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Formulation, Evaluation and Optimization of Nitrofurantoin Delayed Release Matrix Tablets

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Abstract: The aim of the present work was to develop an extended-release dosage form Nitrofurantoin tablets were prepared using hydrophobic and hydrophilic polymers like Badham Gum, Cashew nut tree gum and synthetic polymers Eudragit L- 100 and HPMC K4M, prepared by direct compression method and evaluated for various pre and post compression parameters. Hydrophobic matrix tablets failed to prolong the drug release, whereas Hydrophilic based matrix tablets showed good drug release. Whereas from the dissolution studies it was evident that the formulation (F7) showed better and desired drug release pattern i.e., 99.10 % in 12 hours. It contains the Eudragit L-100 as extended release material. It followed peppas release kinetics mechanism.

Keywords: Nitrofurantoin, Badham Gum, Cashew nut tree gum, Eudragit L-100, HPMC K4M, direct compression and Extended release system.

1. INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes. All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of the mode of delivery (Immediate, Extended or Controlled release) and the design of dosage forms (either solid, dispersion, or liquid), must be developed within the intrinsic characteristics of GI physiology.

A drug delivery system is defined as a formulation or a device that enables the introduction of a therapeutic substance in the body and improves its efficacy and safety by controlling the rate, time, and place of release of drugs in the body. This process includes the administration of the therapeutic product, the release of the active ingredients by the product, and the subsequent transport of the active ingredients across the biological membranes to the site of action. The term therapeutic substance also applies to an agent such as gene therapy that will induce in vivo production of the active therapeutic agent. Drug delivery system is an interface between the patient and the drug. It may be a formulation of the drug to administer it for a therapeutic purpose or a device used to deliver the drug. This distinction between the drug and the device is important, as it is the criterion for regulatory control of the delivery 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 in to better patient compliance, as well as enhanced clinical efficacy of the drug for its intended use.

System by the drug or medicine control agency. If a device is introduced into the human body for purposes other than drug administration, such as therapeutic effect by a physical modality or a drug may be incorporated into the device for preventing complications resulting from the device, it is regulated strictly as a device. Traditional drug delivery system has been characterized by immediate release and repeated dosing of the drug which might lead to the risk of dose fluctuation, this arises the need of a formulation with control release that maintain a near-constant or uniform blood level. The desire 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. Sustained release, sustained action, prolong action, controlled release, extended action, depot are terms used to identify drug delivery systems that are designed to achieve prolong therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose.

Oral administration is the mainstay of antiepileptic drug (AED) delivery for patients with chronic epilepsy.[1] Efforts to enhance the ease of administration are important because lack of adherence or partial adherence to medication can have immediate detrimental consequences, such as uncontrolled or recurrent seizures,[2] or can lead to adverse effects (AEs) associated with restarting a previous dose without titration.

Some drugs are inherently long lasting and require only once a day oral dosing to sustain adequate drug blood levels and the desired therapeutic effect. These drugs are formulated in the conventional manner in the form of immediate release dosage forms. However, many other drugs are not inherently long lasting and require multiple daily dosing to achieve the desired therapeutic results. Multiple daily dosing is inconvenient for the patient and can result in missed doses, made up doses and non compliance with the regimen. When conventional immediate-release dosage forms are taken on schedule and more than once daily, they cause sequential therapeutic blood level peaks and valleys (troughs) associated with the administration of each dose. However, when doses are not administered on schedule, the resulting peaks and valleys reflect less than optimum drug therapy. For example, if doses are administered too frequently, minimum toxic concentrations of drug may be reached, resulting in toxic side effects. If doses are missed, periods of sub therapeutic drug blood levels or those below the minimum effective concentration may result, with no benefit to the patient. Extended-release tablets and capsules are commonly taken only once or twice daily, compared to their counterpart conventional forms which may have to be taken three or four times daily to achieve the same therapeutic effect. Typically, extended release products provide an immediate release of drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period. The sustained plasma drug levels provided by extended release products often at times eliminate the need for night dosing which benefits not only the patient but also the caregiver. It form produces wide range of fluctuation in drug concentration in the blood stream and tissues with consequent undesirable toxicity and poor efficiency. The maintenance of concentration of drug in plasma within therapeutic index is very critical for effective treatment.

METHODOLOGY

7.1. Analytical method development:

Buffer Preparation:

Preparation of 0.2M Potassium dihydrogen orthophosphate solution: Accurately weighed 27.218 gm of monobasic potassium dihydrogen orthophosphate was dissolved in 1000mL of distilled water and mixed.

Preparation of 0.2M sodium hydroxide solution: Accurately weighed 8 gm sodium hydroxide pellets were dissolved 1000ml of distilled water and mixed.

Preparation of pH 6.8 Phosphate buffer: Accurately measured 250ml of 0.2M potassium Dihydrogen ortho phosphate and 112.5 ml 0.2M NaOH was taken into the 1000ml volumetric flask. Volume was made up to 1000ml with distilled water.

a) Determination of absorption maxima:

100mg of Nitrofurantoin pure drug was dissolved in 100ml of 0.1N HCL (stock solution-1). 10ml of above solution was taken and make up with 100 ml by using 0.1 N HCL (stock solution-2 i.e 100µg/ml). From this 10ml was taken and make up with 100 ml of 0.1 N HCL (10µg/ml). Scan the 10µg/ml using Double beam UV/VIS spectrophotometer in the range of 200 – 400 nm.

b) Preparation calibration curve:

100mg of Nitrofurantoin pure drug was dissolved in 15ml of Ethanol and volume make up to 100ml with 0.1N HCL (stock solution-1). 10ml of above solution was taken and make up with100ml by using 0.1 N HCl (stock solution-2 i.e 100µg/ml). From this take 0.2, 0.4, 0.6, 0.8 and 1 ml of solution and make up to 10ml with 0.1N HCL to obtain 2, 4, 6, 8 and 10 µg/ml of Nitrofurantoin per ml of solution. The absorbance of the above dilutions was measured at 360nm 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 (R^2) which determined by least-square linear regression analysis. The above procedure was repeated by using pH 6.8 phosphate buffer solutions.

7.2 Formulation development of Extended release Tablets:

All the formulations were prepared by direct compression method. The compositions of different formulations are given in Table 7.1. The tablets were prepared as per the procedure given below and aim is to prolong the release of Nitrofurantoin.

Procedure:

1. Nitrofurantoin 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 7.1: Formulation of Extended release tablets

INGREDIENTS (MG)	FORMULATION CODES											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Nitrofurantoin	240	240	240	240	240	240	240	240	240	240	240	240
Badham Gum	100	200	300	-	-	-	-	-	-	-	-	-
Cashew nut tree gum	-	-	-	100	200	300	-	-	-	-	-	-
Eudragit L- 100	-	-	-	-	-	-	100	200	300	-	-	-
HPMC K4M	-	-	-	-	-	-	-	-	-	100	200	300
PVP K 30	10	10	10	10	10	10	10	10	10	10	10	10
MCC102	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Mg. stearate	8	8	8	8	8	8	8	8	8	8	8	8
Talc	9	9	9	9	9	9	9	9	9	9	9	9
Total Weight (mg)	650	650	650	650	650	650	650	650	650	650	650	650

7.3 Evaluation Parameters

7.3.1 Pre Compression parameters

Bulk density (D_B)

Bulk density is the ratio between a given mass of the powder and its bulk volume.

Bulk density = Mass of Powder / Bulk volume of the powder

Bulk density (D_B) = W / V_0

Procedure: An accurately weighed quantity of granules (w) (which was previously passed through sieve No: 40) was carefully transferred into 250 ml measuring cylinder and measure the bulk volume.

Tapped Density (D_T)

Tapped density is the ratio between a given mass of powder (or) granules and the constant (or) fixed volume of powder or granules after tapping.

Procedure: An accurately weighed quantity of granules (w) (which was previously passed through sieve No: 40) was carefully transferred into 250 ml measuring cylinder and the cylinder was tapped on a wooden surface from the height of 2.5 cm at two second intervals. The tapping was continued until no further change in volume (until a constant volume) was obtained (V_f). The tapped density was calculated by using the formula

Tapped density = mass of the powder/ tapped volume

Tapped density (D_T)=W/V_f

Hausner's ratio

Hausner's ratio[47] is an indirect index of ease of powder flow and was calculated by the formula,

$$\textbf{Hausner ratio}\ \frac{Dt}{Db}\quad \textbf{ratio} = D_T/D_B$$

Where, D_T is the tapped density

D_B is the bulk density

Compressibility index

Compressibility index (CI) was determined by measuring the initial volume (V_o) and final volume (V_f) after hundred tapping's of a sample in a measuring cylinder. It indicates the powder flow properties and expressed in terms of percentage and given in table no. 14 and calculated by using the formula

% Compressibility index = V_o - V/V_o x 100

Angle of repose

Angle of repose was measured by fixed funnel method. It determines flow property of the powder. It is defined as maximum angle formed between the surface of the pile of powder and the horizontal plane.

The powder was allowed to flow through the funnel fixed to a stand at definite height (h). By measuring the height and radius of the heap of powder formed (r), angle of repose was calculated by using formula given below and the calculated values obtained was shown in table no. 14

$$\theta = \tan^{-1} (h / r)$$

Where, θ is the angle of repose

h is the height in cm

r is the radius in cm

Flow property

Table 7.2: The flow property of powder blend

Flow property	Angle of repose	Compressibility index (%)	Hausner's ratio
Excellent	25-30	<10	1.00-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very poor	56-65	32-37	1.46-1.59
Very very poor	>66	>38	>1.60

7.3.2 Post Compression parameters

Weight variation test

Twenty tablets were randomly selected and weighed, to estimate the average weight and that were compared with individual tablet weight. The percentage weight variation was calculated as per Indian Pharmacopoeial Specification. Tablets with an average weight 250 mg so the % deviation was ±5 %.

Table 7.3: IP standards of uniformity of weight

S. No.	Average weight of tablet	% of deviation
1	≤ 80 mg	10
2	> 80 mg to <250 mg	7.5
3	≥ 250 mg	5

Friability test

Twenty tablets were weighed and subjected to drum of friability test apparatus. The drum rotated at a speed of 25 rpm. The friabilator was operated for 4 minutes and reweighed the tablets. % loss (F) was calculated by the following formula.

$F = 100 (W0-W)/W0$

Where W0 = Initial weight, W = Final weight

Hardness test

The hardness of tablets was measured by using Monsanto hardness tester. The results were complies with IP specification.

Thickness test

The rule of physical dimension of the tablets such as sizes and thickness is necessary for consumer acceptance and maintain tablet uniformity. The dimensional specifications were measured by using screw gauge. The thickness of the tablet is mostly related to the tablet hardness can be used as initial control parameter.

Drug content

The amount of drug in tablet was important for to monitor from tablet to tablet, and batch to batch is to evaluate for efficacy of tablets. For this test, take ten tablets from each batch were weighed and powdered. Weighed equivalent to the average weight of the tablet powder and transferred into a 100 ml volumetric flask and dissolved in a suitable quantity of media. The solution was made up to the mark and mixed well. Then filter the solution. A portion of the filtrate sample was analyzed by UV spectrophotometer.

***In vitro* drug release studies**

Apparatus -- USP-II, Paddle Method

Dissolution Medium -- 0.1 N HCl, p H 6.8 Phosphate buffer
RPM -- 50
Sampling intervals (hrs) -- 0.5, 1, 2, 3, 4, 5, 6, 7, 8,9, 10, 11 and 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 media 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. Then 0.1 N HCl was replaced with pH 6.8 phosphate buffer and process was continued up to 12 hrs at 50 rpm. At specific time intervals, withdrawn 5 ml of sample and again 5ml media was added to maintain the sink condition. Withdrawn samples were analyzed at wavelength of drug using UV-spectrophotometer.

7.4 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.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_o' 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.

$$M_t/ M_\infty = K\ t^n$$

Where, M_t/ 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 (M_t/ M_∞) versus log (time) is linear.

7.4. Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy:

Drug excipient interaction studies are significant for the successful formulation of every dosage form. Fourier Transform Infrared (FTIR) Spectroscopy studies were used for the assessment of physicochemical compatibility and interactions, which helps in the prediction of interaction between drug and other excipients. In the current study 1:1 ratio was used for preparation of physical mixtures used for analyzing of compatibility studies. FT-IR studies were carried out with a bruker FTIR facility.

8. RESULTS AND DISCUSSION

The present work was designed to developing extended tablets of Nitrofurantoin using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

8.1 Analytical Method

8.1.1 Standard graph of Nitrofurantoin in 0.1N HCl:

The scanning of the 10µg/ml solution of Nitrofurantoin in the ultraviolet range (200-400 nm) against 0.1 N HCl blank gave the λ_{max} as 360nm. The standard concentrations of Nitrofurantoin (2-10µg/mL) prepared in 0.1N HCl showed good linearity with R^2 value of 0.998, which suggests that it obeys the Beer-Lamberts law.

Table 8.1: Standard curve of Nitrofurantoin in 0.1N HCl

Concentration (µg/ mL)	Absorbance
0	0
2	0.128
4	0.254

6	0.376
8	0.481
10	0.599

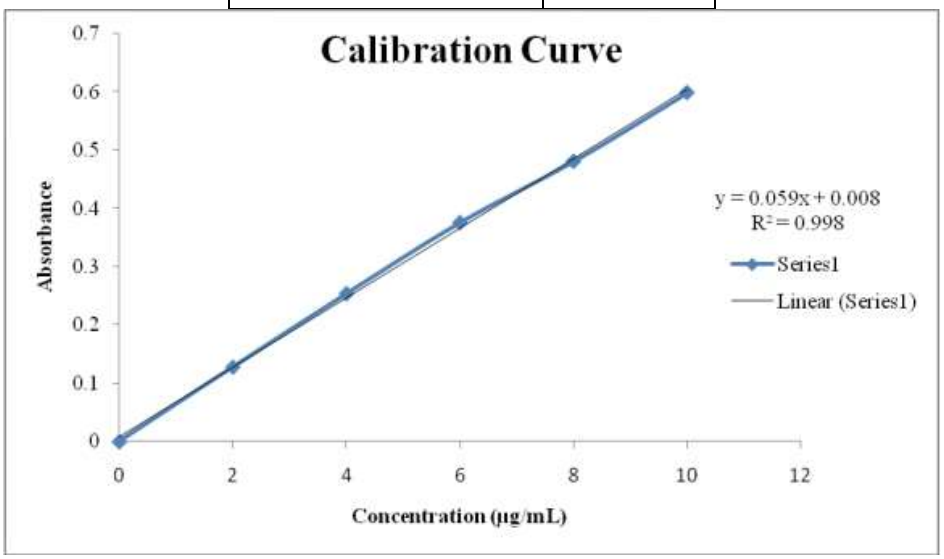

Fig. 8.1: Calibration curve of Nitrofurantoin in 0.1 N HCl at 360 nm

8.1.2 Standard Curve of Nitrofurantoin in Phosphate buffer pH 6.8

The scanning of the 10µg/ml solution of Nitrofurantoin in the ultraviolet range (200-400nm) against 6.8 pH phosphate buffer as blank gave the λ_{max} as 362 nm. The standard concentrations of Nitrofurantoin (2-10µg/ml) prepared in 6.8 pH phosphate buffer showed good linearity with R^2 value of 0.999, which suggests that it obeys the Beer-Lamberts law.

Table 8.2: Standard curve of Nitrofurantoin in Phosphate buffer pH 6.8

Concentration (µg / ml)	Absorbance
0	0
2	0.149
4	0.269
6	0.412
8	0.541
10	0.678

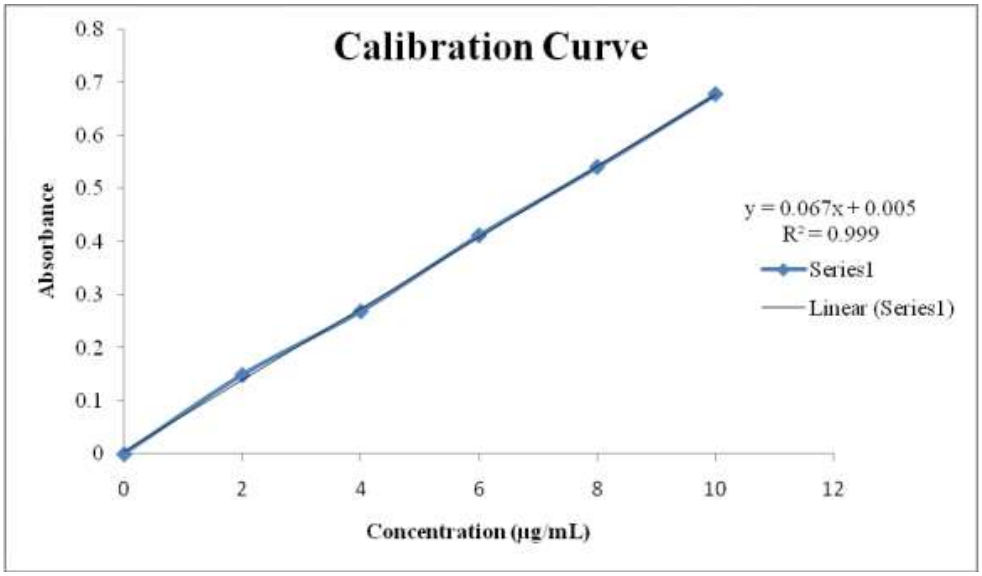

Fig.8.2: Calibration of Nitrofurantoin in Phosphate buffer pH 6.8

8.2 EVALUATION PARAMETERS

8.2.1 Pre-compression parameters

Table 8.3: Pre-compression parameters of powder blend

Formulation Code	Pre-compression parameters of powder blend				
	Angle of Repose	Bulk density (gm/cm^3)	Tapped density (gm/ cm^3)	Carr's index (%)	Hausner's Ratio
F1	25.8^0	0.532	0.657	19.45	1.17
F2	27.5^0	0.476	0.594	25.22	1.24
F3	29.5^0	0.456	0.633	27.51	1.38
F4	29.7^0	0.488	0.685	24.84	1.40
F5	29.9^0	0.461	0.661	27.75	1.43
F6	26.8^0	0.588	0.720	22.24	1.22
F7	27.3^0	0.567	0.705	18.33	1.24
F8	28.4^0	0.543	0.711	17.13	1.30
F9	29.6^0	0.477	0.660	23.52	1.38
F10	30.5^0	0.449	0.654	21.44	1.45
F11	30.3^0	0.484	0.698	18.71	1.44
F12	29.2^0	0.503	0.685	17.83	1.36

Tablet powder blend was subjected to various pre-compression parameters. The angle of repose values was showed from 25.8^0 to 30.5^0; it indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.449 -0.588 (gm/cm^3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.594 - 0.720 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 17.13 to 27.75 which showed that the powder has good flow properties. All the formulations were showed the hausner ratio ranging from 1.17 to 1.45 indicating the powder has good flow properties.

8.2.2 Post Compression parameters for tablets

Table 8.4: Post compression parameters of tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	648.53	5.2	0.24	5.15	98.32
F2	647.82	4.9	0.63	5.65	97.56
F3	649.31	4.6	0.41	5.41	98.75

F4	646.96	5.1	0.46	5.82	98.11
F5	649.20	5.8	0.30	5.44	98.24
F6	647.18	4.7	0.42	5.50	98.57
F7	648.37	4.5	0.21	5.82	98.46
F8	649.56	5.0	0.46	5.46	97.20
F9	648.75	4.3	0.52	5.28	96.38
F10	647.60	4.9	0.64	5.19	97.90
F11	648.10	5.2	0.42	5.22	98.51
F12	649.83	4.1	0.16	5.64	95.72

Weight variation and thickness: All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 8.4. The average tablet weight of all the formulations was found to be between 646.96 to 649.83**.** The maximum allowed percentage weight variation for tablets weighing >650 mg is 1.5% and no formulations are not exceeding this limit. Thus all the formulations were found to comply with the standards given in I.P. And thickness of all the formulations was also complying with the standards that were found to be between 5.15 to 5.82.

Hardness and friability: All the formulations were evaluated for their hardness, using monsanto hardness tester and the results are shown in table 8.4. The average hardness for all the formulations was found to be between **(**4.1 to 5.8**)** Kg/cm^2 which was found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using roche friabilator and the results were shown in table 8.4. The average percentage friability for all the formulations was between 0.16 and 0.64, which was found to be within the limit.

Drug content: All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 8.4. The drug content values for all the formulations were found to be in the range of **(**95.72to 98.75**).** According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the FDT formulations comply with the standards given in IP.

In vitro drug release studies

The formulations prepared with different natural polymers by wet granulation method. The tablets dissolution study was carried out in paddle dissolution apparatus using 0.1N HCl for 2 hours and 6.8 pH phosphate buffers for remaining hours as a dissolution medium.

Table 8.5: Dissolution Data of Nitrofurantoin Tablets

TIME (H)	CUMULATIVE PERCENT DRUG RELEASED											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	10.58	14.79	18.58	21.51	08.85	11.38	33.60	17.86	10.31	12.59	20.15	07.51
1	18.31	16.14	20.89	27.37	12.43	16.52	38.19	20.62	15.10	20.13	23.96	16.39
2	26.15	28.70	28.37	30.14	19.99	21.81	49.52	27.31	22.68	28.35	30.36	21.04
3	32.28	36.57	35.21	43.71	26.51	27.68	53.96	30.53	30.78	32.52	35.98	27.58
4	40.98	39.96	42.79	48.96	31.97	35.50	60.37	37.94	35.48	38.98	41.99	34.65
5	45.65	44.25	47.65	57.21	38.74	37.49	67.82	48.36	41.94	43.11	45.69	41.21
6	51.23	53.57	56.35	60.15	43.59	43.21	72.65	53.78	46.87	45.95	50.99	46.57
7	63.82	58.12	63.17	65.89	50.24	48.15	79.29	60.33	52.10	49.31	57.10	52.78
8	70.65	61.24	68.20	70.64	56.30	53.25	81.66	63.39	60.87	54.68	62.98	60.14
9	76.87	66.59	79.48	75.40	61.25	57.92	84.25	67.59	65.85	58.29	65.74	63.97
10	80.41	70.17	85.90	85.76	66.71	62.79	90.33	71.48	70.32	66.91	79.90	68.72
11	84.05	89.56	90.10	91.24	72.95	65.57	96.21	76.55	73.92	78.39	85.81	71.49
12	90.79	96.32	98.14	96.46	87.20	71.83	99.10	84.95	79.40	81.89	97.89	75.35

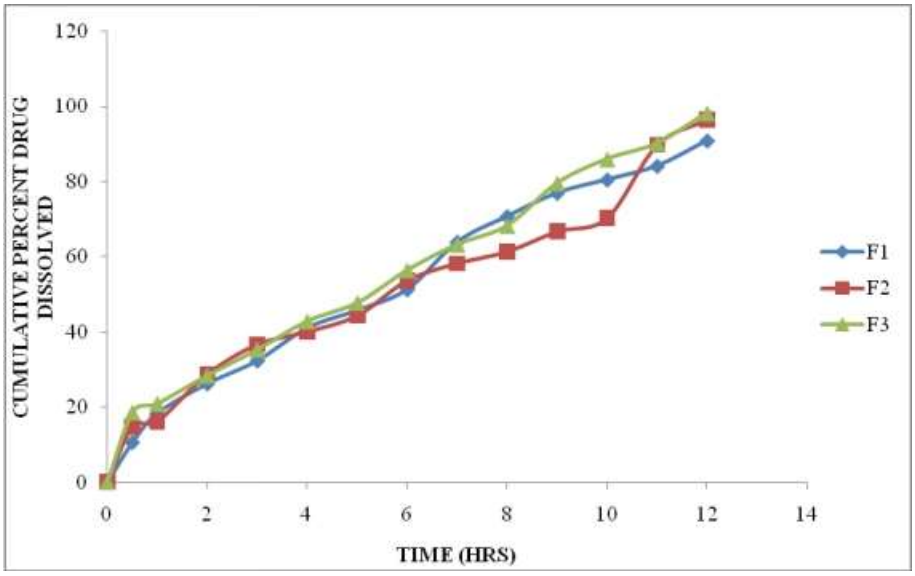

Fig 8.3: Dissolution study of Nitrofurantoin Extended tablets (F1 to F3)

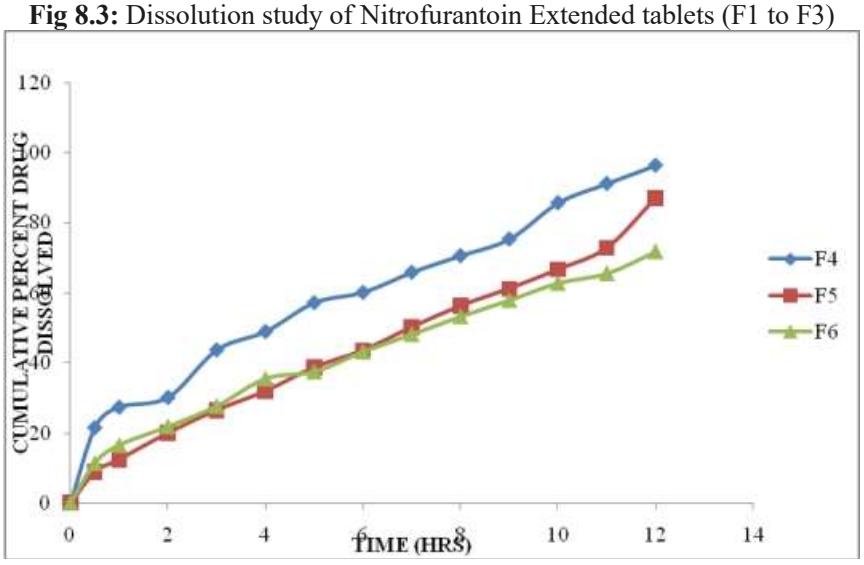

Fig 8.4: Dissolution study of Nitrofurantoin tablets (F4 to F6)

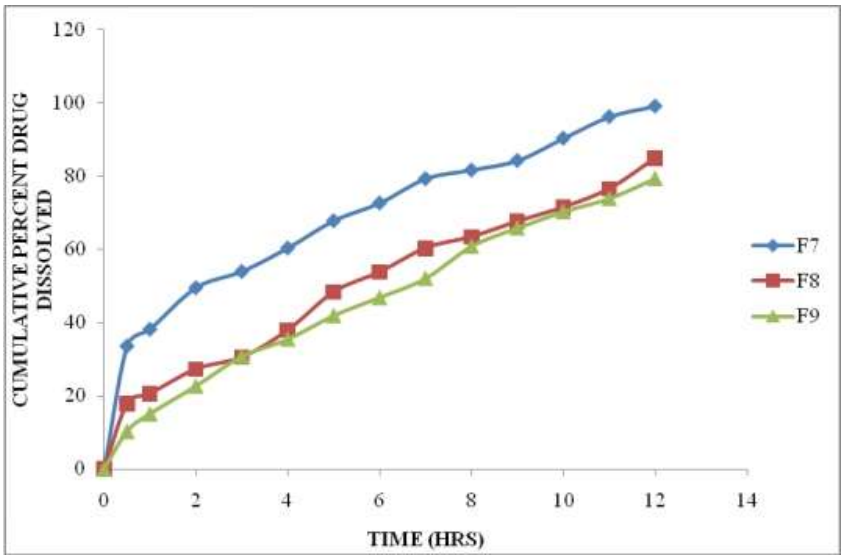

Fig 8.5: Dissolution study of Nitrofurantoin tablets (F7 to F9)

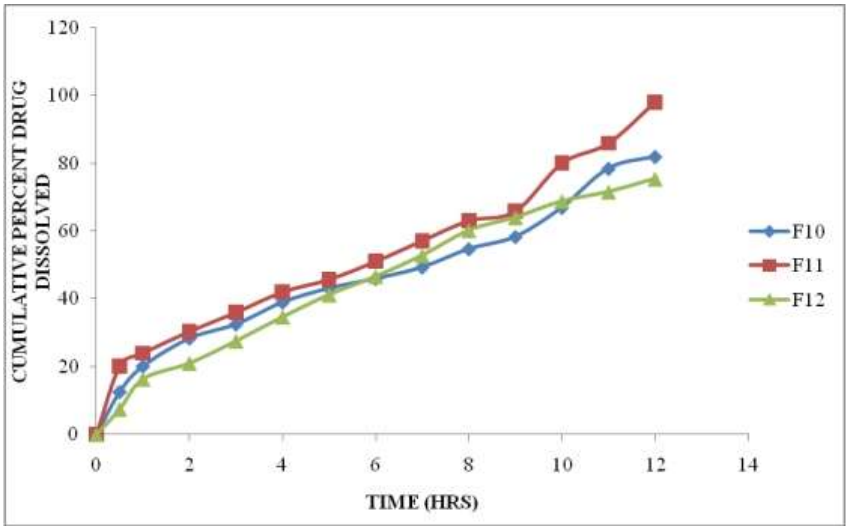

Fig 8.5: Dissolution study of Nitrofurantoin tablets (F10 to F12)

From the dissolution data it was evident that the formulations prepared with Badham Gum as polymer were retarded the drug release more than 12 hours.

Whereas the formulations prepared with lower concentration of Cashew nut tree gum retarded the drug release up to 12 hours in the concentration 100 mg. In higher concentrations the polymer was unable to retard the drug release.

The Formulation Containing Eudragit L- 100 in 100 mg Concentration Showed good retarding nature with required drug release in 12 hours i.e 99.10 %.

Whereas the formulations prepared with lower concentration of HPMC K4M retarded the drug release up to 12 hours in the concentration 200 mg. In higher concentrations of the polymer was unable to retard the drug release.

Hence from the above dissolution data it was concluded that F7 formulation was considered as optimised formulation because good drug release (99.10%) in 12 hours.

8.3 Application of Release Rate Kinetics to Dissolution Data

Data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Nitrofurantoin release from Extended tablets. The data was fitted into various kinetic models such as Zero, First order kinetics; Higuchi and Korsmeyer peppas mechanisms and the results were shown in below table

Table 8.6: Release kinetics data for optimised formulation (F7)

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	Q0 1/3	Qt 1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
33.6	0.5	0.707	1.526	-0.301	1.822	67.200	0.0298	-0.474	66.4	4.642	4.049	0.592
38.19	1	1.000	1.582	0.000	1.791	38.190	0.0360	-0.418	61.81	4.642	3.954	0.688
49.52	2	1.414	1.695	0.301	1.703	24.760	0.0202	-0.305	50.48	4.642	3.696	0.946
53.96	3	1.732	1.732	0.477	1.663	17.987	0.0185	-0.268	46.04	4.642	3.584	1.058
60.37	4	2.000	1.781	0.602	1.598	15.093	0.0166	-0.219	39.63	4.642	3.409	1.232
67.82	5	2.236	1.831	0.699	1.508	13.564	0.0147	-0.169	32.18	4.642	3.181	1.461
72.65	6	2.449	1.861	0.778	1.437	12.108	0.0138	-0.139	27.35	4.642	3.013	1.629

79.29	7	2.646	1.899	0.845	1.316	11.327	0.0126	-0.101	20.71	4.642	2.746	1.895
81.66	8	2.828	1.912	0.903	1.263	10.208	0.0122	-0.088	18.34	4.642	2.637	2.004
84.25	9	3.000	1.926	0.954	1.197	9.361	0.0119	-0.074	15.75	4.642	2.507	2.135
90.33	10	3.162	1.956	1.000	0.985	9.033	0.0111	-0.044	9.67	4.642	2.130	2.511
96.21	11	3.317	1.983	1.041	0.579	8.746	0.0104	-0.017	3.79	4.642	1.559	3.082
99.1	12	3.464	1.996	1.079	-0.046	8.258	0.0101	-0.004	0.9	4.642	0.965	3.676

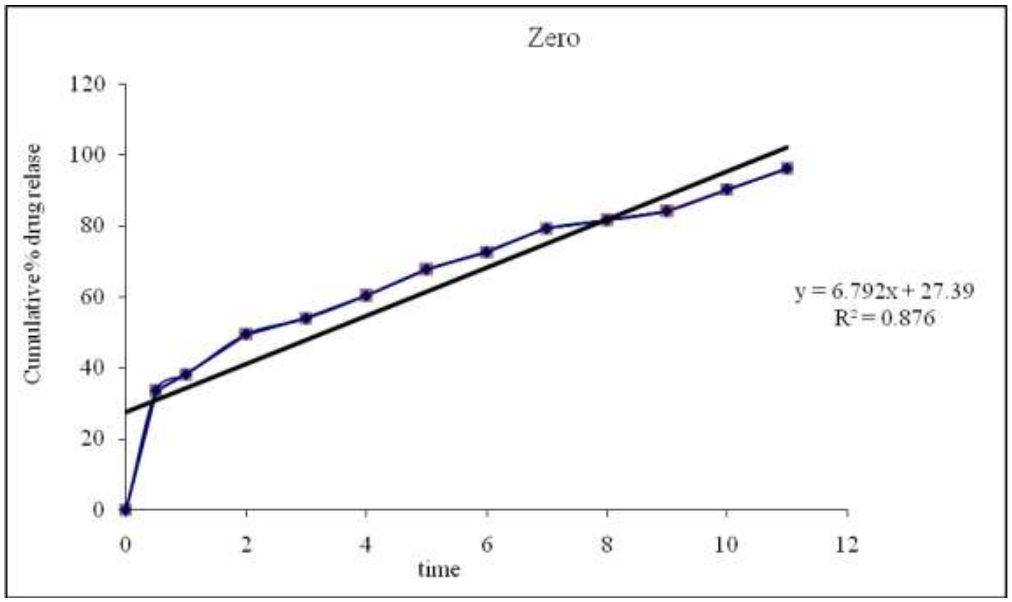

Fig 8.6: Graph of zero order kinetics

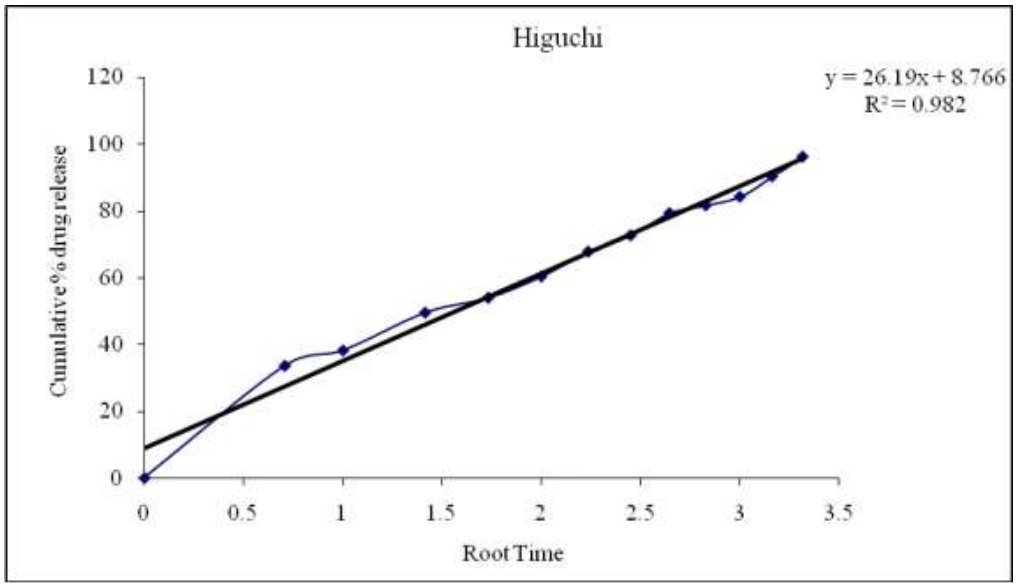

Fig 8.7: Graph of higuchi release kinetics

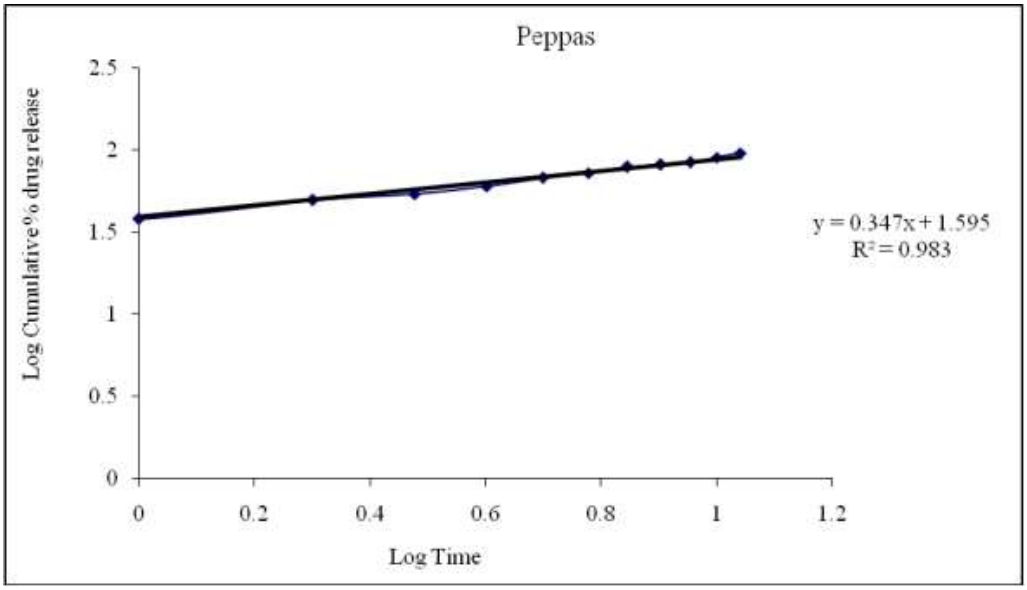

Fig 8.8: Graph of peppas release kinetics

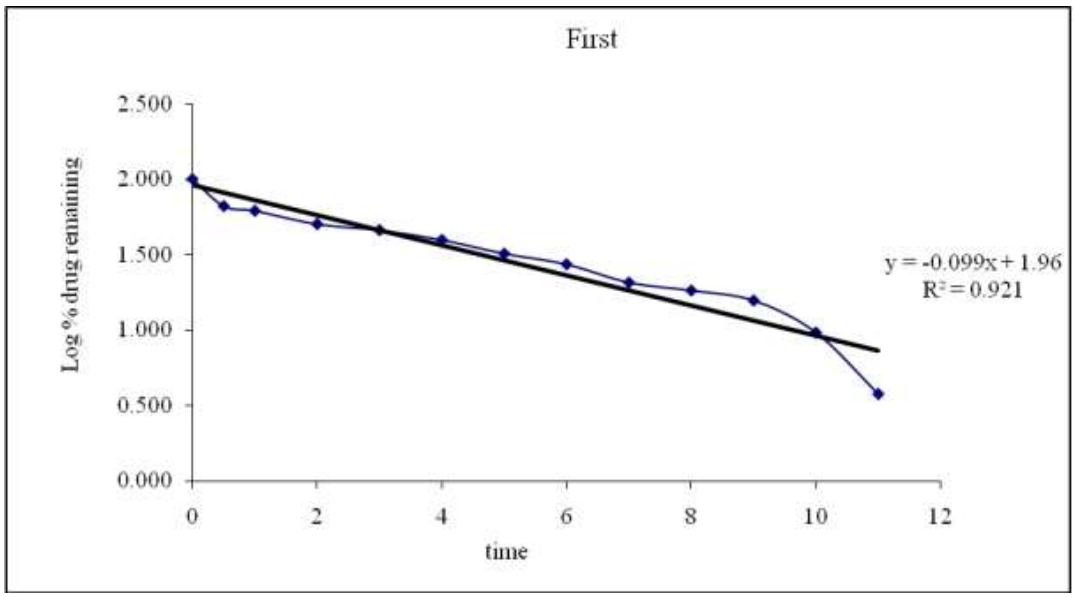

Fig 8.9: Graph of first order release kinetics

Optimised formulation F7 was kept for release kinetic studies. From the above graphs it was evident that the formulation F7 was followed peppas release mechanism.

8.4 Drug and Excipient Compatability Studies

FTIR STUDY

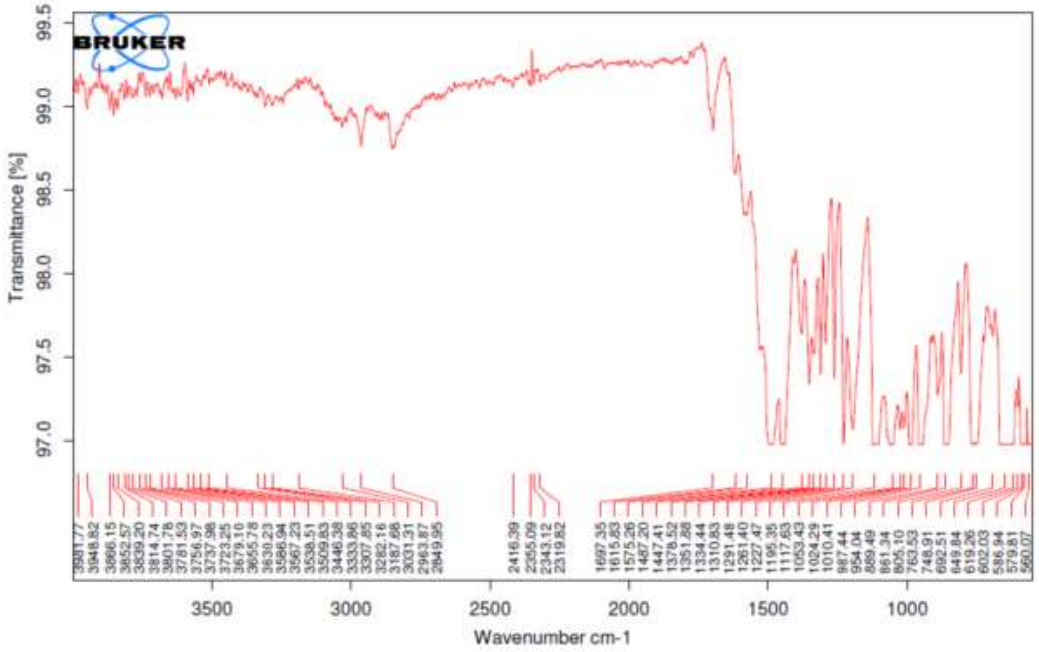

Fig 8.10: Ftir graph of pure drug of Nitrofurantoin

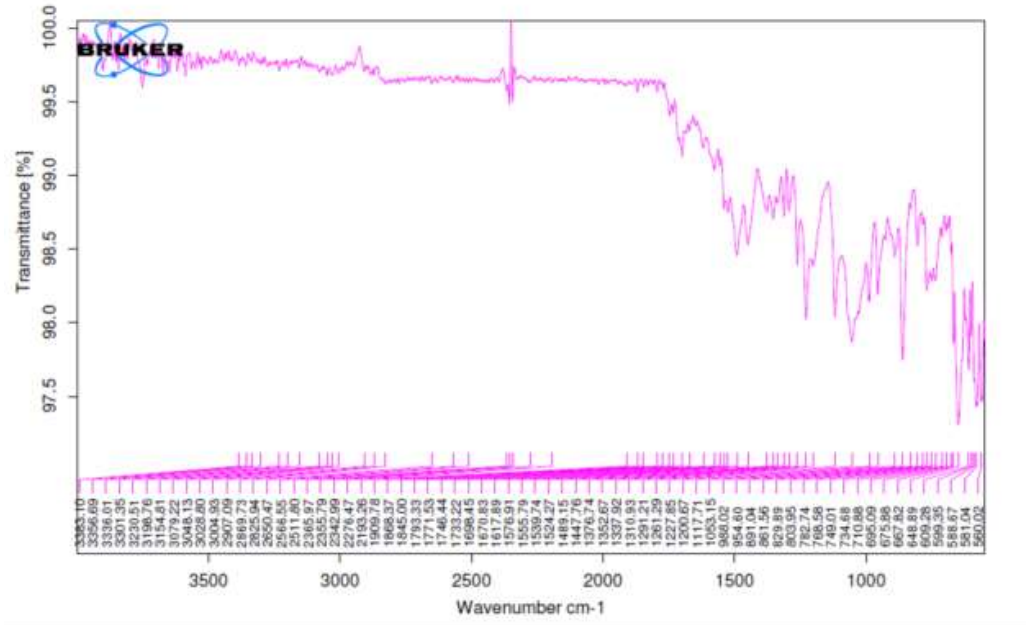

Fig 8.11: FTIR Spectrum of optimised formulation

From the above studies it was found that there was no shifting in the major peaks which indicated that there were no significant interactions occurred between the Nitrofurantoin and excipients used in the preparation of different Nitrofurantoin extended release formulations. Therefore the drug and excipients are compatible to form stable.

Formulations under study, The FTIR spectra of Nitrofurantoin and physical mixture used for optimized formulation were obtained and these are depicted in above figures. From the FTIR data it was evident that the drug and excipients doses not have any interactions. Hence they were compatible.

CONCLUSION:

The formulation, evaluation, and optimization of Nitrofurantoin delayed-release matrix tablets using various polymers, specifically Badham Gum and Cashew Nut Tree Gum, have led to significant insights into the development of effective controlled-release dosage forms.

The study demonstrated that both Badham Gum and Cashew Nut Tree Gum can be utilized effectively to create delayed-release matrix tablets for Nitrofurantoin. The use of these natural gums facilitated the development of matrices that successfully achieved the desired drug release profile. Specifically:

Formulation Efficacy: Both polymers contributed to the creation of tablets with delayed-release characteristics, though the extent and consistency of release varied between the two. The matrix systems formed with Badham Gum and Cashew Nut Tree Gum displayed the ability to control the release of nitrofurantoin over an extended period, aligning with the therapeutic goals of reducing dosing frequency and enhancing patient compliance.

Evaluation Results: The tablets exhibited satisfactory physicochemical properties, including uniformity in weight, hardness, and friability. In-vitro dissolution studies indicated that the tablets formulated with Badham Gum and Cashew Nut Tree Gum released nitrofurantoin in a controlled manner, although the release profiles differed slightly between the two polymers.

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