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Formulation, Development and Evaluation of Extended-Release Tablets of Fenbendazole

Srimukhi Tangellapally*, B.Prashanth, K.Karthik, Ch.Manoj, T.Srinivas, M.Naresh

Surabhi Dayakar Rao College of Pharmacy, Rimmanaguda, Telanagana, India.
Corresponding Author: Srimukhi Tangellapally, M. Pharm.,
Assistant Professor, Department of Pharmacology, Surabhi Dayakar Rao College of Pharmacy

***ABSTRACT**: This study aimed to formulate, develop, and evaluate extended-release tablets of Fenbendazole using various polymers, including Hydroxypropyl Methylcellulose K15 (HPMC K15), Ethyl Cellulose, and Tragacanth. The objective was to enhance the sustained release profile of Fenbendazole while ensuring compliance with the Indian Pharmacopoeia (IP) limits for both pre-compression and post-compression parameters. Different formulations were prepared by the direct compression technique, and their physical characteristics, such as hardness, friability, weight variation, and thickness, were assessed. Additionally, drug content uniformity, in vitro dissolution studies, and evaluations were conducted. The results showed that all formulations met the IP specifications for pre-compression and post-compression parameters. Among the various formulations, the one containing a combination of HPMC K15, Ethyl Cellulose, and Tragacanth demonstrated an optimal drug release profile, with a cumulative drug release of 99.56% at the 12-hour mark (F6 formulation). This formulation displayed a highly satisfactory release pattern, making it the most optimized among all tested formulations. The study concludes that the F6 formulation offers a promising extended-release system for Fenbendazole with sustained therapeutic effects over an extended period, meeting the necessary Pharmacopoeial standards for oral drug delivery systems.*

***KEYWORDS:** Fenbendazole, HPMC K15, Ethyl Cellulose, and Tragacanth*

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I. INTRODUCTION

For many years, oral drug delivery has been recognized as the most popular method of administration. Because standard drug delivery systems are characterized by fast release and repeated dosing of the medication, which may raise the hazard of dose variation, a formulation with regulated release that maintains a blood level that is almost constant or uniform must be developed. Due to the fast release and frequent dosing of the medication that characterize typical drug delivery methods, which may raise the risk of dose variation, a formulation with regulated release that maintains a blood level that is almost constant or uniform must be developed. Better patient compliance and increased clinical efficacy of the medicine for its intended purpose are frequently the results of giving a single dose of a medication that is released over a long period of time to maintain a nearly constant or uniform blood level of the drug. 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. Extended-release medications usually offer an initial release of the medication that quickly achieves the intended therapeutic impact, followed by a progressive release of more medication to sustain this effect for a predefined amount of time. A dosage form that is intended to release the medication in a controlled manner over a prolonged period of time at a specific rate, duration, and site after administration is known as an ER, according to the USP. These extended drug delivery systems use both diffusion-controlled and dissolution-controlled mechanisms to continuously release the medication.

To regulate the release of the pharmaceuticals, which have different physical properties, the drug is distributed in swellable hydrophilic materials, an insoluble matrix of hard non-swellable hydrophobic materials, or plastic materials. For treatment to be effective, the drug's plasma concentration must be kept within the therapeutic index[1]. Antiepileptic medications (AEDs) are most frequently administered orally to patients with persistent epilepsy[1]. Because insufficient or partial medication adherence can lead to immediate undesirable consequences, such as uncontrolled or recurring seizures[2], or adverse effects (AEs) from continuing a previous dose without titrating, it is imperative to improve the convenience of administration

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[3]. Because non-adherence or partial adherence to medicine can have immediate negative repercussions, such uncontrolled or repeated seizures, efforts to improve the ease of administration are crucial[3].

Conventional dosage forms are of the immediate release variety, while non-immediate release delivery methods can be easily categorized into the following groups:[4]

1) Delayed Release
2) Sustained Release
3) Controlled Release
4) Prolonged Release
6) Site-specific and Receptor release

The disadvantages of the conventional dosage form include: [5]

• Patient noncompliance, which increases the likelihood of missing a dose of a prescription with a short half-life that requires frequent administration;
• The inevitable variations in drug concentration might result in either an excess or a shortage of medication.
• The characteristic peak-valley plasma concentration time profile that is obtained makes it challenging to achieve steady-state conditions.
• Any time overmedication occurs, the variations in drug levels may cause negative effects to occur sooner, particularly if the medicine has a low Therapeutic Index (TI).

By continually releasing medication over a prolonged period of time following the administration of a single dose, oral controlled release dosage forms are intended to achieve a chronic therapeutic impact that may result in repeatable and efficient plasma concentrations in vivo. Technologies for modified release formulations provide an effective way to maximize the medications' bioavailability and the ensuing blood concentration time profiles. Modified releases will be divided into two categories: extended or prolonged release and delayed release[6].

Fenbendazole, Methyl N-(6-phenylsulfanyl-1H-benzoimidazol-2-yl) carbamate, works by binding to tubulin, a protein that is part of the microtubules in the cells of parasites. The development and function of microtubules are disturbed by this interaction, which makes it impossible for the parasites to take nutrition and ultimately causes their demise. Fenbendazole is effective against numerous parasitic worms in both their adult and larval stages because of this mode of action.

The primary aim of this study is to formulate, develop, and evaluate extended-release tablets of Fenbendazole using different polymers, such as Hydroxypropyl Methylcellulose (HPMC K15), Ethyl cellulose, and Tragacanth. The goal is to achieve an extended-release profile of Fenbendazole that enhances therapeutic efficacy, improves patient compliance, and reduces the frequency of administration.

II. METHODOLOGY

1.Analytical method development:

a) Determination of absorption maxima:

100mg of Fenbendazole pure drug was dissolved in 15ml of Methanol and make up to 100ml with 0.1N HCL (stock solution-1). 10 ml of the above solution was taken and made up to 100 ml by using 0.1 N HCL (stock solution-2, i.e., 100µg/ml). From this, 10 ml was taken and made up with 100 ml of 0.1 N HCL (10µg/ml). Scan the 10µg/ml using a double-beam UV/VIS spectrophotometer in the range of 200 – 400 nm.

b) Preparation of calibration curve:

100mg of Fenbendazole pure drug was dissolved in 15ml of Methanol 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 1.0, 2.0, 3.0, 4.0, and 5.0 ml of solution and make up to 10 ml with 0.1N HCl to obtain 10, 20, 30, 40, and 50 µg/ml of Fenbendazole per ml of solution. The absorbance of the above dilutions was measured at 296nm by using a UV-Spectrophotometer, taking 0.1N HCl as blank. Then a graph was plotted by taking Concentration on the X-axis and Absorbance on the Y-axis, which gives a straight line. Linearity of the standard curve was assessed from the square of the correlation coefficient (R^2), which was determined by least-squares linear regression analysis. The above procedure was repeated by using pH 6.8 phosphate buffer solutions.

2.Formulation Development of Extended-Release Tablets:

All the formulations were prepared by the direct compression method. The compositions of different formulations are given in Table 1. The tablets were prepared as per the procedure given below, and the aim is to prolong the release of Fenbendazole.

Procedure:

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

Table 1: Formulation of Extended-release tablets

INGREDIENTS	FORMULATION CODE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Fenbendazole	90	90	90	90	90	90	90	90	90
HPMC K15	30	60	90	-	-	-	-	-	-
Ethyl cellulose	-	-	-	30	60	90	-	-	-
Tragacanth	-	-	-	-	-	-	30	60	90
P.V.P.K.30	25	25	25	25	25	25	25	25	25
Aerosil	15	15	15	15	15	15	15	15	15
Talc	10	10	10	10	10	10	10	10	10
Mg. Stearate	10	10	10	10	10	10	10	10	10
MCC	220	190	160	220	190	160	220	190	160
Total weight	400	400	400	400	400	400	400	400	400

3.Evaluation Parameters

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 a 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 a 250 ml measuring cylinder, and the cylinder was tapped on a wooden surface from a 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,

Hausner's ratio = D_T/D_B

Where D_T is the tapped density, D_B is the bulk density

Compressibility index:

The compressibility index (CI) was determined by measuring the initial volume (V_o) and final volume (V_f) after a hundred taps of a sample in a measuring cylinder. It indicates the powder flow properties and is 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:

The angle of repose was measured by the fixed funnel method. It determines the flow property of the powder. It is defined as the 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 a definite height (h). By measuring the height and radius of the heap of powder formed (r), the angle of repose was calculated by using the formula given below, and the calculated values obtained were 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 No.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

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 the individual tablet weight. The percentage weight variation was calculated as per the Indian Pharmacopoeial Specification. Tablets with an average weight of 250 mg, so the % deviation was ±5 %.

Table No.3: IP standards of uniformity of weight

S. No.	Average weight of a 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 the drum of the friability test apparatus. The drum rotated at a speed of 25 rpm. The friabilator was operated for 4 minutes and 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 the Monsanto hardness tester. The results were compliant with the IP specification.

Thickness test:

The rules of physical dimensions of the tablets, such as sizes and thickness, are necessary for consumer acceptance and maintaining tablet uniformity. The dimensional specifications were measured by using screw gauge. The thickness of the tablet is mostly related to the tablet's hardness can be used as an initial control parameter.

Drug content:

The amount of drug in a tablet was important to monitor from tablet to tablet, and batch to batch is to evaluate for efficacy of tablets. For this test, 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 analysed by a UV spectrophotometer.

***In vitro* drug release studies**

Apparatus	--	USP-II, Paddle Method
Dissolution Medium	--	0.1 N HCl, pH 6.8 Phosphate buffer
RPM	--	50
Sampling intervals (hrs)	--	1, 2, 3, 4, 5, 6, 7, 8, 9,10, 11, and 12
Temperature	--	37°c ± 0.5°c

Procedure:

900ml 0f 0.1 HCl was placed in a vessel, and the USP apparatus II (Paddle Method) was assembled. The media was allowed to equilibrate to temp of 37°c $\pm$ 0.5°c. The tablet was placed in the vessel and the apparatus was operated for 2 hours. Then, 0.1 N HCl was replaced with pH 6.8 phosphate buffer, and the process was continued up to 12 hrs at 50 rpm. At specific time intervals, 5 ml of sample and again, 5 ml of media were added to maintain the sink condition. Withdrawn samples were analysed at the wavelength of the drug using a UV-spectrophotometer.

3.3 Application of Release Rate Kinetics to Dissolution Data:
Various models were tested for explaining the kinetics of drug release. To analyse 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 models.

Zero order release rate kinetics:
To study the zero–order release kinetics, the release rate data are 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 the 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 the 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 a 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 the case of Fickian diffusion, n = 0.5; for zero-order release (case II transport), n = 1; and for super case II transport, n > 1. In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

3.4. 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 interactions between the drug and other excipients. In the current study 1:1 ratio was used for the preparation of physical mixtures used for analyzing compatibility studies. FT-IR studies were carried out with a Bruker FTIR facility.

III. RESULT & DISCUSSION

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

1.Analytical Method

1.1 Standard graph of Fenbendazole in 0.1N HCl:
The scanning of the 10µg/ml solution of Fenbendazole in the ultraviolet range (200-400 nm) against a 0.1 N HCl blank gave the λ_{max} as 296 nm. The standard concentrations of Fenbendazole (10-50 µg/mL) prepared in 0.1N HCl showed good linearity with an R^2 value of 0.997, which suggests that it obeys Beer-Lambert's law.

Table No.4: Standard curve of Fenbendazole in 0.1N HCl

Concentration (µg/ mL)	Absorbance
0	0
10	0.107
20	0.218
30	0.318
40	0.419
50	0.525

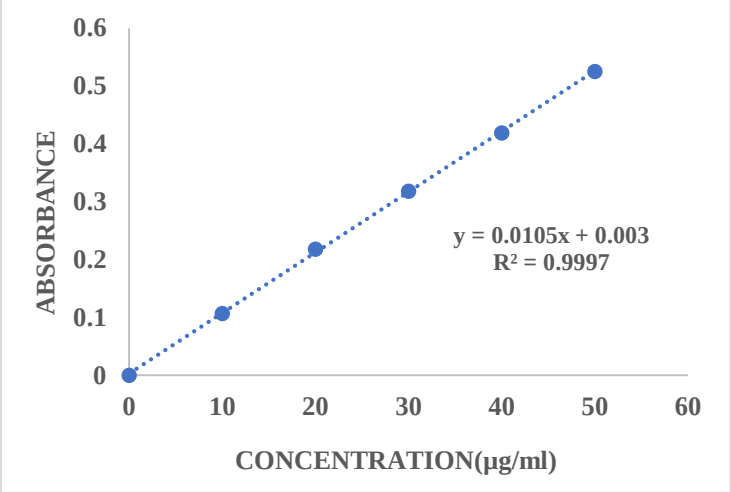

Fig.1: Calibration curve of Fenbendazole in 0.1 N HCl at 296 nm

1.2 Standard Curve of Fenbendazole in Phosphate buffer pH 6.8

The scanning of the 10µg/ml solution of Fenbendazole in the ultraviolet range (200-400nm) against 6.8 pH phosphate buffer as blank gave the λ_{max} as 296 nm. The standard concentrations of Fenbendazole (10-50µg/ml) prepared in 6.8 pH phosphate buffer showed good linearity with an R^2 value of 0.998, which suggests that it obeys Beer-Lambert's law.

Table No.5: Standard curve of Fenbendazole in Phosphate buffer pH 6.8

Concentration (µg / ml)	Absorbance
0	0
10	0.141
20	0.281
30	0.415
40	0.549
50	0.679

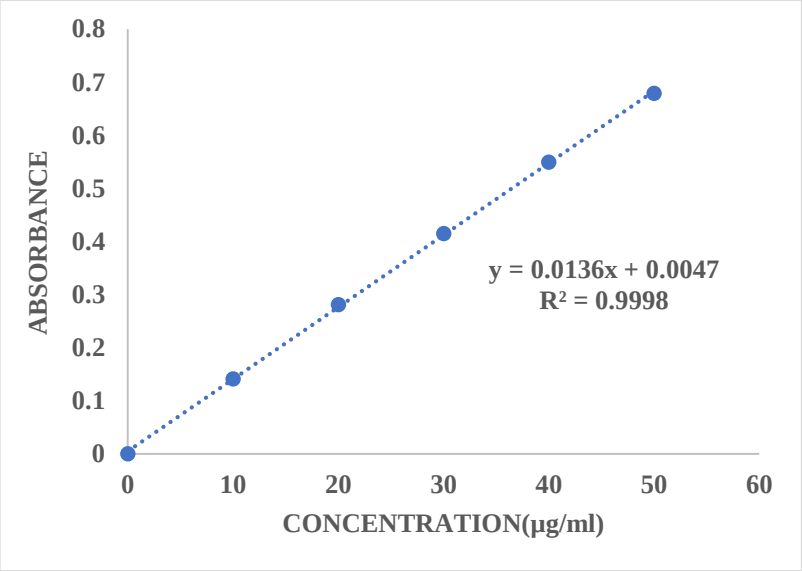

Fig.2: Calibration of Fenbendazole in Phosphate buffer pH 6.8

2 EVALUATION PARAMETERS

2.1 Pre-compression parameters

Table No.6: Pre-compression parameters of powder blend

Formulation Code	Angle of Repose	Bulk density (gm/cm^3)	Tapped density (gm/ cm^3)	Carr's index (%)	Hausner's Ratio
F1	26.78 ±0.42	0.41 ±0.10	0.50 ±0.13	18 ±0.37	1.21 ±0.51
F2	26.78 ±0.29	0.41 ±0.16	0.50 ±0.15	18 ±0.12	1.21 ±0.39
F3	29.34 ±0.54	0.50 ±0.29	0.58 ±0.08	13.79 ±0.24	1.16 ±0.23
F4	28.23 ±0.10	0.47 ±0.23	0.55 ±0.12	14.54 ±0.09	1.17 ±0.52
F5	29.34 ±0.22	0.50 ±0.24	0.58 ±0.37	13.79 ±0.35	1.16 ±0.08
F6	26.71 ±0.23	0.46 ±0.11	0.55 ±0.24	16.36 ±0.29	1.19 ±0.29
F7	29.34 ±0.64	0.50 ±0.15	0.58 ±0.40	13.79 ±0.42	1.16 ±0.21
F8	28.23 ±0.41	0.47 ±0.26	0.55 ±0.32	14.54 ±0.37	1.17 ±0.31
F9	27.91 ±0.12	0.45 ±0.18	0.55 ±0.23	18.18 ±0.45	1.22 ±0.24

The tablet powder blend was subjected to various pre-compression parameters. The angle of repose values were shown from 26.78 ±0.29 to 29.34 ±0.64; 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 0.41 ±0.10 - 0.50 ±0.24 (g/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 0.50 ±0.13 - 0.58 ±0.40, showing the powder has good flow properties. The compressibility index of all the formulations was found to range from 1.16 ±0.08 to 1.22 ±0.24, which showed that the powder has good flow properties. All the formulations showed the Hausner ratio ranging from 1.16 to 1.25, indicating the powder has good flow properties.

2.2 Post-Compression Parameters for Tablets

Table No.7: Post-Compression Parameters of Tablets

Formulation codes	Weight variation(mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	398.12	4.12	0.29	2.57	98.37
F2	401.38	4.36	0.31	2.64	99.55
F3	397.45	4.22	0.39	2.51	99.62
F4	400.37	4.29	0.24	2.48	97.22

F5	399.22	4.31	0.33	2.41	98.71
F6	400.89	4.18	0.12	2.38	99.28
F7	405.62	4.39	0.19	2.59	98.38
F8	397.47	4.25	0.27	2.66	97.44
F9	399.71	4.15	0.35	2.73	98.89

Weight variation and thickness:
All the formulations were evaluated for uniformity of weight using an 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 397.45 to 405.62**.** The maximum allowed percentage weight variation for tablets weighing >400 mg is 1.5%, and no formulations exceed this limit. Thus, all the formulations were found to comply with the standards given in I.P., And the thickness of all the formulations was also complying with the standards that were found to be between 2.38 to 2.73.

Hardness and friability:
All the formulations were evaluated for their hardness, using the Monsanto hardness tester, and the results are shown in Table 8.4. The average hardness for all the formulations was found to be between **(**4.12 to 4.39**)** $Kg/cm^{2,}$ which was found to be acceptable.
Friability was determined to estimate the ability of the tablets to withstand abrasion during packing, handling, and transporting. All the formulations were evaluated for their percentage friability using the Roche friabilator, and the results are shown in Table 8.4. The average percentage friability for all the formulations was between 0.12 to 0.39, which was found to be within the limit.

Drug content:
All the formulations were evaluated for drug content according to the procedure described in the methodology section, and the results are shown in Table 7.4. The drug content values for all the formulations were found to be in the range of 97.22 to 99.62**.** 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 polymers using by Direct compression method. The tablets' dissolution study was carried out in a paddle dissolution apparatus using 0.1N HCl for 2 hours and 6.8 pH phosphate buffers for the remaining hours as a dissolution medium.

Table No.8: Dissolution Data of Fenbendazole Tablets Prepared With HPMC K15 in Different Concentrations

TIME (hrs)	**CUMULATIVE PERCENT DRUG RELEASED**		
	F1	**F2**	**F3**
0	0	0	0
1	11.65	9.17	13.51
2	14.58	18.62	19.25
3	21.41	26.69	29.76
4	27.65	29.85	38.36
5	32.64	37.76	45.39
6	43.12	45.45	54.46
7	48.25	51.54	63.62
8	59.37	56.37	71.55
9	68.54	64.66	75.38
10	74.48	76.82	82.72
11	82.66	82.17	88.89
12	86.72	89.55	92.43

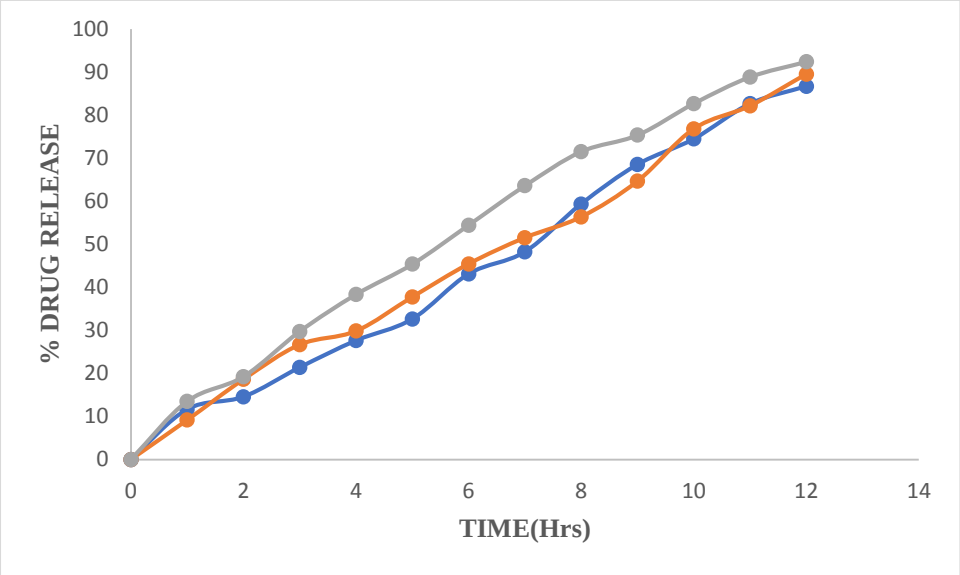

Fig 3: Dissolution study of Fenbendazole Extended tablets (F1 to F3)

Table No.9: Dissolution Data of Fenbendazole Tablets Prepared with Ethyl cellulose in Different Concentrations

TIME (hrs)	**CUMULATIVE PERCENT DRUG RELEASED**		
	F4	**F5**	**F6**
0	0	0	0
1	08.56	12.27	11.41
2	17.43	19.81	15.56
3	28.35	22.72	26.39
4	37.58	28.63	38.53
5	44.36	37.79	43.27
6	48.77	53.51	55.22
7	61.65	62.44	64.19
8	73.51	74.52	75.08
9	77.72	79.49	84.81
10	85.49	84.78	89.42
11	89.18	89.23	92.47
12	92.71	95.79	99.52

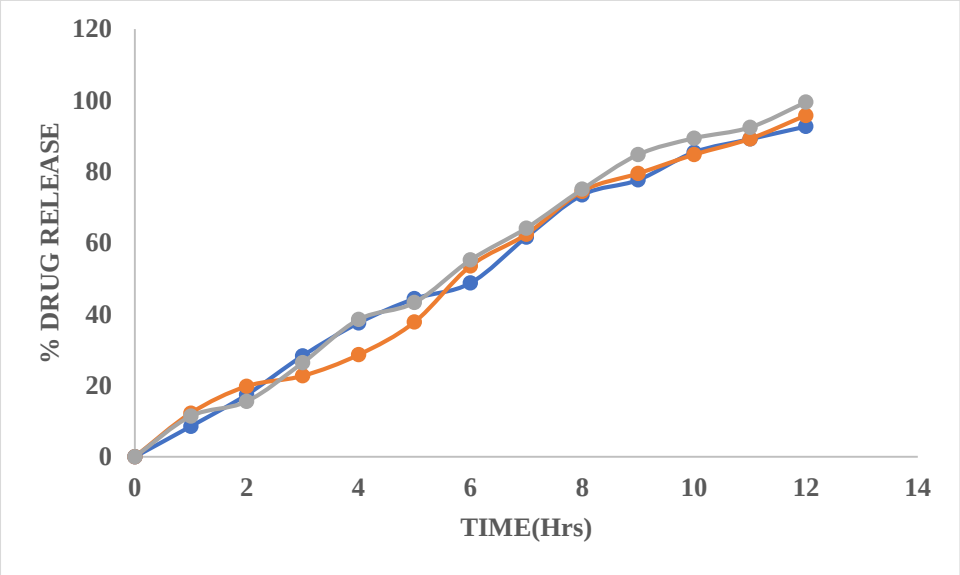

Fig 4: Dissolution study of Fenbendazole tablets (F4 to F6)

Table No.10: Dissolution Data of Fenbendazole Tablets Prepared with Tragacanth in Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED		
	F7	F8	F9
0	0	0	0
1	6.25	9.49	7.72
2	18.41	17.25	15.69
3	26.29	21.45	28.82
4	36.36	25.31	39.46
5	46.52	35.42	48.17
6	58.18	49.51	55.27
7	68.55	53.35	67.63
8	71.42	62.68	76.33
9	75.37	75.59	82.64
10	82.36	78.47	89.77
11	85.59	87.35	92.58
12	92.88	97.69	94.26

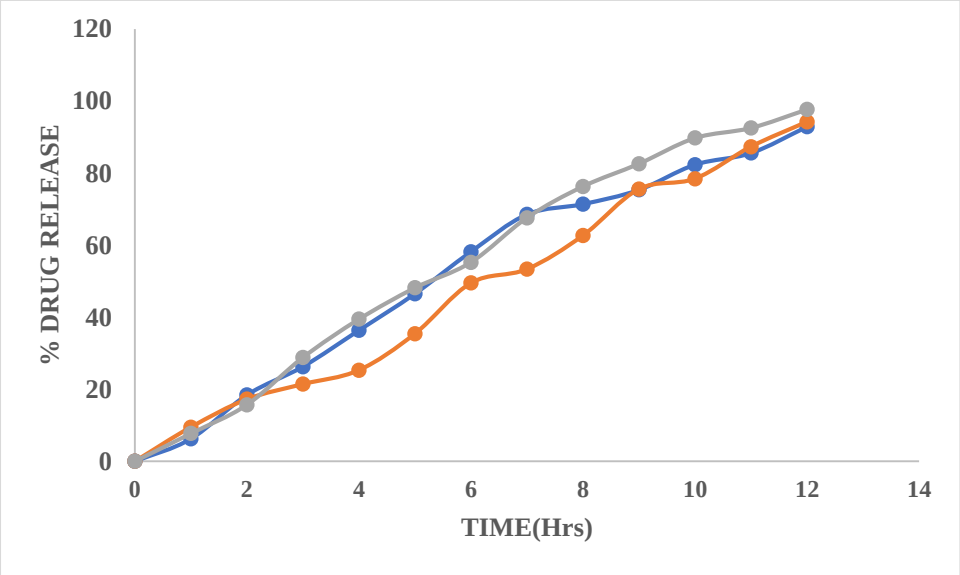

Fig 5: Dissolution study of Fenbendazole tablets (F7 to F9)

Formulations prepared with HPMC K15 retarded the drug release in the concentration of 90mg (F3 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 92.43 % in 12 hours with good retardation.
From the dissolution data it was evident that the formulations prepared with different concentrations as 30, 60 and 90 mg polymer were retard the drug release up to desired period i.e., 12 hours.

Formulations prepared with Ethyl cellulose retarded the drug release in the concentration of 90mg (F6 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.52 % in 12 hours with good retardation.
From the dissolution data it was evident that the formulations prepared with different concentrations as 30, 60 and 90 mg polymer were retard the drug release up to desired period i.e., 12 hours.

Formulations prepared with Tragacanth retarded the drug release in the concentration of 60mg (F8 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 97.69 % in 12 hours with good retardation.
From the dissolution data it was evident that the formulations prepared with different concentrations as 30, 60 and 90 mg polymer were retard the drug release up to desired period i.e., 12 hours.

Hence, from the above dissolution data, it was concluded that the F6 formulation was considered as the optimized formulation because good drug release (99.52 %) in 12 hours.

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 Fenbendazole from Extended tablets. The data was fitted into various kinetic models such as Zero, First order kinetics, Higuchi and Korsmeyer papas mechanisms, and the results are shown in table below

Table No.11: Release kinetics data for optimized formulation (F6)

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	Q01/3	Qt1/3	Q01/3-Qt1/3
0	**0**	0			2.000				100	4.642	4.642	0.000
11.41	1	1.000	1.057	0.000	1.947	11.410	0.0876	-0.943	88.59	4.642	4.458	0.184
15.56	2	1.414	1.192	0.301	1.927	7.780	0.0643	-0.808	84.44	4.642	4.387	0.254
26.39	3	1.732	1.421	0.477	1.867	8.797	0.0379	-0.579	73.61	4.642	4.191	0.451
38.53	4	2.000	1.586	0.602	1.789	9.633	0.0260	-0.414	61.47	4.642	3.947	0.695
43.27	5	2.236	1.636	0.699	1.754	8.654	0.0231	-0.364	56.73	4.642	3.842	0.799
55.22	6	2.449	1.742	0.778	1.651	9.203	0.0181	-0.258	44.78	4.642	3.551	1.091
64.19	7	2.646	1.807	0.845	1.554	9.170	0.0156	-0.193	35.81	4.642	3.296	1.345
75.08	8	2.828	1.876	0.903	1.397	9.385	0.0133	-0.124	24.92	4.642	2.921	1.721
84.81	9	3.000	1.928	0.954	1.182	9.423	0.0118	-0.072	15.19	4.642	2.477	2.165
89.42	10	3.162	1.951	1.000	1.024	8.942	0.0112	-0.049	10.58	4.642	2.195	2.446
92.47	11	3.317	1.966	1.041	0.877	8.406	0.0108	-0.034	7.53	4.642	1.960	2.682
99.52	12	3.464	1.998	1.079	-0.319	8.293	0.0100	-0.002	0.48	4.642	0.783	3.859

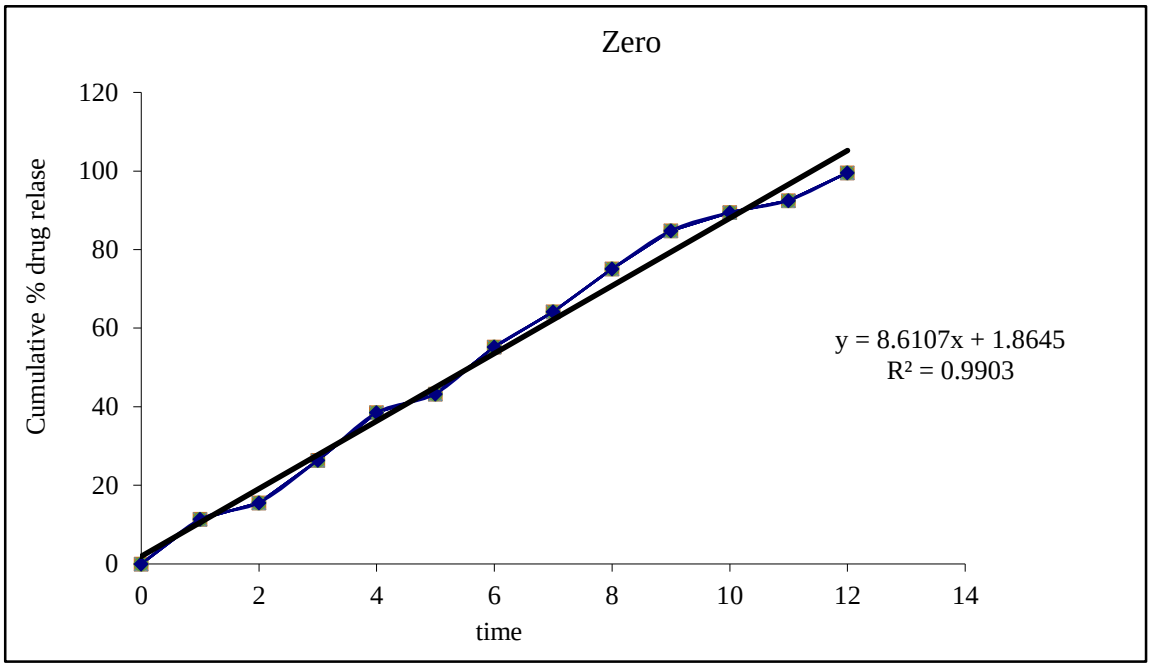

Fig 6: Graph of zero-order kinetics

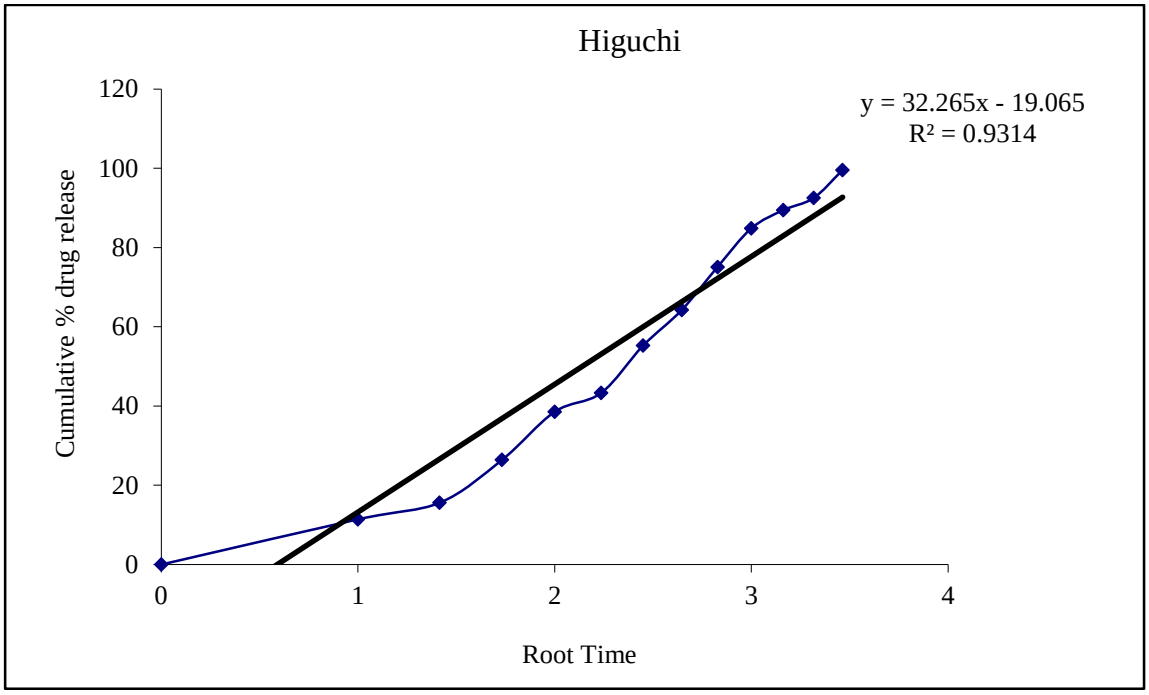

Fig 7: Graph of Higuchi release kinetics

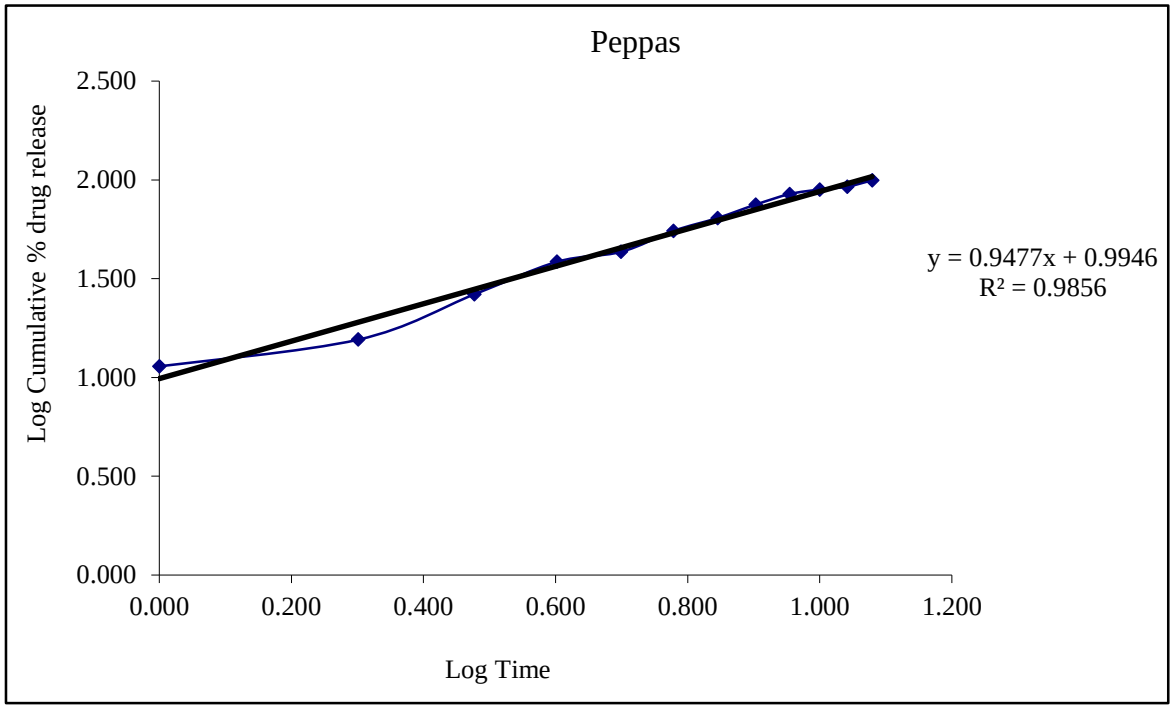

Fig 8: Graph of Peppas release kinetics

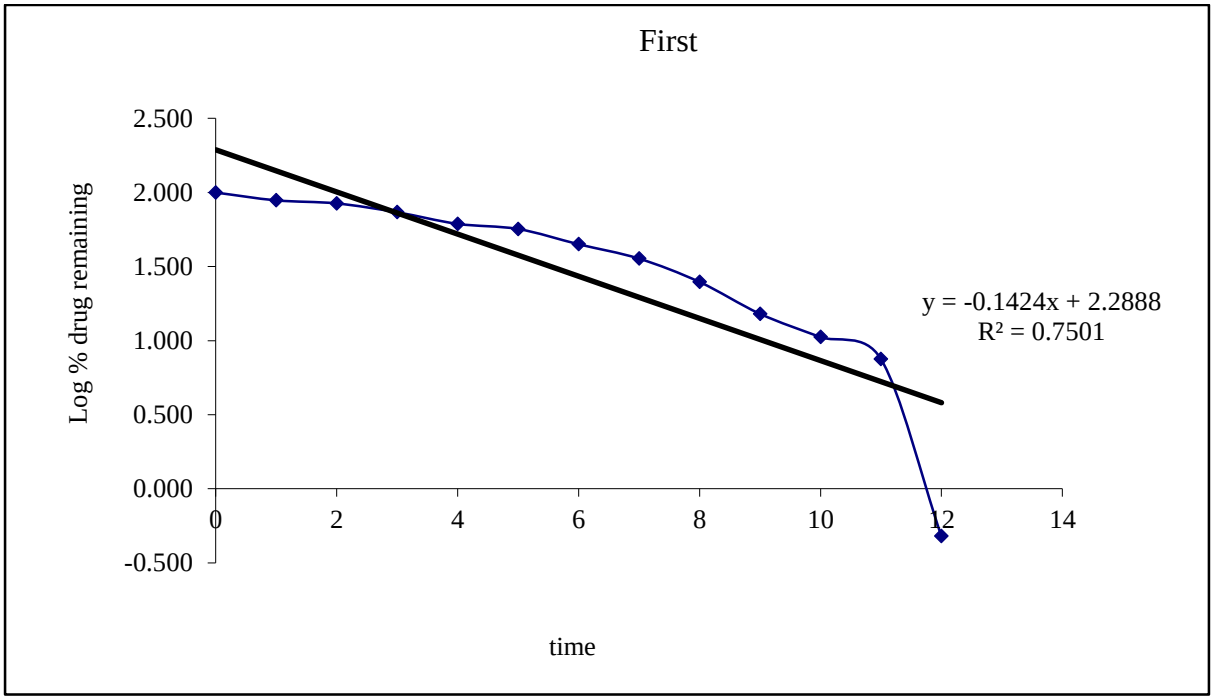

Fig 9: Graph of first-order release kinetics

Optimised formulation F6 was kept for release kinetic studies. From the above graphs, it was evident that the formulation F6 followed the Peppas release mechanism.

4. Drug and Excipient Compatibility Studies

FTIR study

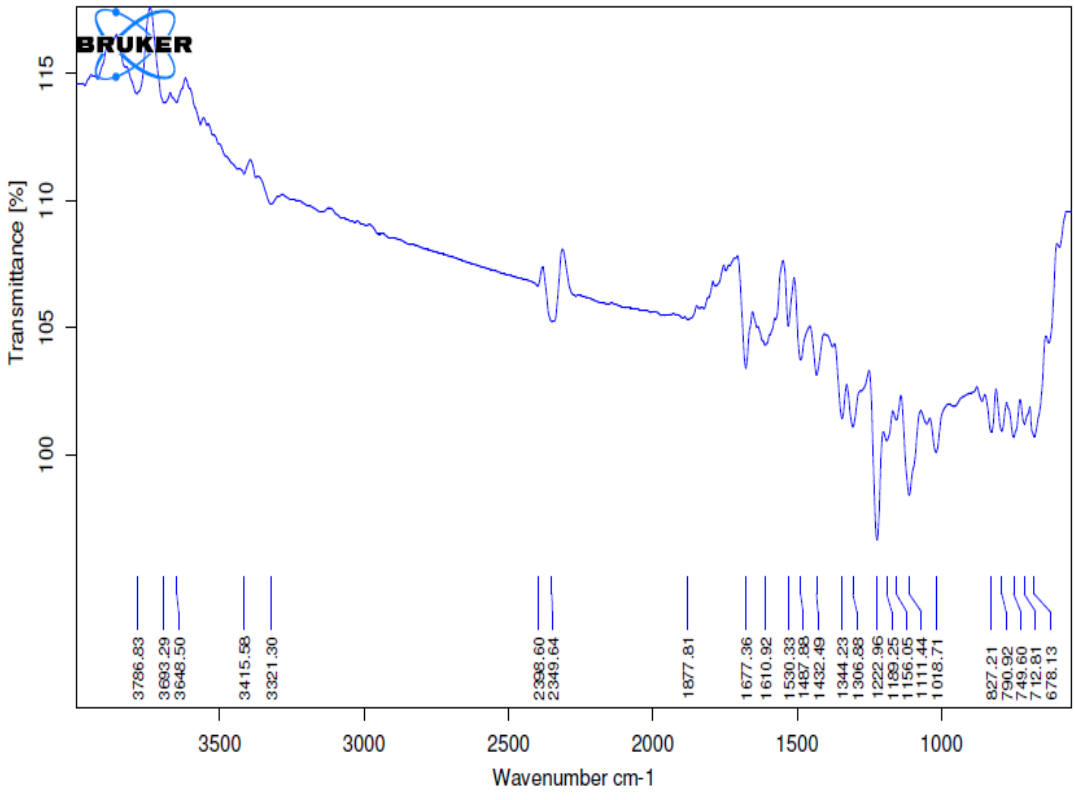

Fig 10: FTIR Graph of Pure Drug of Fenbendazole

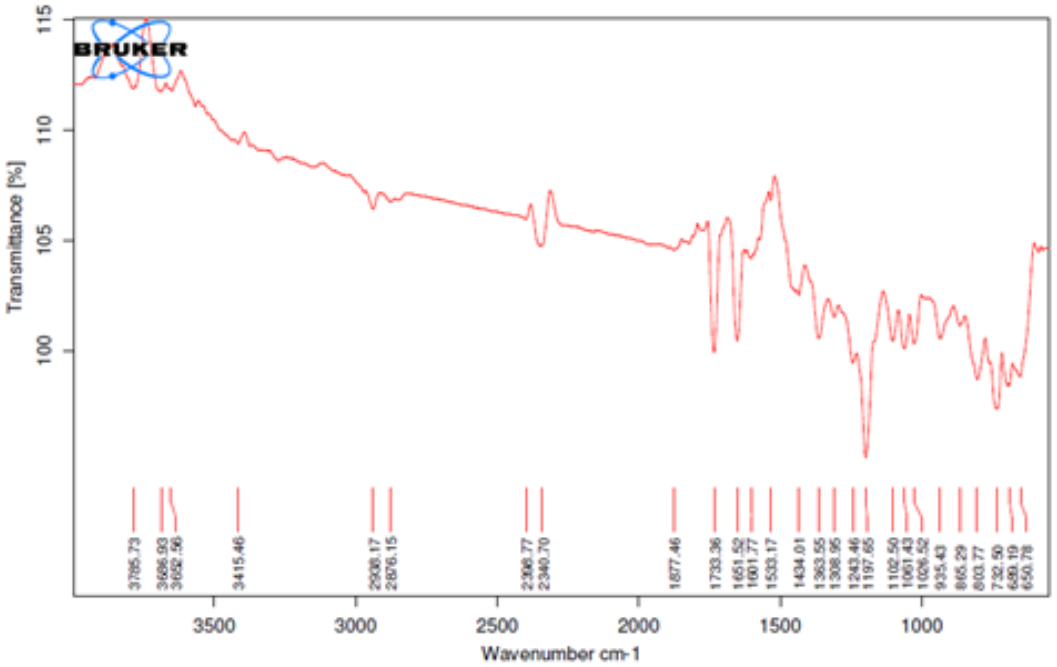

Fig 11: FTIR Graph of Pure Drug of Fenbendazole Optimized Graph

There is no incompatibility of pure drugs and excipients. There is no disappearance of peaks of pure drug in the optimized formulation.

9. CONCLUSION

In conclusion, the formulation, development, and evaluation of extended-release tablets of fenbendazole have demonstrated promising results in enhancing the drug's therapeutic efficacy. By employing appropriate excipients and techniques, such as controlled release mechanisms, the developed tablets offer the potential for prolonged drug release, which can help maintain therapeutic plasma concentrations over extended periods. This approach not only improves patient compliance by reducing the frequency of dosing but also minimizes fluctuations in drug levels, leading to more consistent pharmacological effects. The successful evaluation of various formulation parameters, including release kinetics and in vitro performance, suggests that the extended-release fenbendazole tablets are a viable alternative to conventional dosage forms.

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