International Journal of Research and Development in Pharmacy and Life Sciences
Available online at http//www.ijrdpl.com
October - November, 2015, Vol. 4, No.6, pp 1827-1834
ISSN (P): 2393-932X, ISSN (E): 2278-0238

Research Article

FORMULATION AND CHARACTERIZATION OF FAST DISSOLVING TABLET OF THIABENDAZOLE

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(Received: July 21, 2015; **Accepted:** September 13, 2015**)**

ABSTRACT

Thiabendazole is an anthelmintic drug inhibits the enzyme fumarate reductase and thus provide cidal action to the helminth. Thiabendazole have low bioavailability about 30 to 40%. The main aim of the present investigation was to increase the bioavailability of the drug and to provide the cidal action against the helminth by preparing fast dissolving tablet. Thiabendazole is effective in helminthic infection in children and fast dissolving tablets are most suitable for the children due to ease of administration and no water requirement. Fast Dissolving Tablet of Thiabendazole provide rapid onset of action with better release. Fast dissolving tablets of Thiabendazole was prepared by Direct compression method and evaluated by pre-compression and post-compression parameter. Benzimidazole derivatives are less soluble in water and for fast dissolving tablets the water solubility is prime requirement and that can be achieved by using Acrysol K-150 Polymer. Among all the formulation the tablet ODT6 that contains Co-proceed super disintegrants Kyron T-314 with maximum amount of microcrystalline cellulose and Acrysol K-150 was considered to be best formulation and which release upto 98.75% within 3 Minutes.The tablet that contains combination of sodium starch glycolate and croscarmellose sodium (ODT8) is found as second best tablet and Provide 97.78% Drug release.

Keywords: Thiabendazole, ODT, Release, Acrysol K-150, Kyron T-314 etc.

INTRODUCTION

Fast dissolving tablets are new generation tablet and accepted by all age group patients due to the unit dose and increased patient compliance, they do not require water and most suitable for the patient that are older in age(Geriatric) and elder in age (Pediatric). Fast dissolving tablets are also known as mouth dissolving tablets(MDT) or oral disintegrating tablets (ODT). They rapidly melt in the mouth and provide rapid onset of action (1,2,3). Thiabendazole {2-(1,3-thiazol-4-yl)-1H-1,3-benzodiazole} is basically an anthelmintic drug and used to prevention and the treatment of Helminthiasis. It belongs to the class Benzimidazole. Thiabendazole is most effective drug for the children and it is used for the treatment of strongyloidiasis (threadworm infection), cutaneous larva migrans (creeping eruption), and visceral larva migrans alone or in conjunction with enterobiasis (pinworm)(4,5).

Direct compression is one of the simplest method for preparation of the tablet it eliminates the number of steps during tablet preparation. Direct compression method was used in the present investigation with a number of superdisintegrants for preparing Fast dissolving tablet of Thiabendazole. Co- Proceed super disintegrants, Kyron T-314 was used to provide the rapid release of the drug.

MATERIAL AND METHODS

Acrysol K-150 and Kyron T -314 was obtained as a gift sample from Corel Pharma Chem, The Drug Thiabendazole was obtained from Oasis Laboratory Pvt. Ltd and all other Ingredients are provided by the institution. The drug Thiabendazole is poorly soluble in the water the solubility of

Thiabendazole is increased by using Acrysol K-150 Polymer. Kyron T- 314 is used as a Co-proceed superdisintegrants. Aspartame is used as a sweetening agent. Poly vinyl pyrrolidone used as a binding agent, Talc is used as a glidant, magnesium stearate is used as lubricant, Sorbitol and Mannitol are used as Diluent and Remaining sodium starch glycolate, Croscarmellose sodium are used as super disintegrants.

Preparation of Fast Dissolving Tablet

The critical parameters to formulate fast dissolving tablet are choice of super disintegrants and optimization of concentration of superdisintegrants. The main criteria for fast dissolving tablets is to disintegrate or dissolve rapidly in oral cavity in 15-60 seconds, without need of water and should have pleasant mouth feel.

The Fast dissolving tablet of Thiabendazole are prepared by using direct compression method with the incorporation of superdisintegrants like Microcrystalline cellulose (MCC), Sodium starch glycolate, Croscarmellose Sodium (CCS), Polyvinyl Pyrrolidone. with Acrysol K-150 and Thiabendazole equivalent to 250 mg, Mannitol and Microcrystalline Cellulose are mixed thoroughly in glass mortar using a pestle. Superdisintegrants were incorporated in the powder mixture according to each formulation in the tablets and finally Aspartame, and Magnesium stearate was added. The whole mixture was passed through Sieve No. 60 twice. Tablets were prepared by using Shakti Pharmatech 10 station punching machine. The compression force was constant during Punch(6,7).

Table 1: Thiabendazole Fast Dissolving Tablets by direct compression method.

Ingredients	ODT_1	ODT_2	ODT_3	ODT_4	ODT_5	ODT_6	ODT_7	ODT_8
Thiabendazole	250	250	250	250	250	250	250	250
SSG	15	20	-	-	-	-	-	-
CCS	-	-	15	20	-	-	-	-
Kyron T-314	-	-	-	-	15	20	-	-
SSG+CCS	-	-	-	-	-	-	15	20
Acrysol K-150	10	15	10	15	10	15	10	15
Avicel pH-102	30	25	30	25	30	25	30	25
PVP	4	3	4	3	4	3	4	3
Talc	2	2	2	2	2	2	2	2
Magnesium stearate	3	3	3	3	3	3	3	3
Aspartame	2	2	2	2	2	2	2	2
Mannitol/Sorbitol	34	30	34	30	34	30	34	30
Total wt. (mg)	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**

CHARACTERIZATION OF DRUG

Calibration curve of Thiabendazole

The calibration curve of Thiabendazole was prepared in Sorenson's Buffer pH 6.8 at 290 nm and the absorbance values of different concentrations of Thiabendazole solutions in methanolic Sorenson's Buffer pH 6.8 .

Table 2 : Calibration Curve Data of Thiabendazole

Concentration(mcg/ml)	Absorbance (290 nm)
0.0	0
2.0	0.176
4.0	0.306
6.0	0.498
8.0	0.639
10.0	0.809
12.0	0.920
14.0	1.08

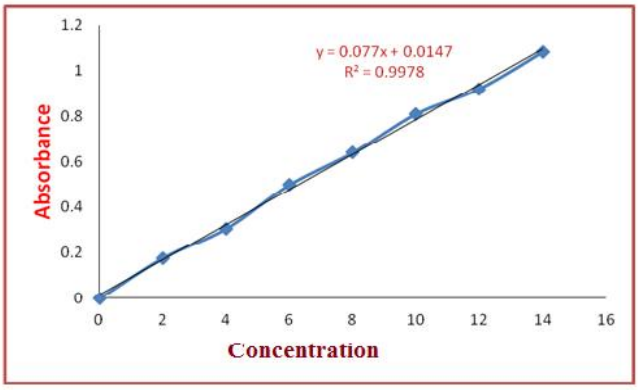

Figure 1: Calibration Curve of Thiabendazole

FT-IR Spectroscopy

The identity of a compound was confirmed by comparison with that of an authentic sample and verification of the presence of functional groups in an unknown molecule was done by IR spectra. The IR spectra obtained was elucidated for important chromophore groups.

The pellet of approximately 01 mm diameter of the drug was prepared grinding 3-5 mg of sample with 100-150 mg of Potassium Bromide in pressure compression machine. The sample pellet was mounted in IR compartment and scanned at wavelength 4000 cm-1 – 400 cm-1. The IR spectra of Thiabendazole showed peaks at 1408, 906, 740, 3487 cm-1.

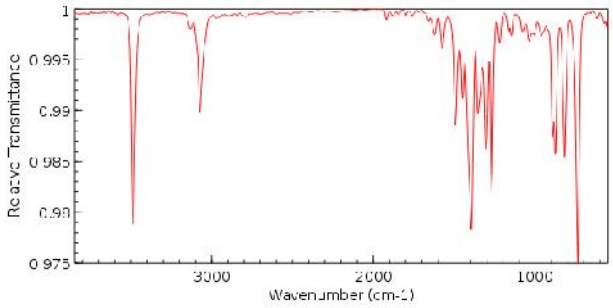

Figure 2: IR Spectra of Thiabendazole

EVALUATION OF FAST DISSOLVING TABLETS

Pre-compression studies (Evaluation of blends)

The evaluation of Pre-compression studies of formulated Fast dissolving tablets Thiabendazole were done as per standard procedures. Tablets were made from blends by direct compression method. The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends.

Bulk Density

A sample of about 50 cm3 (blend) is carefully introduced in a 100ml graduated cylinder. The cylinder is dropped onto a hard wood surface five 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.

Bulk density(Bd) = Mass of the powder (M) / Bulk Volume (Vb)

Tapped density

It is the ratio of total mass of powder to the tapped volume of powder. The volume was measured by tapping the powder for 100 times. It is expressed by given formula.

Tapped density (Td) = Mass of the powder (M) / Tapped Volume (Vt)

Compressibility index

It is the simple indication of the flow property of the blend. It can be determine with the help of bulk density and tapped density. It can be calculated by following formula:

$$\% \text{ Compressibility} = Td\text{-}Bd / Td \times 100$$

Where Td and Bd are tapped density and bulk density respectively.

Hausner ratio

Hausner ratio is the indirect index of the powder flow. It can be determined by given formula:

Hausner ratio = Td / Bd

Where, Td is the tapped density and Bd is the bulk density. Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Angle of Repose

Angle of repose is the Maximum angle between the surface of a cone of the powder and the horizontal plane. Angle of repose is determined by the following formula (8)

$\tan \theta = h/r$

Therefore $\theta = \tan^{-1} h/r$ Where θ = Angle of repose

h = height of the cone

r = Radius of the cone base

POST-COMPRESSION PARAMETER

Tablet Thickness and Diameter

Ten tablets were selected randomly from each formulation and their thickness was measured with Vernier caliper . The mean ± SD values were also calculated.

Tablet hardness test

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. Hardness of the tablet of each formulation was determined using Monsato Hardness tester. The force was measured in Kg/ cm^2.

Friability

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure.

The preweighed amount of the tablet was placed in Roche friabilator that is rotating with the speed 25 RPM. In Roche friabilator tablets are falling from 6 inch height in each round upto 4 Minutes and after that the tablets are reweighed and the loss in the weight of tablet is the measure of friability and is expressed in percentage as:

% Friability = loss in weight / Initial weight X 100

Friability = (W1-W2) / W1 X 100

Where W1 = weight of the tablet before test, W2= weight of the tablets after test (9)

Weight Variation:

Twenty tablets were randomly selected from each batch, individually weighed, the average weight and standard deviation of 20 tablets was calculated.

% Deviation = Individual weight –Average weight / Average weight X 100

Content uniformity:

Ten randomly selected tablets were weighed and average weight was calculated, the tablets were powdered in a glass mortar. The weight equivalent to 10 mg Thiabendazole was weighed. The weighed amount was dissolved in 10 ml of methanol in separate volumetric flask using magnetic stirrer,

Table 3: Characterization of blend of Thiabendazole tablet

Parameters Formulation	Bulk density (mg/ml)	Tapped Density (mg/ml)	Hausners Ratio	Compressibilty Index (%)	Angle of Repose
ODT_1	0.537±0.002	0.615±0.002	1.145±0.11	12.68±0.34	25.18±1.37
ODT_2	0.551±0.003	0.637±0.003	1.150±0.12	13.50±0.40	22.13±0.96
ODT_3	0.557±0.005	0.617±0.004	1.107±0.09	9.72±0.45	21.94±0.98
ODT_4	0.568±0.003	0.638±0.002	1.123±0.10	10.97±0.70	25.49±0.99
ODT_5	0.561±0.004	0.625±0.001	1.114±0.11	10.24±0.49	28.19±1.17
ODT_6	0.558±0.002	0.643±0.006	1.152±0.13	13.21±0.57	23.12±1.19
ODT_7	0.564±0.007	0.639±0.004	1.132±0.12	11.73±0.67	22.17±1.09
ODT_8	0.571±0.003	0.669±0.005	1.171±0.11	14.64±0.22	27.18±1.36

Table 4: Characterization of Thiabendazole fast dissolving tablet

Parameter / Formulation	Diameter (mm) ±SD	Thickness (mm) ±SD	Weight Variation (mg) ±SD	Hardness (Kg/cm²) ±SD	Friability (%)±SD
ODT_1	8±0.040	6±0.019	351.25±0.19	2.9±0.3	0.70±0.14
ODT_2	8±0.038	6±0.022	347.89±0.74	2.8±0.4	0.43±0.21
ODT_3	8±0.029	6±0.017	348.26±0.98	2.7±0.2	0.48±0.19
ODT_4	8±0.033	6±0.038	347.12±1.18	2.5±0.4	0.55±0.17
ODT_5	8±0.054	6±0.041	348.86±1.08	2.9±0.3	0.51±0.11
ODT_6	8±0.029	6±0.017	349.86±0.96	3.0±0.1	0.47±0.21
ODT_7	8±0.047	6±0.028	345.97±1.81	2.8±0.3	0.45±0.17
ODT_8	8±0.052	6±0.033	347.98±1.91	2.6±0.3	0.57±0.11

Table 5 : Drug Content in the Fast Dissolving Tablet of Thiabendazole

Parameters Formulation	Drug Content (mg per Tablet)	% Drug Content
ODT_1	240.55±0.026	96.22
ODT_2	247.88±0.048	99.15
ODT_3	259.88±0.121	103.95
ODT_4	242.85±0.726	97.14
ODT_5	257.33±0.389	102.93
ODT_6	249.87±0.256	99.94
ODT_7	242.98±0.567	97.19
ODT_8	251.85±0.389	100.74

Table 6: Release Rate of Thiabendazole with different formulation at different time interval

Time (Min)	Release rate of Thiabendazole at different time interval							
	ODT1	ODT2	ODT3	ODT4	ODT5	ODT6	ODT7	ODT8
0	0	0	0	0	0	0	0	0
0.5	35.78	39.9	30.89	32.88	45.49	48.96	40.85	45.86
1.0	65.67	68.96	57.89	59.88	72.15	75.98	71.05	73.80
1.5	73.88	75.41	62.48	63.97	78.82	85.63	75.97	82.82
2.0	82.85	86.92	66.85	67.88	88.90	90.55	88.78	89.09
2.5	86.45	90.81	71.88	73.89	92.23	96.62	90.78	93.51
3.0	90.92	91.23	76.88	78.38	93.78	98.75	92.80	97.78

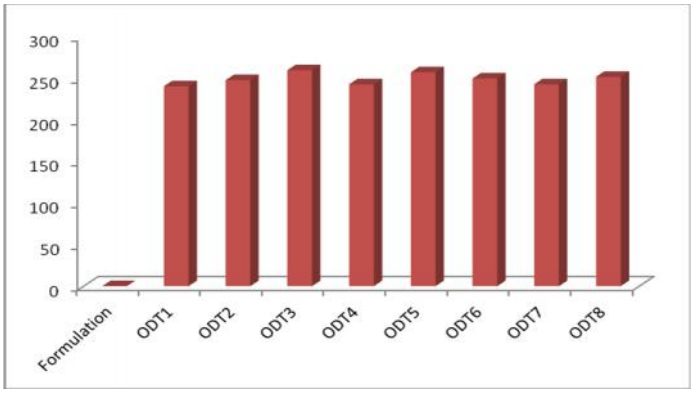

Fig 3: Graphical Representation of percent Drug Content

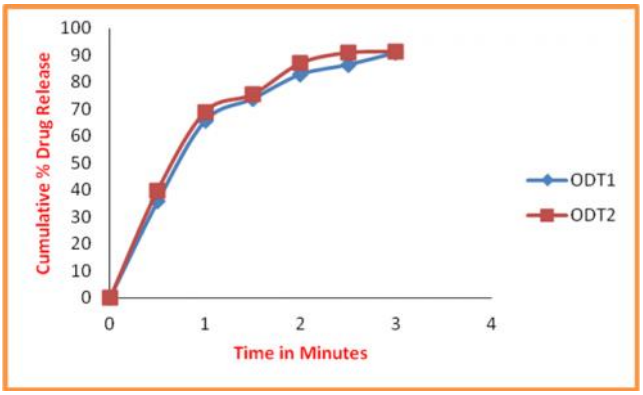

Fig 4: In vitro release curve of Thiabendazole tablet [Zero Order Release (ODT1 & ODT2)]

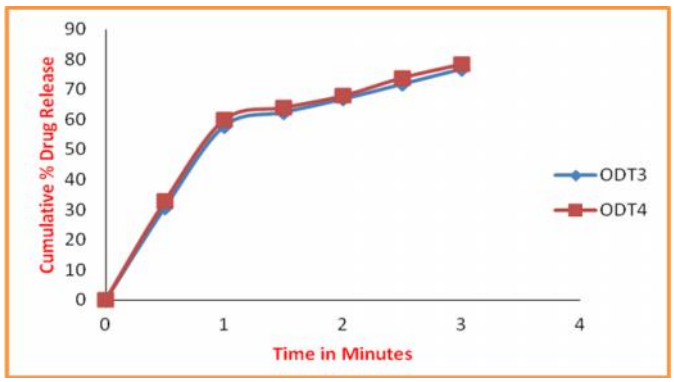

Fig 5: In vitro release curve of Thiabendazole tablet -Zero Order Release (ODT3 & ODT4)

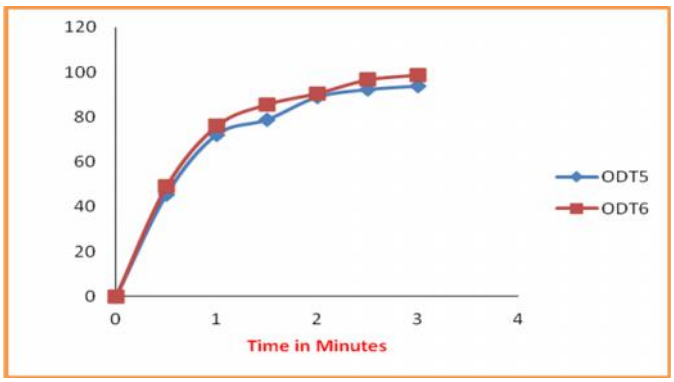

Fig 6: In vitro release curve of Thiabendazole tablet -Zero Order Release (ODT5 & ODT6)

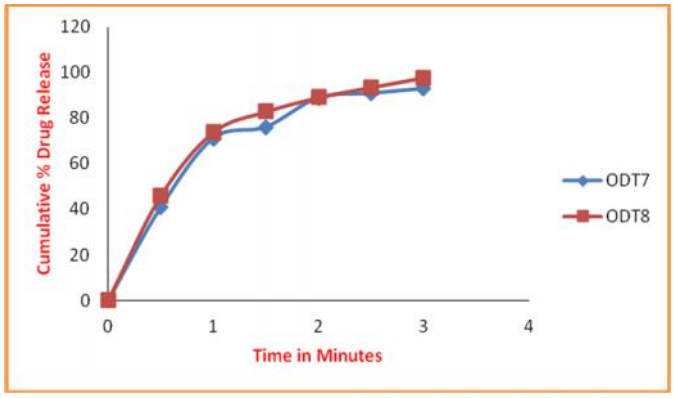

Fig 7: In vitro release curve of Thiabendazole tablet -Zero Order Release (ODT7 & ODT8)

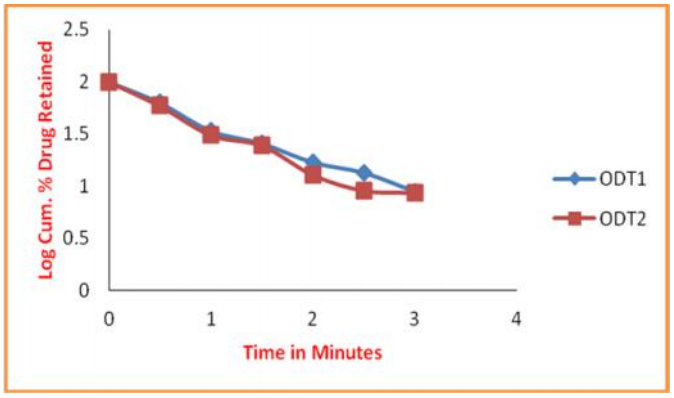

Fig 8: In vitro release curve of Thiabendazole tablet -First Order Release (ODT1 & ODT2)

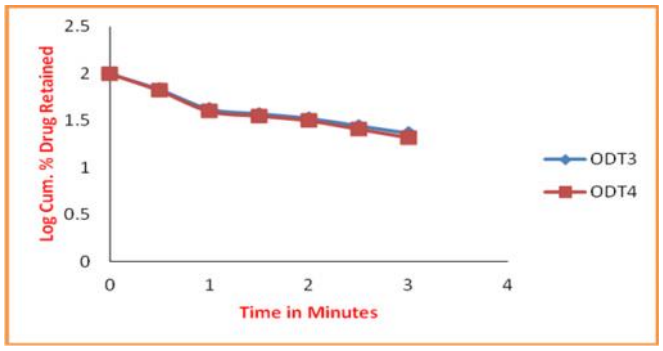

Fig 9: In vitro release curve of Thiabendazole tablet -First Order Release (ODT3 & ODT4)

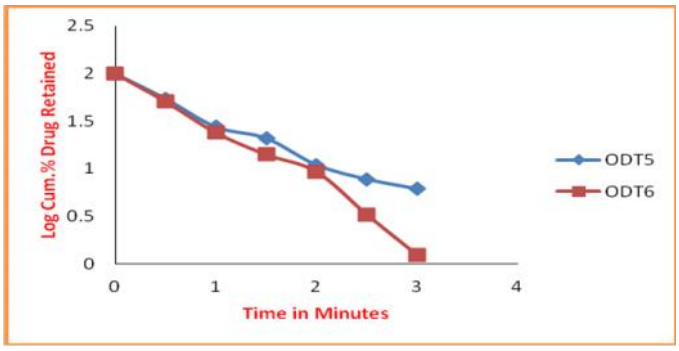

Fig 10: In vitro release curve of Thiabendazole tablet -First Order Release (ODT5 & ODT6)

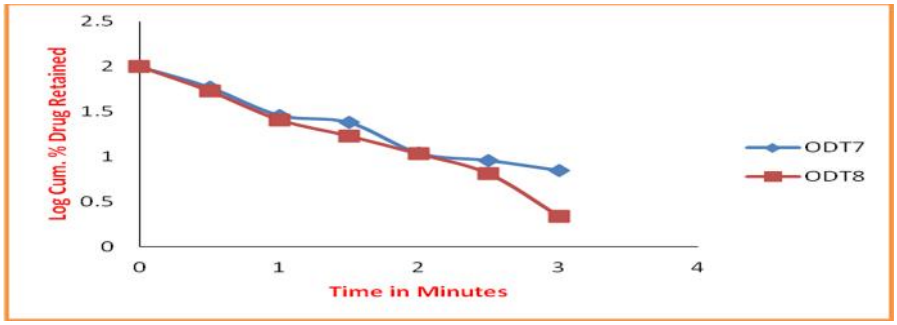

Fig 11: In vitro release curve of Thiabendazole tablet -First Order Release(ODT7 & ODT8)

the volume was adjusted with Methanol, the solution was filtered and UV absorbance was measured at 290 nm by using Double beam spectro photometer 2203(SYSTRONICS). Drug concentration was determined from standard graph.

Disintegration time

The test was carried out by using 6 tablets in distilled water at 37±20 C and the time in seconds was recorded when no residue remaining in the apparatus(10).

Wetting time

A piece of paper (12 cm X 10.75 cm) folded twice was kept in a Petri dish containing 6 ml of purified water. A tablet placed on the tissue paper. The time for complete wetting was measured on the upper surface of the tablet was recorded as the wetting time(11).

Parameter / Formulation	Disintegration time (Sec) ±SD	Swelling time (Sec) ±SD
ODT_1	44±4	23±1
ODT_2	47±2	20±2
ODT_3	48±1	25±1
ODT_4	42±1	22±1
ODT_5	38±1	27±2
ODT_6	36±1	24±2
ODT_7	38±3	20±2
ODT_8	39±3	17±3

In vitro Drug Release

In vitro drug Release rate for all the tablets were carried out using LAB INDIA DS8000 at 75 rpm in 900 ml of Sorenson's buffer pH 6.8 as dissolution media, maintained at 37±0.50C. The sample was withdrawn at different time interval and filtered through whatmann filter paper and assayed spectrophotometrically at 290 nm. An equal volume of fresh medium, which was prewarmed at 370C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test(12).

The various kinetic treatments are given to in vitro release data, The in vitro data obtained are put in different kinetic models like Zero order, First Order, Higuchi and Korsemeyer equation. It indicates the release profile and release mechanism.

RESULT & DISCUSSION

Pre-compression parameters

1. Bulk Density and Tapped Density of the Blend were found as 0.537 to 0.571 and 0.615 to 0.669 respectively.
2. Carr's index of the prepared blend fall in the range of 9.72 to 14.64% and this is also supported by Hausner's factor values which were in the range of 1.110 to 1.171.Hence the prepared blends posses good flow property and can be used for manufacturing of the tablet.
3. The values of angle of repose were found in the range of 21.94 to 28.19.

Post-compression Parameter

All the tablets were prepared under similar experimental conditions. All the formulation exhibited white colour, odourless, flat shaped with almost smooth surfaces.

1. The average weight of the fast dissolving tablet was 345.97 to 351.25mg.
2. Hardness of prepared tablet was between 2.5 to 3.0 kg/cm2
3. The percent friability of formulations was found to be 0.43 to 0.70 (less than 1.0%) and thus hardness and friability of all formulation are found within acceptable limits.
4. The quick disintegration may assist quick swallowing and drug absorption in buccal cavity, thus greater bioavailability of the drug. Disintegration time of prepared fast dissolving tablet was found in the range of 38 to 48 seconds.
5. Wetting time of tablet was in the range of 17 to 27 seconds
6. Assay of the prepared formulation was performed to determine drug content uniformity and it was found between 96.22 to 103.95%.
7. The release of drug followed first order kinetics and mechanism of drug release was found to be diffusion controlled.

ODT6 > ODT8 > ODT5 > ODT7 > ODT2 > ODT1>ODT4>ODT3

CONCLUSION

Fast Dissolving Tablet of Thiabendazole was successfully prepared by Direct compression method using Super disintegrants with the Aim to provide quick onset of action and effective treatment. The Relative efficiency of these superdisintegrants to improve the dissolution and drug release of the tablet. The efficiency of the super disintegrants found as in given order

Kyron T-314 > Sodium Starch glycolate > Croscarmellose sodium

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