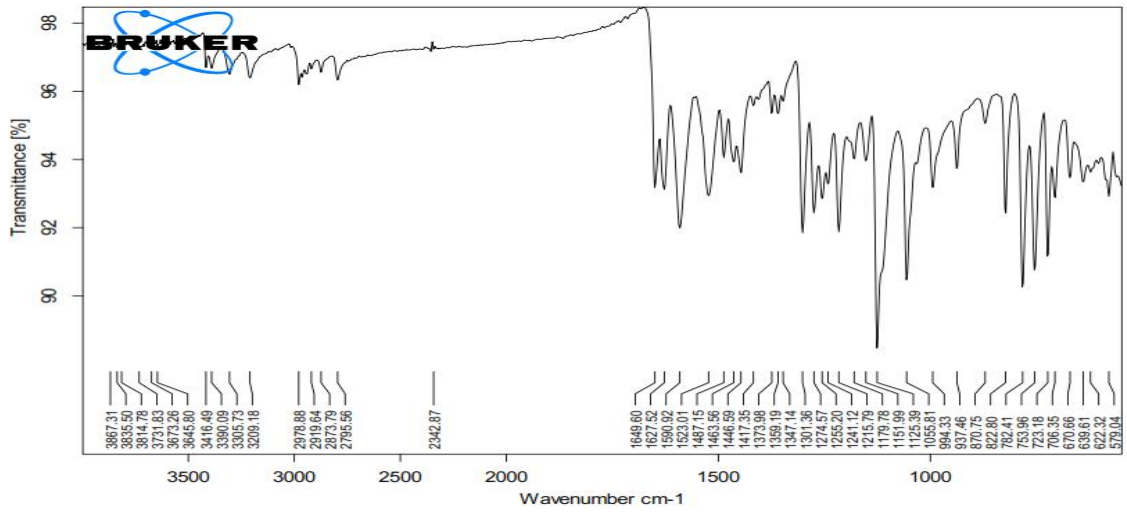

Fig3: FT-IR Spectrum of Fesoterodine Fumarate pure drug

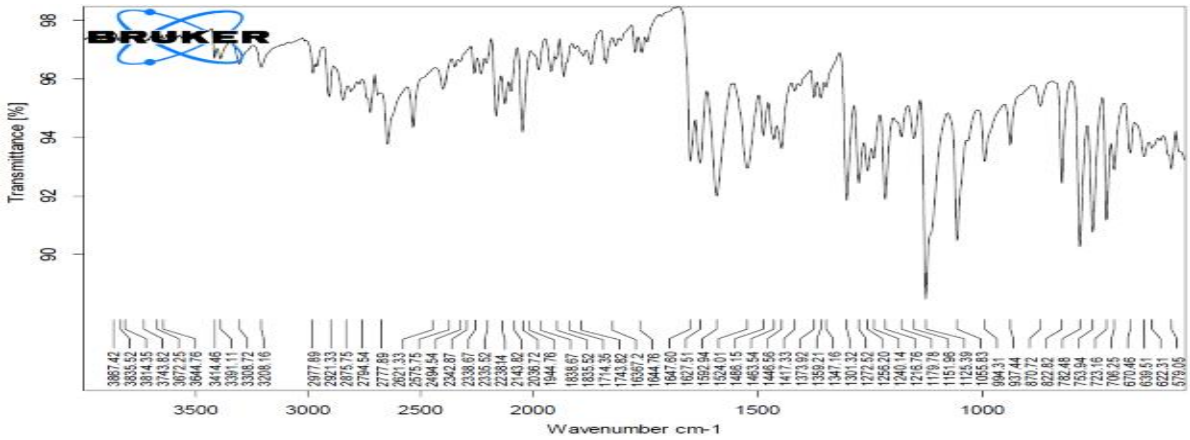

Fig4: FT-IR Spectrum of Optimised Formulation

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

Fesoterodine Fumarate are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

Preformulation parameters of powder blend

Table 7: Pre-formulation parameters of Core blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	25.01	0.49	0.57	14.03	1.16
F2	26.8	0.56	0.67	16.41	1.19
F3	27.7	0.52	0.64	18.75	1.23
F4	25.33	0.54	0.64	15.62	1.18
F5	25.24	0.53	0.65	18.46	1.22
F6	28.12	0.56	0.66	15.15	1.17
F7	27.08	0.58	0.69	15.94	1.18
F8	25.12	0.48	0.57	15.78	1.18
F9	26.45	0.54	0.65	16.92	1.2

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.48 to 0.58 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.57 to 0.69 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 14 to 18 which shows that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0 to 1.25 indicating the powder has good flow properties.

Quality Control Parameters For tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression coated tablet.

Table 8 : *In vitro* quality control parameters for tablets

Formulation codes	Average Weight (mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	99.5	4.5	0.50	3.8	99.8
F2	101.2	4.5	0.51	3.9	99.1
F3	99.5	4.4	0.51	3.9	99.8
F4	100.6	4.5	0.55	3.9	99.7
F5	101	4.4	0.56	3.7	99.3
F6	100	4.5	0.45	3.7	99.5
F7	99.5	4.1	0.51	3.4	99.8
F8	99.5	4.3	0.49	3.7	99.8
F9	100	4.5	0.55	3.6	99.4

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

***In Vitro* Drug Release Studies**

Table 9: Dissolution Data of Fesoterodine Fumarate Tablets Prepared With Locust Bean Gum Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED		
	F1	F2	F3
0	0	0	0
0.5	28.18	23.93	18.4
1	34.47	31.68	22.3
2	50.38	39.77	29.5
3	79.33	44.51	32.3
4	84.38	52.97	41.3
5	89.45	59.84	52.6
6	93.4	65.81	59.4
7	96.8	70.91	65.2
8	99.2	78.29	72.3
9		83.94	79.5
10		89.88	82.5
11		93.82	89.1
12		99.65	91.2

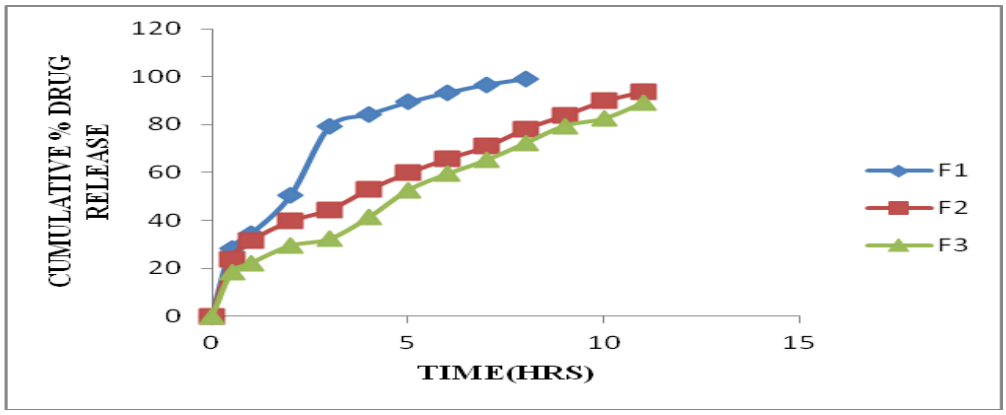

Fig. 5: Dissolution profile of Fesoterodine Fumarate (F1, F2, F3 formulations).

Table 10: Dissolution Data of Fesoterodine Fumarate Tablets Prepared With Gum Cyamposis In Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED		
	F4	F5	F6
0	0	0	0
0.5	37.25	34.24	30.62
1	48.26	43.37	34.86
2	54.16	48.63	40.35
3	71.01	65.04	48.45
4	88.26	70.25	54.80
5	99.10	87.33	59.25
6		94.41	65.24
7		98.56	70.73
8			78.34
9			85.52
10			99.17

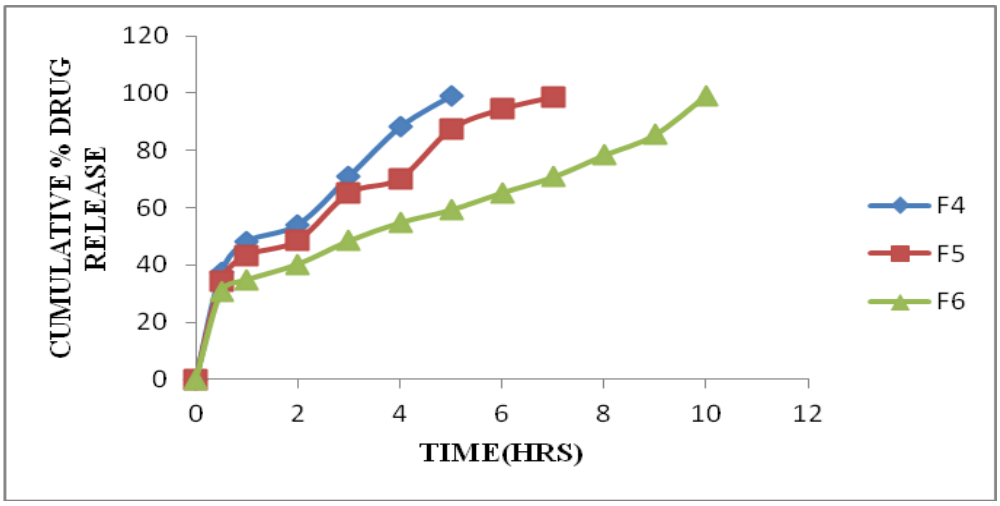

Fig.6: Dissolution profile of Fesoterodine Fumarate (F4, F5, F6 formulations)

Table 11: Dissolution Data of Fesoterodine Fumarate Tablets Prepared With Corn Sugar Gum In Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED		
	F7	F8	F9
0	0	0	0
0.5	8.2	3.2	1.9
1	13.2	8.9	2.2
2	16.3	12.3	8.3
3	22.4	17.4	12.3
4	26.3	19.3	17.4
5	29.5	22.4	19.3
6	32.8	25.6	22.4
7	38.4	32.3	25.6
8	42.5	37.6	32.9
9	48.15	42.8	37.5
10	56.36	52.6	42.7
11	73.46	62.3	52.3
12	85.51	72.3	62.8

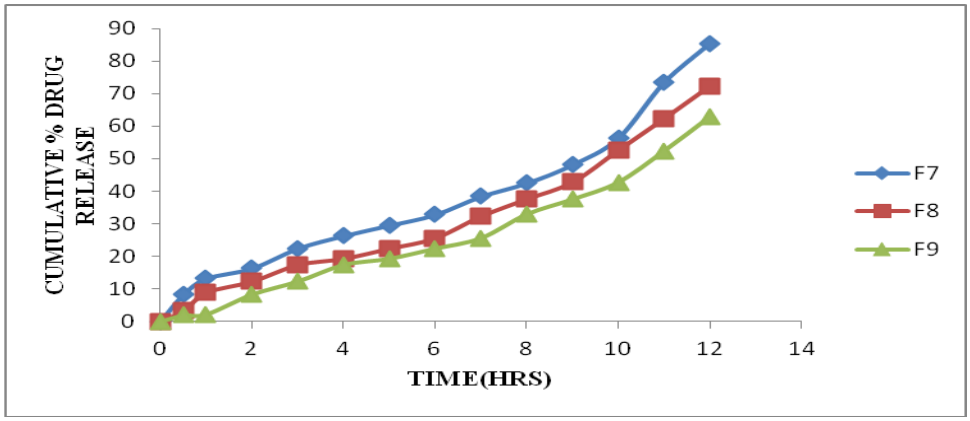

Fig .7: Dissolution profile of Fesoterodine Fumarate (F7, F8, F9 formulations) From the dissolution data, it was revealed that formulations prepared with Gum Cyamposis did not retard the drug release up to 12 hrs. Hence those formulations did not take into consideration.

Formulations prepared with Corn Sugar Gum retard the drug release more than 12hrs. These formulations also did not take into consideration.

Formulations prepared with Locust Bean Gum were revealed that increase in the concentration retards the drug release. Among all formulations F2 formulation was considered as optimised formulation. It was shown 99.65% drug release at 12hrs.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Table 12 : Release kinetics data for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining
0	0	0			2.000				100
23.93	0.5	0.707	1.379	-0.220	1.881	47.860	0.0418	-0.621	76.07
31.68	1	1.000	1.501	0.000	1.835	31.680	0.0316	-0.499	68.32
39.77	2	1.414	1.600	0.220	1.780	19.885	0.0251	-0.400	60.23
44.51	3	1.732	1.648	0.477	1.744	14.837	0.0225	-0.352	55.49
52.97	4	2.000	1.724	0.602	1.672	13.243	0.0189	-0.276	47.03
59.84	5	2.236	1.777	0.699	1.604	11.968	0.0167	-0.223	40.16
65.81	6	2.449	1.818	0.778	1.534	10.968	0.0152	-0.182	34.19
70.91	7	2.646	1.851	0.845	1.464	10.130	0.0141	-0.149	29.09
78.29	8	2.828	1.894	0.903	1.337	9.786	0.0128	-0.106	21.71
83.94	9	3.000	1.924	0.954	1.206	9.327	0.0119	-0.076	16.06
89.88	10	3.162	1.954	1.000	1.005	8.988	0.0111	-0.046	10.12
93.82	11	3.317	1.972	1.041	0.791	8.529	0.0107	-0.028	6.18
99.65	12	3.464	1.998	1.079	-0.456	8.222	0.0100	-0.002	0.35

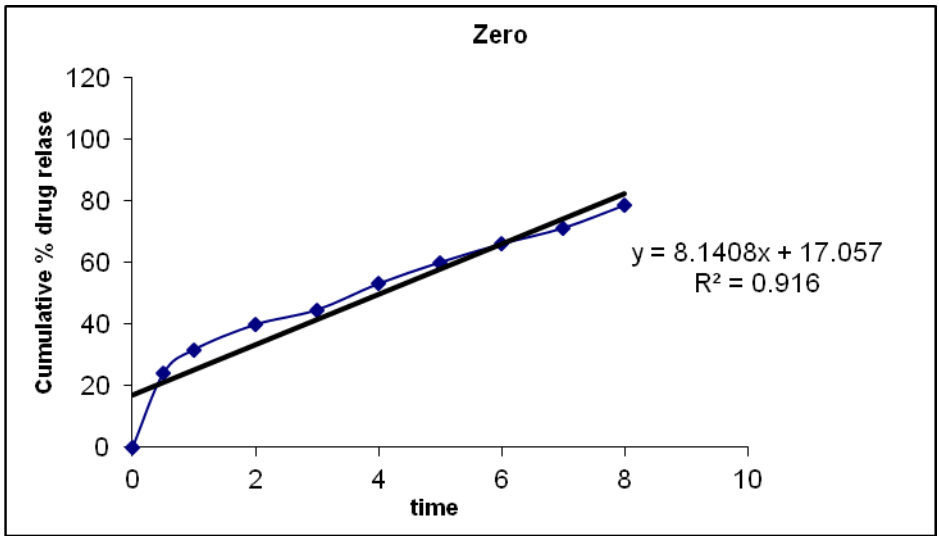

Fig.8 : Zero order release kinetics graph

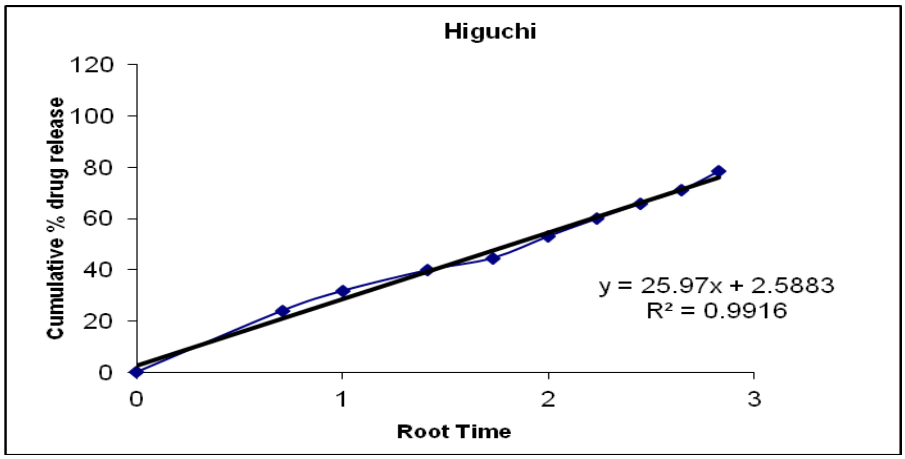

Fig.9 : Higuchi release kinetics graph

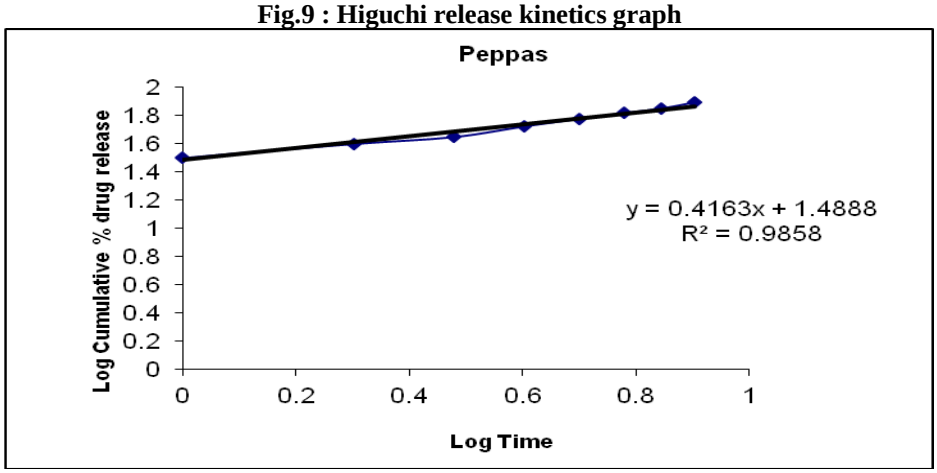

Fig 10: Kars mayer peppas graph

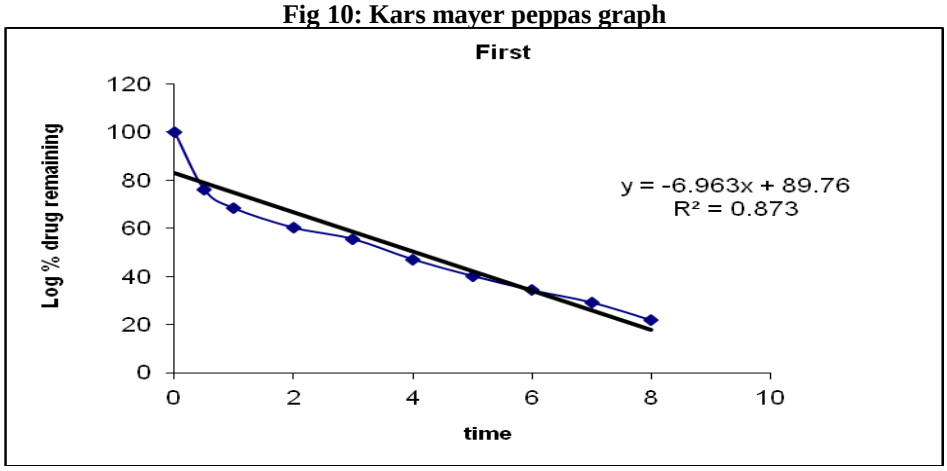

Fig11: First order release kinetics graph

From the above graphs it was evident that the formulation F2 was followed Higuchi release kinetics.

CONCLUSION:

In the present research work the sustained release matrix formulation of Fesoterodine Fumarate by using various polymers. Initially analytical method development was done for the drug molecule. Absorption maxima were determined and calibration curve was developed by using different concentrations.

The formulation was developed by using various polymers such as Locust Bean Gum, Gum Cyamposis, Corn Sugar Gum. The formulation blend was subjected to various preformulation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations prepared by using Gum Cyamposis were unable retard drug

release up to 12 hours. Hence those formulations did not take into consideration. Formulations prepared with Corn Sugar Gum retard the drug release more than 12 hrs. These formulations also did not take into consideration. Formulations prepared with Locust Bean Gum were revealed that increase in the concentration retards the drug release. Among all formulations F2 formulation was considered as optimised formulation. It was shown 99.65% drug release at 12hrs. The optimised formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed Higuchi mechanism of drug release.

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