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FORMULATION AND *IN VITRO* EVALUATION OF EFFERVESCENT TABLET OF ALBENDAZOLE

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ABSTRACT

The present study was made to formulate and evaluate the effervescent tablet of Albendazole using wet granulation method to overcome the problems occurred in other marketed formulation of Albendazole and to determine the percentage release profile of drug. In this present study formulation were prepared from Albendazole as an active ingredient with effervescent bases in different concentrations and the flow characteristics are increased by adding microcrystalline cellulose as a bulking agent. The effervescent tablet is prepared by wet granulation method. In present work Preformulation studies were performed and prepared effervescent tablet of Albendazole were evaluated for hardness, friability, weight variation, disintegration time, FTIR. The formulation obtained from wet granulation method having improved flowability and dissolution rate. The dissolution studies were performed for three doses and the percentage release profile of three dose concentration F1, F2, F3 were found to be 99.7%, 89.75%, 83.25% respectively. In this, F1 dose give better release at the end of 15 mins. The percentage release profile of chewable tablet was found to be 99.87%, at the end of 30mins. So that effervescent tablet of albendazole was formulated and has improved percentage release profile within 15 mins.

KEYWORDS

Albendazole, Effervescent tablet, Microcrystalline cellulose and Percentage release profile.

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INTRODUCTION

Oral route of drug administration is the most appealing route of drug delivery of drugs[1]. In the current trend, the people are very busy with their schedules and have less time to care for health. For the treatment, they always prefer the quick relief and easily administrable formulations. One such formulation is effervescent tablet. Effervescent tablet is dissolved or dispersed in water before

administration. The tablet provides less irritation, tolerability, swallowing can be prevented and more stability is achieved, improved therapeutic effect[2]. The Effervescent tablet is added into a glass of water just before administration and the drug solution or dispersion is to be drunk immediately. The formulated tablet is quickly broken apart by internal release of CO2 in water due to interaction between Tartaric acid and Citric acid with alkali metal carbonates or bicarbonates in presence of water. Due to liberation of CO2 gas, the dissolution of active pharmaceutical ingredient in water as well as taste masking effect is enhanced[3]. The disease helminthiasis is an infestation by macroparasitic worms in human and other animals in which the part of body is infected[4]. Albendazole is an anthelmintic or anti-worm medication. It is used for the treatment of variety of parasitic worm infection[5].

Drug Profile[6]

ALBENDAZOLE,

Molecular Formula

$C_{12}H_{15}N_3O_2$

Chemical Name

Methyl 5-(propylthio)-2 benzimidazole carbamate.

Molecular Weight

265.34.

Description

Albendazole is used to treat Neurocysticercosis, an infection of the nervous system caused by PORK tape worms. This medicine is also used to treat cystic hydatid disease of the liver, lung, and peritonenum, an infection caused by dog tape worms.

Solubility

Freely soluble in anhydrous formic acid and very slightly soluble in ether. And methylene chloride. Albendazole is practically insoluble in alcohol and water.

Melting Point

207ºC to 211ºC.

Mechanism of Action

Albendazole intracellular transport are also disrupted. At higher concentrations, it disrupts the metabolic pathways of Helminths by inhibiting metabolic enzymes such as MALATE DEHYDROGNASE and FUMARATE REDUCTASE, with inhibition of the latter leading to less energy produced by the Krebs cycle. Due to diminished ATP production, the parasite is immobilizing and eventually dies. Some parasites have evolved to have some resistance to Albendazole by having a different set of acids comprising beta-tubulin, decreasing the binding affinity of Albendazole.

Polymer Profile[7]

Micro crystalline cellulose[13]

Chemical name

Cellulose.

Function Category

Emulsifier, stabilizer, Anti caking and dispersing agent.

Description

Fine, white or almost white, odourless, free flowing crystalline powder.

MATERIAL AND METHODS

Albendazole was procured from Kniss lab (Chennai), sodium bicarbonate, sodium carbonate, citric acid and tartaric acid was procured from Scientific labs (Chennai), polyvinyl pyrrolidone, simethicone procured from Kniss lab, saccharine sodium, sodium benzoate, magnesium stearate and microcrystalline cellulose procured from Chem o Labs (Chennai).

Pre-Formulation[1,8,9]

These studies could focus on physico-chemical properties of drug that could affect drug performance and development of efficacious dosage form.

The various properties studied are:

1. Angle of repose,
2. Bulk Density,
3. Tapped Density,
4. Compressibility Ratio,
5. Hausner's Ratio,
6. Solubility test.

Angle of Repose

The frictional force in loose powder can be measured by the angle of repose Θ. It is defined as the maximum angle possible between the surface of

the pile of the powder and the horizontal plane. To the pile the extra added powder slides down the sides of the pile until the mutual friction of the particles producing a surface angle Θ, is in equilibrium with the gravitational force. Funnel method is suggested for the determination of angle of repose by Newman. Angle of repose is determined by the following formula.

$\tan \Theta = h/r$

Therefore $\Theta = \tan^{-1} h/r$

Where Θ= Angle of repose

H = Height of the cone

R = radius of the cone base

Angle of repose less than 30° shows the free following of the material.

Bulk Density

Generally, density is the weight per unit volume. The mass of the powder divided by the bulk volume is known as Bulk Density (P_b), and is expressed as gm/cm^3. The Bulk Density of a powder primarily depends on particle size distribution, particle shape and tendency of the particles to adhere together. There are two types of Bulk Density. The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of bulk density. Shifting of smaller particles between the large particles resulting in heavy powder of high bulk density. Bulk Density is very important in the size of containers needed for handling, shipping, and storage of raw materials and blend. It is also important in size blending equipment. Weighed 50 cm^3sample blend is introduced in a100ml graduated cylinder. The cylinder is dropped on to a hard wood surface three times from a height of 1 inch at two second interval. The bulk density is then obtained by dividing the weight of sample in gms by final volume in cm^3.

$P_b = M/V_p$

Where,

P_b = Bulk Density

M = Weight of sample in gm

V_b = Final Volume of blend in cm^3

Tapped Density

Generally, the ratio of total mass of powder to the tapped volume of powder is denoted as Tapped density. Volume was measured by tapping the powder for 750 times and tapped volume was noted. It is the difference between the two volumes is less than 2%. If it is more than 2% tapping is continued until successive volume is less than 2%. It is expressed in gm/ml.

$D_t = M/V_t$

Where,

D_t = Tapped density

M = mass of powder

V_t = tapped volume

Compressibility Ratio

It indicates powder flow characteristics. It is expressed in percentage (%). Weigh accurately an accurate measure of sample and transfer into 50cc graduated measuring cylinder and note down the initial volume and calculate the initial or untapped bulk density using the formula.

Weight of granules / Initial volume

Fix the cylinder in bulk density apparatus until the volume of sample becomes constant. Note the final volume and calculate its tapped or final bulk density.

Initial bulk density (P_O) = Weight of sample/Initial volume

Final bulk density (P_t) = Weight of sample/Final volume

Compressibility ratio= $Pt\text{-}P_0/P_t*100$

Hausner's Ratio

It is measured by determining the bulk density and tapped density. It is determined by using the formula.

Hausner's Ratio = Tapped Density/Bulk Density.

Solubility Test

A little amount of drug is mixed in different solvents water, acetone, methanol, chloroform and its solubility are found out.

METHODOLOGY

Wet Granulation Method[10]

The powdered and mixed tablet ingredients namely the drug Albendazole, excipients like Sodium bicarbonate, Microcrystalline cellulose, Magnesium stearate, PVP are converted into a wet coherent mass. The coherent mass is forced through #40

mesh screen for granulation. The wet granules are dried in an oven and finally screened through #20 mesh screen.

Acid Granulation

Citric acid and Tartaric acid are blend together and pass through the Sieve no.40. Simethicone and Methylene chloride are mixed together then acid portion and pass through the Sieve no.20 and dried at 60ºC for 1 hour. IR (L.O.D) at 105ºC for 5 mins. L.O. D<1%.

Base Granulation

Sodium bicarbonate and Sodium carbonate are blend together and then pass through the Sieve no.40. PVP and Methylene chloride are mixed with base portion to form coherent mass and then pass through the sieve No.20 dried at 60 ^{0}C for 1 hour. Same as above (acid granulation).

Lubricant of acid and base granulation

Mix the acid and base granules. Add Albendazole and each Saccharin sodium, Sodium benzoate, Microcrystalline cellulose and mix it well.

Steps Involved in Tablet Making

1. Wet granulation the Albendazole and the intra-granular Sodium bicarbonate in a high shear granulator using an aqueous solution of Methylene chloride.
2. Drying result of step 1.
3. Milling result of step 2.
4. Dry blending result of steps 3 with the intra-granular Sodium benzoate and additional excipients.
5. Compressing into tablets the result of step 4.

Evaluation of Effervescent Tablets[8,11]

The tablets were subjected for the following quality control tests:

General appearance

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include tablets size, colour, presence or absence of an odour, taste, surface texture, physical flaws, consistency and legibility of any identifying marking.

Size and shape

The size and shape of the tablet can be dimensionally described, monitored and controlled.

Tablet thickness

The most important characteristic of tablet thickness is reproducing appearance and it is counted by using filling equipment. Five tablets were taken and their thickness was recorded using micrometre.

Weight variation

For weight variation, 20 tablets were weighed using an electronic balance and the average weight was calculated. Finally, the weights of individual tablet were compared with the average weight. Not more than two individual weights deviate from the average weight by more than the percentages shown in following table:

$$\text{Deviation} = \frac{\text{Average weight} - \text{Tablet weight}}{\text{Average weight}} \times 100$$

Tablet hardness

The diameter of chipping, abrasion or breakage under condition of storage transformation is due to the force applied and handling before usage depends on its hardness. Monsanto Hardness tester is usually used to determine the tablet hardness.

Friability

It is measured of mechanical strength of tablets. Friability is determined by Roche friabilator with the following procedure. A pre-weighed tablet was placed in the friabilator. It revolves at 25 rpm and having a plastic-chamber that drops those tablets at a distance of 6 inches with each revolution. The introduced tablets in a friabilator were rotated for at least 4 minutes. At the end of test tablets were dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Loss = Initial Weight-Final Weight / Final Weight x 100

Disintegration Test

The test was carried out on 6 tablets using the disintegration apparatus specified in I.P-1996 distilled water at 37ºC + 2ºC was used as a disintegration media and the time less than a minute is taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

Fourier Transformation Infra-Red (FT-IR) Analysis[12]

Infra-red spectrum of pure drug and polymer were obtained from Sri Ramachandra University. The spectra were scanned over the wave number range of 4200 to 500 cm^{-1}.

Calibration curve of Albendazole[13]

Standard preparation of albendazole

Standard solution was prepared by dissolving 50mg of Albendazole in 100ml of Methanolic glacial acetic acid to get concentration of 500µg/ml. aliquots of standard solution were further diluted with methanolic glacial acetic acid to get working solution of 2.5, 5, 7.5, 10, 12.5, 15, 17.5, 20, 22.5 µg/ml and the working standards were scanning between 150-300nm which shows the maximum absorbance at 235nm.

***In vitro* release studies**[14,15]

Procedure

1. Dissolution studies were using the dissolution apparatus USP DISSO 2000 model using paddle method.
2. Tablet was put into the dissolution apparatus containing a buffer solution at pH 7.4.
3. The speed of paddle was maintained at about 25-30 rpm.
4. Pipetted out 5ml sample and dissolved the sample into acetone at an interval of 5 min, 10min and 15min.
5. The collected sample were filtered and observed the absorbance at 334nm in UV spectrometer.

RESULTS AND DISCUSSION

Pre-formulation study

Identification test

Colour, Odour, Taste and Appearance:

Pre-formulation studies

Solubility

The drug was found to be soluble in acetone and practically insoluble in water.

The angle of repose of the prepared granules was found to be good when compared to the drug before granulation. The bulk density of the drug was found to be reduced after granulation. The tapped density of the drug was found to be reduced after granulation. The compressibility ratio of the drug was found to be fair before granulation and after granulation it was found to be good. From the above value of Hausner's ratio it was found that the drug has good flow property. Post compression parameters like Hardness, Weight variation, Thickness, Friability were evaluated and are found to be within the limit. The disintegration test was performed for the marketed tablet and the prepared the effervescent tablet of Albendazole and are found to be within the limit. FTIR Spectra of Albendazole and the physical mixture of Albendazole and polymers were taken. All the Characteristic peaks of the pure drug were observed and the spectrum of mixture. This indicated that there was no interaction between the drug and polymers. The dissolution studies were performed for the three formulations and marketed tablet. The percentage release profile of F1, F2, F3 and marketed tablet were found to be 99.87%, 89.75%, 83.25% and 98.97% respectively. The F1 gave better release compared to other formulations at the end of 15 mins. Also, F1 shows better release when compared to that of the marketed chewable tablet of Albendazole.

Table No.1: Angle of Repose with flow properties

S.No	Flow properties	Angle of Repose (degrees)
1	Excellent	Up to 20
2	Good	Up to 30
3	Fair/Reasonable	Up to 40
4	Flow with difficulty	Above 50

Table No.2: % Compressibility limit with respect to flow property

S.No	%Compressibility	Flow ability
1	5-12	Excellent
2	12-16	Good
3	18-21	Fair
4	23-25	Poor
5	38-38	Very poor
6	More than	Very very poor

Table No.3: Hausner's Ratio limits

S.No	Hausner's Ratio	Type of flow
1	<1.25	Good flow
2	>1.25	Poor flow

Table No.4: Identification test

S.No	Parameter	Drug
1	Colour	White
2	Odour	Odourless
3	Taste	Tasteless
4	Appearance	Crystalline powder

Table No.5: Pre-formulation studies

S .No	Parameter	F1	F2	F3
1	Angle of Repose	15º12′	20º 17′	24º18′
2	Bulk Density	0.612	0.467	0.419
3	Tapped Density	0.75	0.583	0.5
4	Compressibility	18.4%	19.897%	16.2%
5	Hausner's ratio	1.225	1.248	1.193

Table No.6: Evaluation of tablets

S.No	Thickness	Weight variation	Hardness (kg/cm2)	Friability (%)	Disintegration time (mins)
1	0.6mm	Passes	4.1	0.58	2 mins 30 sec
2	0.6mm	Passes	4.2	0.82	3 mins 18 sec
3	0.6mm	Passes	4.2	1.33	5 mins 27 sec

Table No.7: Concentration and Absorbance values for Albendazole

S.No	CONCENTRATION(µg/ml)	ABSORBANCE (325nm)	EQUATION OF LINE AND REGRESSION
1	0.5	0.11	$Y=0.0298x+0.035 r^2 = 0.09892$
2	1	0.214	
3	1.5	0.311	
4	2	0.437	
5	2.5	0.518	
6	3	0.618	
7	3.5	0.76	

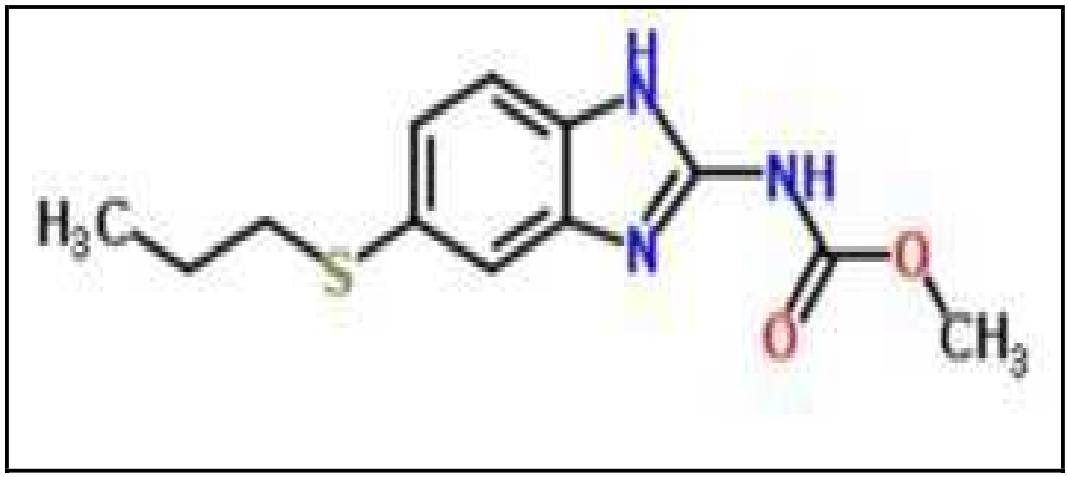
Table No.8: % Drug release of formulated Albendazole effervescent tablet

Formulation	Time (min)	(µg/ml)	Amount of drug release	%Drug release
I	5	0.29	261	65.25
	10	0.35	315	78.75
	15	0.41	369	99.87
II	5	0.28	252	63.07
	10	0.33	297	74.28
	15	0.38	342	89.75
III	5	0.26	234	58.5
	10	0.32	288	72.73
	15	0.37	333	83.25

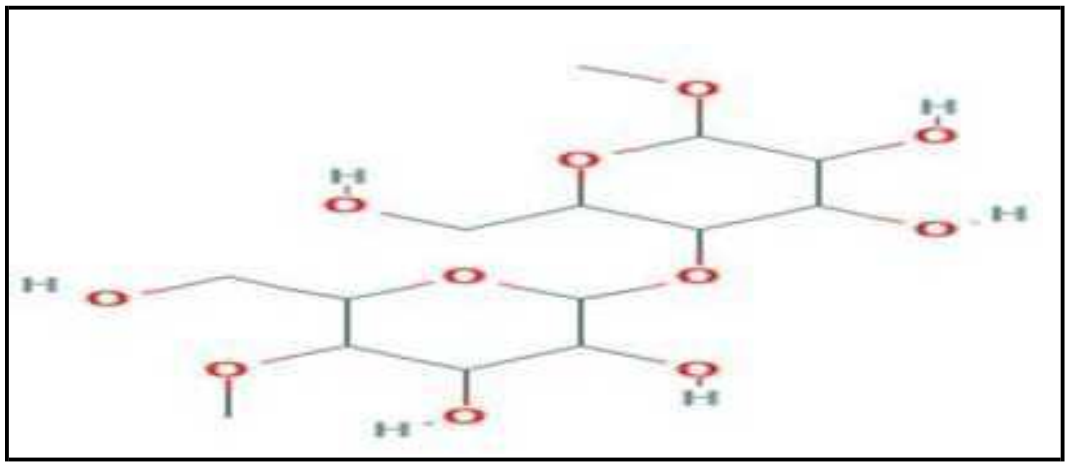
Table No.9: % Drug release of marketed chewable tablet of Albendazole

S.No	Time (min)	Concentration (µg/ml)	Amount of Drug Release	%Drug Release
1	10	0.19	171	44.37
2	20	0.33	297	74.25
3	30	0.4	360	98.97

Structure



Structure



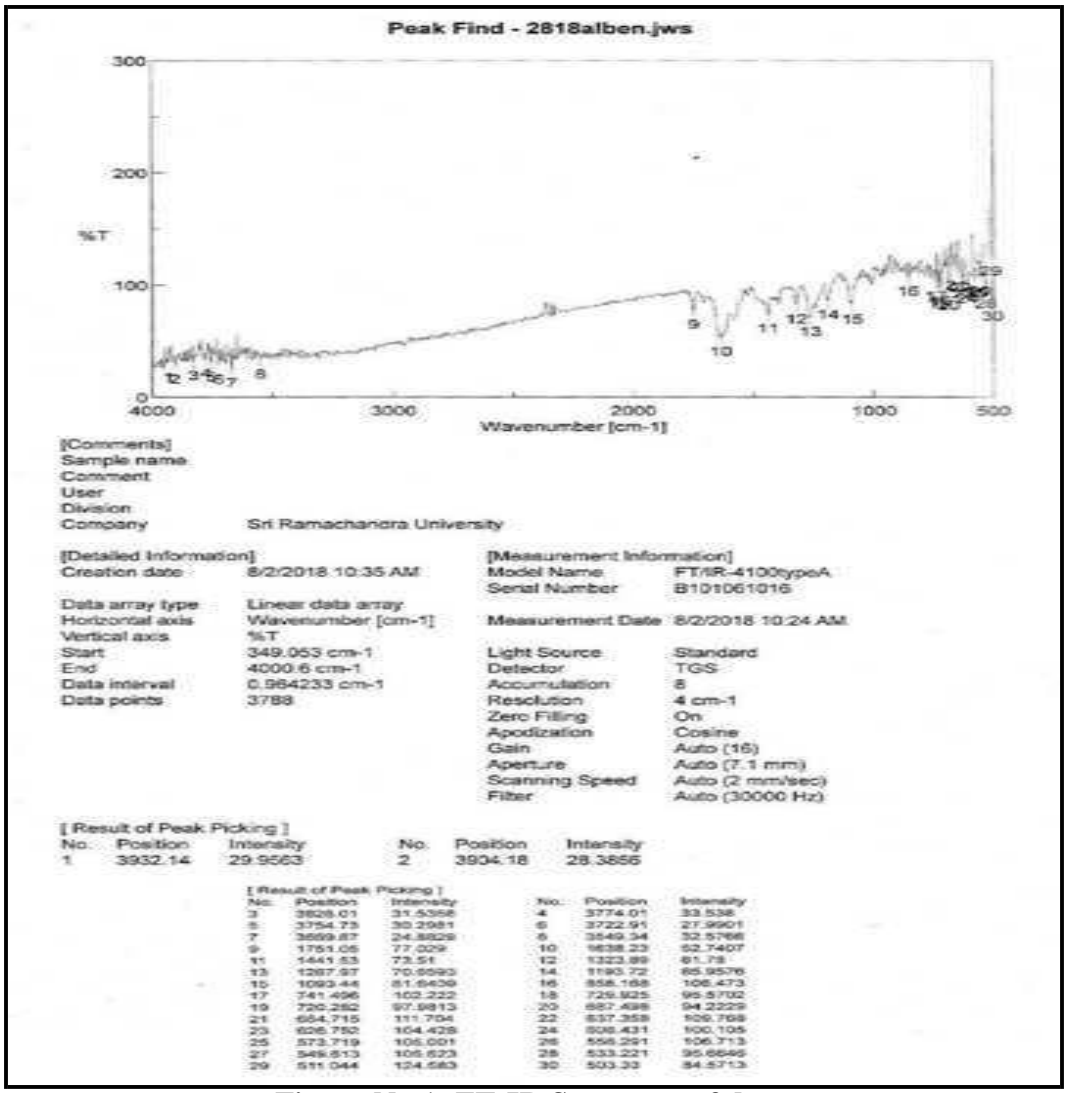


Figure No.1: FT-IR Spectrum of drug

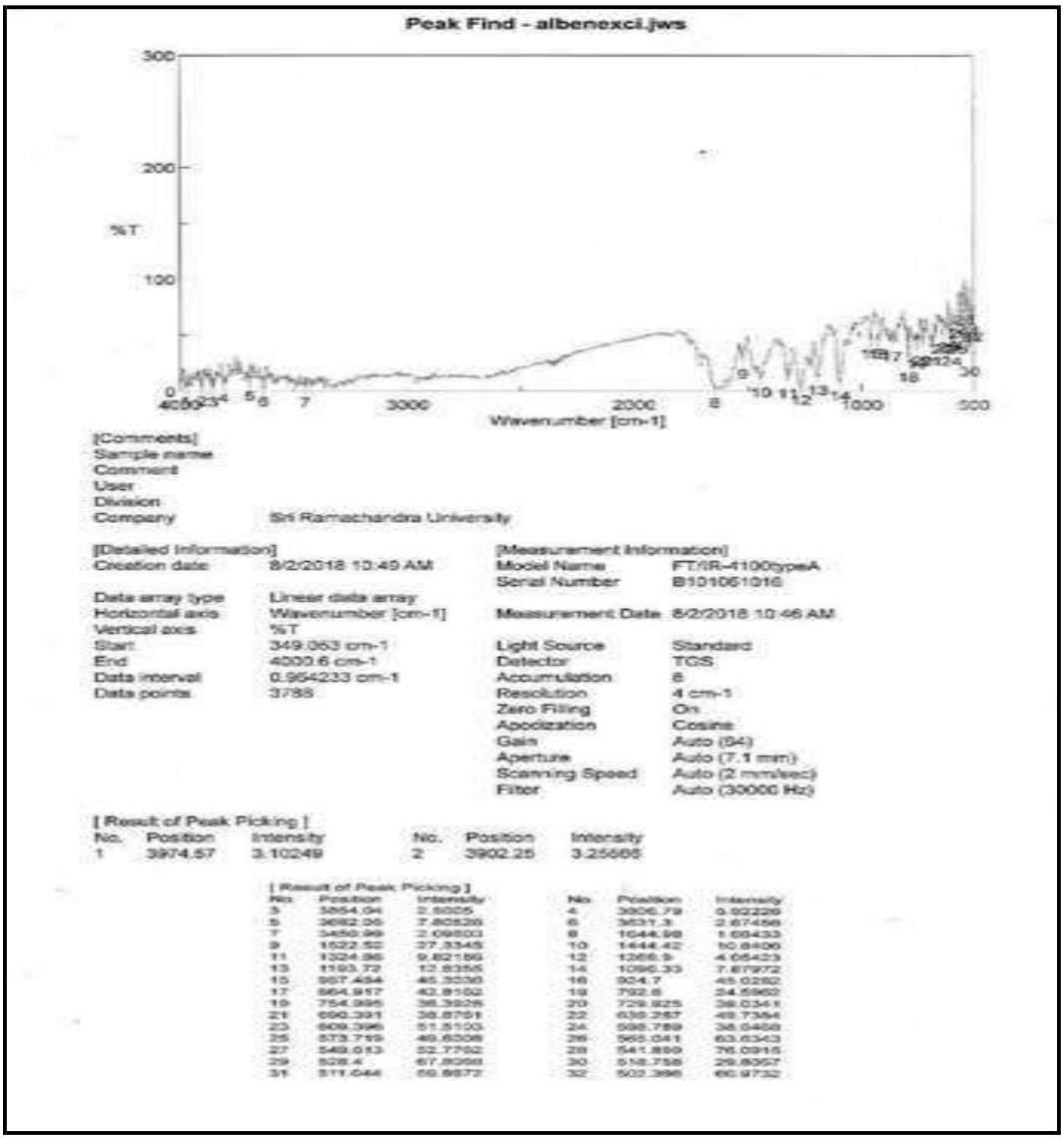


Figure No.2: FT-IR Spectra of Drug and Polymer

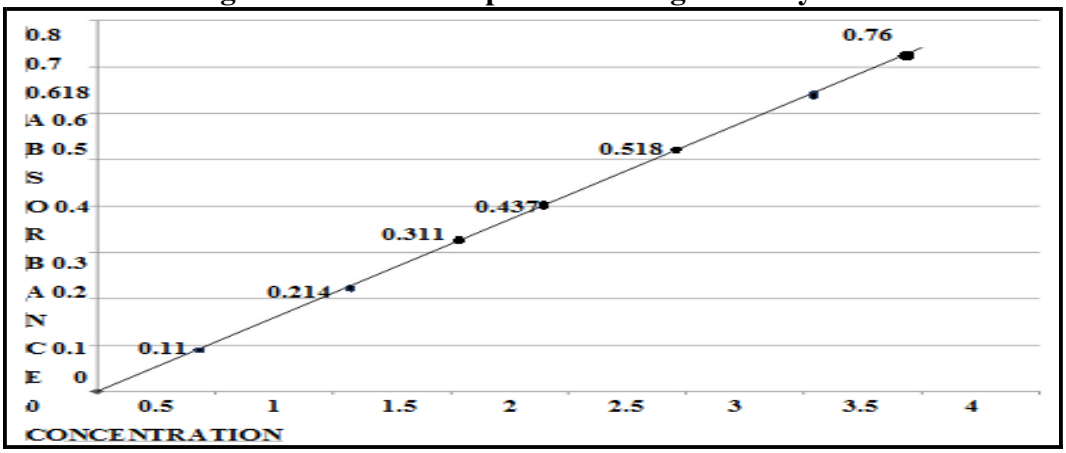


Figure No.3: Standard calibration curve of Albendazole

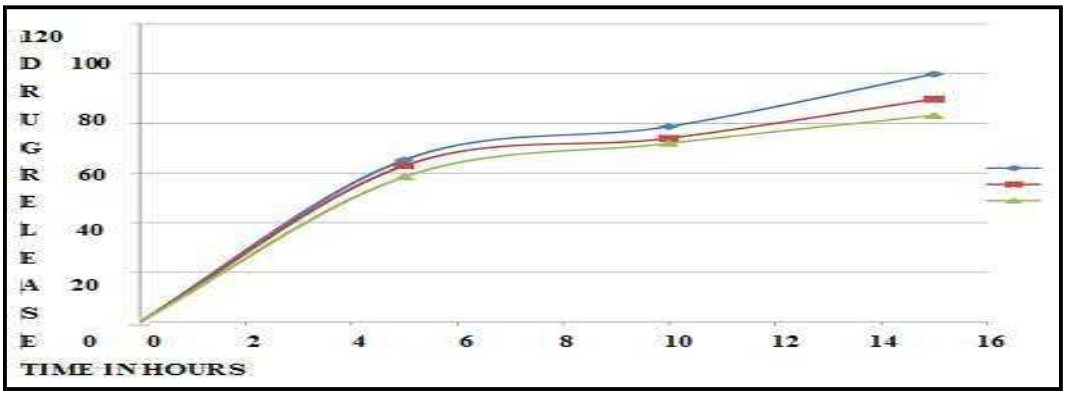


Figure No.4: % Drug release of formulated Albendazole effervescent tablet

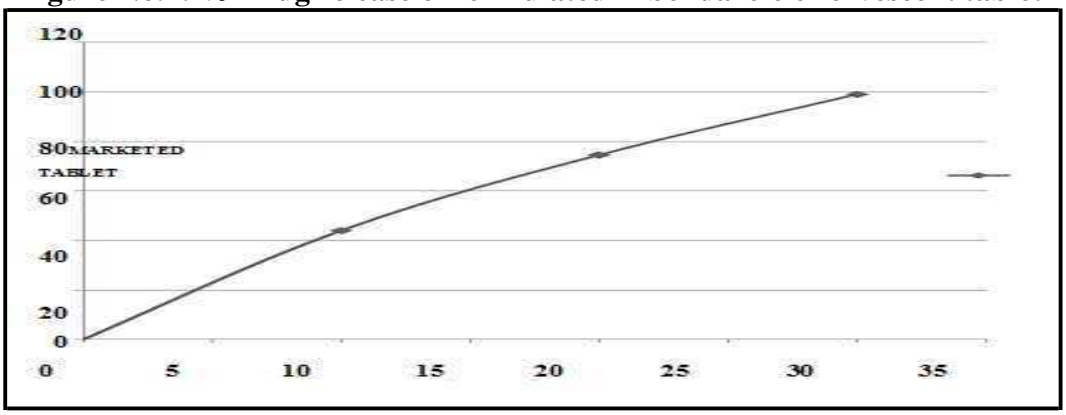


Figure No.5: % Drug release of marketed chewable tablet of Albendazole (DRUG RELEASE VS TIME IN HOURS)

CONCLUSION

Albendazole is an Anti-helminthic drug used in the treatment of Helminthiasis. It is available as Chewable tablet and Suspension. The % Release profile of Chewable tablet of Albendazole was found to be 98.97% at the end of 30 mins. So, that effervescent tablet of Albendazole was formulated. This has improved %release profile within 15 mins. Based on bioavailability studies Albendazole has to be released in a rapid manner (minimum of 80% release in 10-15mins), to achieve rapid absorption and enhanced bioavailability. The formulations were compatible with drug and excipients. Improvement in the rate and extent of dissolution may also lead to the less variation in the pharmacokinetic parameters during the bioequivalence studies.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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