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FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF ALBENDAZOLE

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Abstract:

Albendazole is an oral broad spectrum anthelmintic, antiparasitic agent generally prescribed for the treatment of tissue infections caused by a variety of namatodes, Threadworm, Hookworm, and Tapeworm. It has low bioavailability due to its first pass metabolism. It is water insoluble drug. The purpose of the present research work was to formulate and evaluate the mouth dissolving tablets of Albendazole by direct compression method using different superdisintegrants like sodium starch glycolate, croscarmellose sodium, and crospovidone in different concentrations. FT-IR spectroscopy was used to investigate the physical characteristics of the complex. The blend was evaluated for angle of repose, bulk density, tapped density, Carr's index hausner's ratio. The tablet were evaluated for hardness, weight variation, friability, disintegration time, water absorption ratio, wetting time, drug content uniformity and in-vitro dissolution. The % cumulative release of drug from tablet (F5) was found to be more than 97.06% within 40 minutes. It was concluded from the study that Albendazole may improve patient compliance especially pediatric and geriatric patients and increase the efficacy of drug for treating infections.

Keywords: *Albendazole, Mouth dissolving tablets, Superdisintegrants.*

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INTRODUCTION:

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drug via various pharmaceutical products of different dosage form. The reasons that the oral route achieved such popularity may be part attributed to its ease of administration as well as traditional belief that by oral administration the drug is as well absorbed as the foodstuffs that are ingested daily [1]. Introduction of therapeutic substance into the body to improve its efficacy and safety is known as drug-delivery system which interfaces between the patient and the drug. Drug may be introduced in to human body by various routes, but oral route has been one most popular and used route for both conventional as well as novel drug delivery because of low cost therapy, avoidance self medication ease of ingestion leading to high level compliance and did not require sterile conditions [2]. Drug delivery systems are a strategic tool for expanding markets, extending product life cycle and generating opportunities. Patient compliance, high-precision dosing, and manufacturing efficiency make tablets the solid dosage form of choice. Excipients and equipments choices will be significantly affected should solid dosage form technologies change in response to the unprecedented shifts in the drug discovery such as genomics. Injections generally are not favored for use by patients unless facilitated by sophisticated auto injectors. Inhalation is one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so far has generate predominantly chemical entities with low molecular weights. The development of enhanced oral protein delivery technology by Fast dissolving Tablets which may release these drugs in the mouth are very promising for the delivery of high molecular weight protein and peptide [3]. An ideal dosage regimen in the drug therapy of any diseases is one which immeditely attain the desire therapeutic concentration of drug in plasma and maintain it constant for the entire duration of treatment. Drugs are more frequently taken by oral route. Although few drugs taken orally are intended to be dissolving in mouth, the vast majority of drugs have taken orally swallowed. Compared with alternate routes, the oral route of drug administration is the most popular and has been successfully used for conventional delivery of drug. Fast dissolving tablet is an important and alternative to liquid dosage form [4].

MATERIALS AND METHODS:

List of Materials:

The following materials that were either LR/AR grade or the best possible Pharma grade available were used as supplied by the manufacturer.

Table 1:List of Chemicals used with Suppliers

Sr. No.	Materials	Suppliers
1	Albendazole	Medriech ltd(Meiji seika pharma) Benglore.
2	Crosscarmellose Sodium	S.D. Fine Chemicals, Mumbai
3	Crospovidone	S.D. Fine Chemicals, Mumbai
4	Sodium Starch Glycolate	S.D. Fine Chemicals, Mumbai
5	Microcrystalline cellulose	S.D. Fine Chemicals, Mumbai
6	Mannitol	S.D. Fine Chemicals, Mumbai
7	Aspartame	S.D. Fine Chemicals, Mumbai
8	Magnesium stearate	S.D. Fine Chemicals, Mumbai
9	Talc	S.D. Fine Chemicals, Mumbai

List of Instruments:

The following instruments/equipment's that were available in laboratory were used as supplied by the manufacturer.

Table 2:List of Equipment's

Sr. No	Instrument	Manufacturer
1	Electronic weighing balance	Citizen Limited
2	Tablet compression machine	KarnavatiRimek Mini Press I
3	Tablet Hardness Tester	Precision Dial type
4	Friability Test Apparatus	Lab line
5	Vernier caliper	Mituyoto,Japan
6	Disintegration test apparatus	Lab line
7	Dissolution test apparatus	Electrolab.(Model TDT-08L)
8	UV-Visible Spectrophotometer	Shimadzu 1800
9	FT-IR Spectrophotometer	Shimadzu 1800

Formulation and Development:

Albendazole Mouth Dissolving Table

Development of the formulation in the present study was mainly based on the type and concentration of the polymers and the properties of the drug. Various polymers in different combinations were used so as to get tablets with physical properties. The direct compression technique is preferred for making tablets. Therefore, a pharmaceutical composition containing Albendazole suitable for generating tablets using direct compression.

Manufacture of Albendazole tablets:

Direct compression technique:

Albendazole tablets were manufactured for nine batches F1 to F9 using different ratios of superdisintegrants mentioned in the Table 5.3 keeping the total weight (700 mg) of the tablet constant in all the formulations. Albendazole tablets were prepared by direct compression technique as per the formula given in the Table 5.3. The superdisintegrants such as croscarmellose sodium, crospovidone and sodium starch glycolate were used in different proportions. The drug, Mannitol and Microcrystalline cellulose were mixed thoroughly in glass morter using a pestle. Superdisintegrants were incorporated in the powder mixture according to each formulation in the tablets and finally aspartame, magnesium stearate, talc was added. The whole mixture was passed through sieve no. 60 twice. The mixed blend of drug and the excipients was compressed on tablet compression machine using 12 mm punches.

Table 3:Formulation of Albendazole Mouth Dissolving Tablets Prepared by Direct Compression Method:

Sr No.	Ingredients	Formulation code and quantities(mgs)								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Albendazole	400	400	400	400	400	400	400	400	400
2	Croscarmellose sodium	33	34	35	-	-	-	-	-	-
3	Crospovidone	-	-	-	33	34	35	-	-	-
4	Sodium starch glycolate	-	-	-	-	-	-	33	34	35
5	Microcrystalline cellulose	82	81	80	82	81	80	82	81	80
6	Mannitol	165	165	165	165	165	165	165	165	165
7	Aspartame	5	5	5	5	5	5	5	5	5
8	Magnesium Stearate	10	10	10	10	10	10	10	10	10
9	Talc	5	5	5	5	5	5	5	5	5
10	Total	700	700	700	700	700	700	700	700	700

Analytical Methods:

Preparation of Phosphate Buffer (pH 6.8):

Weigh accurately 28.80 gm of disodium hydrogen phosphate and 11.45gm of potassium dihydrogen phosphate dissolve in sufficient distilled water and make up volume up to 1000 ml with distilled water & filter.

Preparation of Albendazole standard stock solution (100µg/ml) in phosphate buffer

(pH 6.8) solution:

A standard stock solution of Albendazole was prepared by dissolving accurately weighed 10 mg of Albendazole in phosphate buffer (pH 6.8) solution in a 100 ml volumetric flask and the volume was made up to 100 ml by using phosphate buffer (pH 6.8) solution to obtain a stock solution of 100µg/ml.

Determination of analytical wavelength:

From the standard stock solution, 1 ml was taken into 10 ml volumetric flask. The volume was made up to 10 ml with phosphate buffer (pH 6.8) solution. The resulting solution containing 10µg/ml was scanned between 200 to 400 n m. The λ max was found to be 291 nm and was used as an analytical wavelength. This value matches with the literature value of 291 nm.

Calibration curve of Albendazole in phosphate buffer pH 6.8 solution:

An accurately weighed 10 mg of Albendazole was dissolved in 100 ml of phosphate buffer pH 6.8 to get a concentration of 100µg/ml.

From this stock solution, aliquots with suitable dilutions were made in order to get concentration in between the Beer's range of 5-25 µ g/ml. The dilutions of 5 µg/ml, 10µg/ml, 15µg/ml, 20µg/ml and 25µg/ml were prepared . The absorbance was measured at 291 nm using UV visible spectrophotometer. The standard curve was obtained by plotting absorbance V/s concentration in µg /ml.

Pre-formulation Studies:

The following Preformulation studies were performed for Albendazole and polymers;

Determination of melting point of Albendazole.

Drug- polymer compatibility studies.

Determination of melting point:

Melting point was determined by taking small amount of Albendazole in a capillary tube closed at one end. The capillary tube was placed in an electrically operated melting point apparatus and the temperature at which the drug melts was recorded. This was performed thrice and average value was calculated.

Drug-excipients compatibility studies:

Excipients were integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage forms depends on the selection of excipients, which are added to facilitate administration of the drug and protect it from degradation.

FT-IR Studies:

In the preparation of tablet formulations, drug and polymer may interact as they are in close contact with each other, which could lead to the instability of drug. Preformulation studies regarding the drug-polymer interaction are therefore very critical in selecting appropriate polymers. FT-IR spectroscopy was employed to ascertain the compatibility between Albendazole and selected polymers.

The pure drug, drug-polymers combinations and formulations were subjected to FT-IR studies. Potassium bromide Disc method (Shimadzu 1800) used for FTIR studies. The mixtures were then placed in the sample holder of the instrument and the spectra were taken. The spectra were run from 4000 Cm-1 to 400 Cm-1 wave number. FT-IR spectrum of Albendazole was compared with FT-IR spectrum of Albendazole with polymer. The pure drug and the drug with excipients were scanned separately. Disappearance of Albendazole peaks or shifting of peak in any of the spectra was studied.

EVALUATION OF TABLETS:

Pre-compression parameters:

Micromeritic evaluation:
Angle of repose
Bulk density
Tapped density
Percent compressibility
Hausner's ratio
Post-compression parameters:
Shape, Diameter and color of tablets
Uniformity of thickness
Hardness test
Weight variation test
Friability test
Drug content uniformity
Wetting time
Water absorption ratio
In-vitro dispersion time
In-vitro disintegration
In-vitro dissolution studies

Stability studies

Pre-compression parameters: 5-6

Angle of Repose (θ):

The angle of repose values of Albendazole and the tablet blends were determined by funnel method (Reposogram). The accurately weighed drug or tablet blend was taken in a funnel. The height of funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the powder. The powder was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

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

Where,
θ = Angle of repose,
h = the height of the powder cone and r = the radius of the powder cone.
Flow properties for different values of angle of repose are given in table.

Table 4:Relationships between Angle of Repose and Flow Property.

Sr No.	Flow Properties	Angle of repose(θ0)
1	Excellent	25-30
2	Good	31-35
3	Fair	36-40
4	Passable	41-45
5	Poor	46-55
6	Very poor	56-65
7	Very very poor	>66

Bulk density:

It refers to packing of particles. Bulk density is used to determine the amount of powder that occupies the volume in g/ml. Accurately weighed of powder was transferred into 50 ml measuring cylinder without tapping during transfer. The volume occupied by powder was measured.

Tapped density:

Accurately weighed of powder was taken into a graduated cylinder. Volume occupied by the drug was recorded. Then the cylinder was subjected to 100 taps in tap density apparatus.

Compressibility Index:

The compressibility index and Hausner's ratio was measures the property of granules to be compressed. The packing ability of drug was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping.

Hausner's Ratio:

It is measurement of frictional resistance of the granules. It was determined by the ratio of tapped density and bulk density

Table 5:Relationships between % Compressibility, Hausner's ratio and Flowability

Sr No.	Compressibility index (%)	Flow Character	Hausner's ratio
1	≤10	Excellent	1.00-1.11
2	11-15	Good	1.12-1.18
3	16-20	Fair	1.19-1.25
4	21-25	Passable	1.26-1.34
5	26-31	Poor	1.35-1.45
6	32-37	Very poor	1.46-1.59
7	>38	Very very poor	>1.60

Post-compression parameters:[7-8]

Shape, diameter and color of tablets:

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

Uniformity of thickness:

The thickness of the tablets were measured by using Vernier caliper, and expressed in mm. The limit specified was average thickness ± 5% deviation.

Hardness test:

Hardness of tablet is defined as the force applied across the diameter of the tablet to break the tablet. The resistance of the tablet to abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined by using Monsanto hardness tester.

Friability test:

The friability test is performed to access the effect of friction and shocks which may cause tablet to break. Roche friabilator was used to perform the test. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm and dropping the tablets at distance of 6 inches with each revolution. Pre-weighed sample of tablets were placed in the friabilator, which was then operated for 100 revolutions. Tablets were dedusted and reweighed. The percent friability was calculated by using the formula:

% Friability = [(W-W0)/W0] x 100

Where,

W = Initial weight of the tablet

W0 = Weight of the tablet after test.

Weight variation test:

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average weight.

Table 6:Weight variation test:

IP/BP	Limit	USP
80 mg or less	± 10%	130 mg or less
More than 80 mg or less than 250 mg	± 7.5%	130 mg to 324 mg
250 mg or more	± 5%	More than 324 mg

Drug content uniformity:

Two tablets was weighed and powdered. The whole amount of powdered tablet was transferred into a 100 ml volumetric flask. The powdered tablets were dissolved by adding phosphate buffer pH 6.8 in volumetric flask and finally make up the volume to the mark. After few minutes the solution was filtered. The filtered solution after appropriate dilutions with phosphate buffer pH 6.8 was analyzed by UV spectrophotometer at 291 nm. The concentration of Albendazole (µg/ml) was calculated by using the standard calibration curve of Albendazole.

Wetting time:

A piece of tissue paper folded twice was placed in a small Petridish (internal diameter = 6.5 cm) containing 10 ml of simulated saliva pH (phosphate buffer pH 6.8). A tablet was put on the paper and the time required for the complete wetting was measured. Three trials for each batch were performed; average time for wetting with standard deviation was recorded.

Water absorption ratio:

A piece of tissue paper folded twice was placed in a small petridish containing 10 ml of distilled water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then reweighed. Water absorption ratio R, was determined by using equation:-

Three tablets from each formulation were analyzed performed and standard deviation was determined.

In-vitro dispersion time:

Tablet was placed in 10 ml phosphate buffer pH 6.8 solution. Time required for complete dispersion of tablet was measured.

***In-vitro* disintegration time:**

In-vitro disintegration time was performed by disintegration test apparatus specified in USP at 50 rpm. Phosphate buffer pH 6.8, 500 ml was used as a disintegration medium, and the temperature of which maintained at 37±0.50C and the time in second for complete disintegration of tablet with no palpable mass remaining in the apparatus was measured in seconds.

***In-vitro* dissolution studies:**

In-vitro dissolution study was performed by using dissolution test apparatus (electro lab) at 50 rpm. Phosphate buffer pH 6.8, 500 ml was used as dissolution medium which time interval (2 min) and was filtered. The amount of drug dissolved was determined by UV spectrophotometer (Shimadzu 1800, Japan) by measuring the absorbance of the sample at 291 nm and Cumulative percentage drug releases are determined. maintained at 37±0.50C. Aliquot of dissolution medium (5 ml) was withdrawn at specific.

The following procedure was employed throughout the study to determine the in vitro dissolution rate for all the formulations.

Table 7:Requirement for Dissolution Study

Apparatus used	Electro lab
Temperature	37± 0.50C
RPM	50 rpm
Volume withdrawn	5 ml
	5 minutes
λ max	291nm

Stability studies:

The stability of drug has been defined as ability of a particular formulation in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications.

In the present study stability study were carried out at 400C/75% RH for a specific time interval up to 30 days for selected formulations.

RESULTS:

Preformulation Studies:

Melting point:

The melting point of Albendazole was determined by capillary tube method and It was found to be in the range of 2080C.

Solubility:

The albendazole is freely soluble in formic acid, sparingly soluble in dimethylformamide, slightly soluble in chloroform, very slightly soluble in methanol

UV Scanning:

Observed that the drug was shown maxima at 291 nm in phosphate buffers pH 6.8.

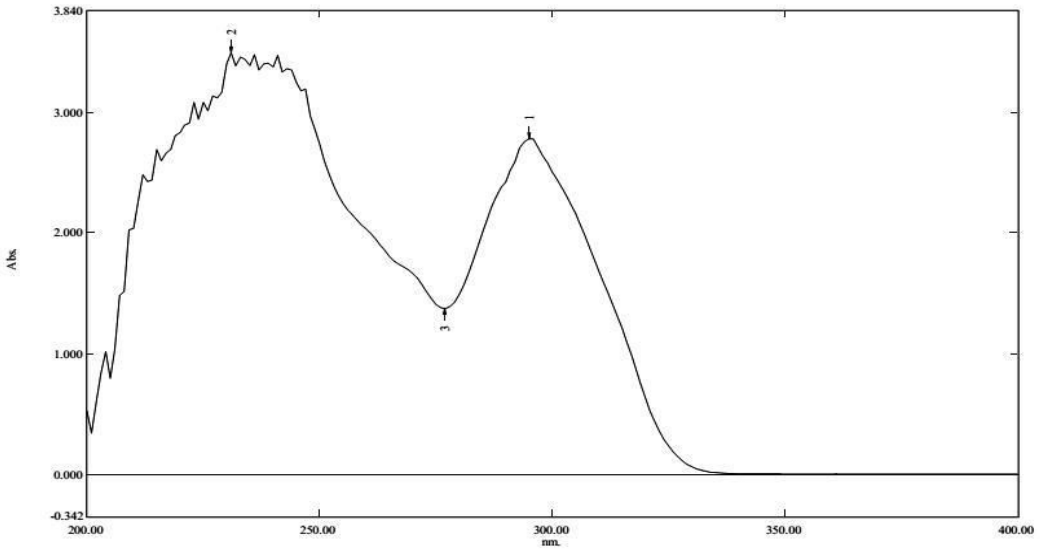

Fig.1: UV spectra of Albendazole.

Standard calibration curve of Albendzole:

Table 8: Standard calibration curve of Albendazole in phosphate buffer pH 6.8:

Sr. No.	Concentration µg/ml	Absorbance at 291 nm
1	0	0
2	5	0.162
3	10	0.355
4	15	0.549
5	20	0.722
6	25	0.855

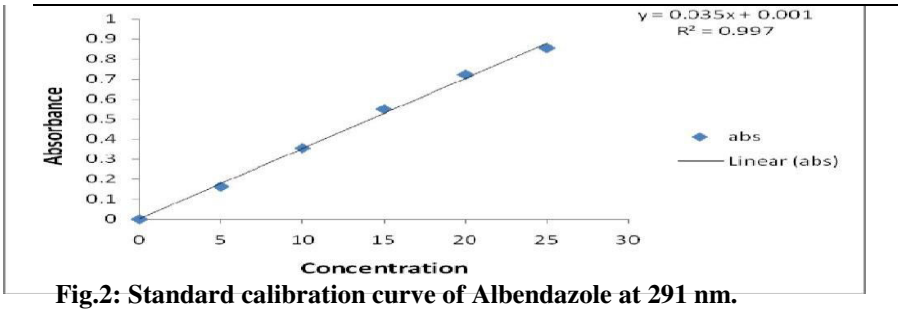

Fig.2: Standard calibration curve of Albendazole at 291 nm.

Compatibility study of Pure Drug and polymers:

Physical mixture of drug and polymer was characterized by FTIR spectral analysis for any physical as well as chemical alteration of the drug characteristics.

Table 9:Comparison of the peaks of functional groups observed in IR spectra of compatibility studies.

IR Spectra	Peak of functional groups[Wavelength(cm-1)]			
	C-H Stretch	N-H Bending	C-N Vibration	C=O group
Reference standard	2962-2853	1640-1550	1220-1020	1750-1730
Albendazole	2955	1587	1224	1709
SSG+Crospovidone+CCS	2956	1587	1224	1629

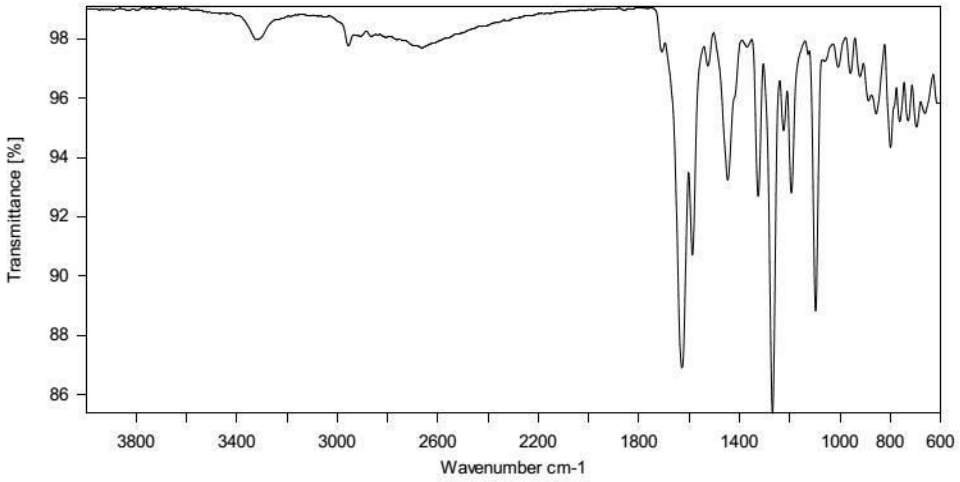

Fig.3: IR spectra of Albendazole

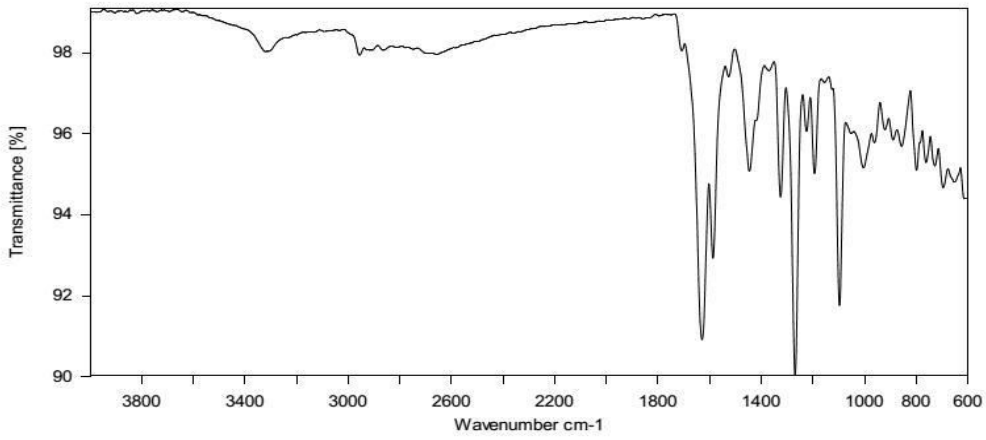

Fig.4: IR spectra of Albendazole + SSG + Crospovidone + CCS

Pre-compression parameters:

Table 10:Angle of Repose, Loose Bulk Density, Tapped Bulk Density and Carr's Compressibility Index, Hausner's ratio:

Formulations	Angle of repose(□)	Loose bulkdensity (gm/ml)	Tappedbulk density (gm/ml)	Percent Compressibility %	Hausner's ratio
F1	30.96±99	0.400±0.006	0.466±0.007	13±0.47	1.15±0.015
F2	34.50±1.01	0.411±0.005	0.482±0.007	14.58±1.39	1.17±0.005
F3	34.21±1.04	0.378±0.004	0.411±0.008	9.75±0.18	1.10±0.009
F4	33.02±0.92	0.358±0.003	0.424±0.003	15.06±1.3	1.18±0.019
F5	31.79±0.20	0.341±0.001	0.424±0.003	14.04±1.05	1.16±0.004
F6	35±0.34	0.388±0.002	0.451±0.009	15.55±0.56	1.18±0.011
F7	29.68±0.14	0.368±0.001	0.411±0.004	12.19±0.004	1.13±0.020
F8	30.11±1.10	0.333±0.009	0.368±0.005	8.33±1.8	1.09±0.035
F9	26.50±1.73	0.350±0.004	0.388±0.009	7.89±0.95	1.08±0.030

Bar graph comparison between angles of repose for Albendazole formulations (F1- F9)

Post-compression parameters:

Table 11: Organoleptic properties

Formulation code	Color	Diameter(m)	Shape
F1	White	12	Flat and circular
F2	White	12	Flat and circular
F3	White	12	Flat and circular
F4	White	12	Flat and circular
F5	White	12	Flat and circular
F6	White	12	Flat and circular
F7	White	12	Flat and circular
F8	White	12	Flat and circular
F9	White	12	Flat and circular

Table 12:Uniformity of thickness, Hardness, Friability, and Weight variation (F1-F9)

Formulation Code	Uniformity of Thickness (mm)	Hardness (kg/cm3)	Friabiliy %	Weight Variation (mg)
F1	4.98±0.019	3.20±0.10	0.28	700 ±3.05
F2	4.86±0.025	3.27±0.025	0.95	697±2.51
F3	5.00±0.01	3.30±0.08	0.88	702±2.0
F4	4.86±0.025	2.50±0.03	0.97	699.8±2.03
F5	4.97±0.019	2.65±0.05	0.48	698.5±1.5
F6	4.87±0.02	2.88±0.035	0.46	699±2.51
F7	4.98±0.030	3.20±0.10	0.48	701±1.52
F8	5.00±0.01	2.50±0.03	0.86	700±1.52
F9	4.97±0.019	3.27±0.08	0.47	699±2.0

All values are expressed as mean ± SD, n=

Table 13: Wetting Time, Water Absorption Ratio

Formulation Code	Wetting Time (n=3)	Water Absorption Ratio (n=3)
F1	45±1.25	71.42±0.42
F2	57.6±2.51	85.71±0.29
F3	52±2.0	73.23±0.23
F4	67±2.0	67.14±0.85
F5	53±1.52	71.18±0.31
F6	64±1.73	85.18±0.81
F7	67.6±2.08	61.89±0.12
F8	67±2.0	64.52±0.47
F9	62±1.52	68.51±0.41

All values are expressed as mean ± SD, n=3

Table 14:Dispersion Time, In-vitro Disintegration Time and Drug Content Uniformity (F1 to F9)

Formulation code	DispersionTime	In-vitro disintegration	Drug content
F1	55±1.5	52±1.0	95.07±1.07
F2	53±1.0	50±1.5	96±0.57
F3	35±2.0	49±1.0	98.10±1.10
F4	51±1.0	47±1.5	96.92±0.91
F5	50±1.5	45±1.5	97.00±1.01
F6	54±1.0	48±1.0	97.22±1.0
F7	53±2.0	53±1.0	96.92±1.07
F8	57±1.0	55±1.5	98.12±0.07
F9	52.07±1.5	57±2.0	98±1.06

All values are expressed as mean ± SD, n=3

Table 15:*In-vitro* Dissolution Profile of the Formulations of Direct Compression Technique (F1-F9)

Time in minutes	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	58.54	59.85	61.13	59.85	64.98	62.41	61.13	62.41	62.93
10	61.13	66.46	63.69	64.98	68.06	66.46	64.73	64.73	66.26
15	64.73	68.85	71.41	70.13	72.18	70.13	67.54	67.54	71.41
20	67.54	74.25	76.54	74.25	82.98	75.26	75.26	74.25	76.54
25	70.13	76.54	80.41	81.38	86.33	81.40	80.21	80.93	80.54
30	75.26	82.98	82.48	85.34	89.93	85.95	84.26	82.98	84.26
35	82.98	85.81	85.54	86.85	95.33	89.33	89.14	86.58	89.93
40	86.85	89.21	89.43	91.38	97.06	96.61	93.26	92.49	94.54

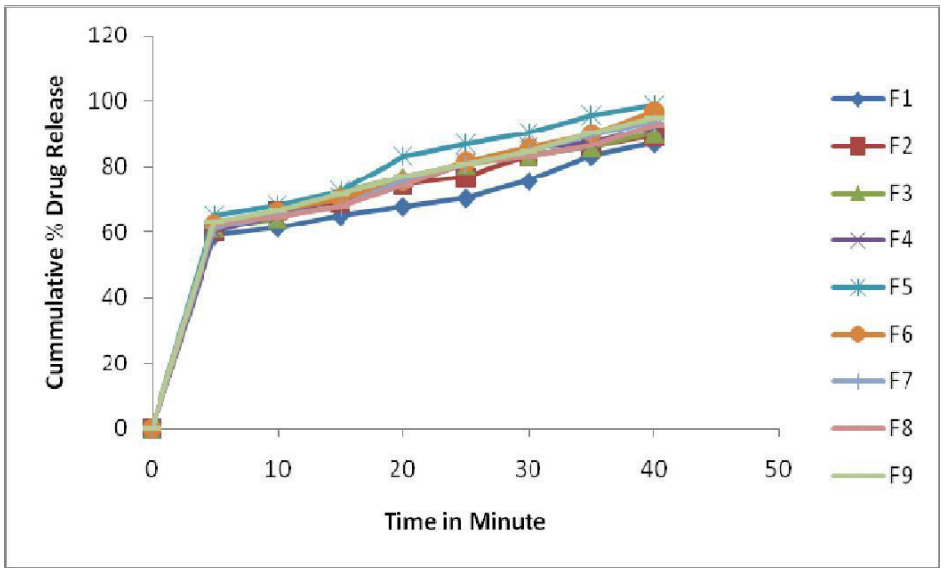

Fig.5: In-vitro cumulative % drug released V/s time for formulations (F1- F9)

Table 16:Results of the stability studies

Evaluation parameters					
Time	**Colour**	**Hardness (kg/cm2)**	**Drug content Uniformity (mg)**	**% CDR**	**Disintegration time (sec.)**
After 1 month	white	2.65±0.05	97.00±1.01	97.06	45±1.5

DISCUSSION:

Preformulation Studies:

Melting point:

The melting point of Albendazole was determined by capillary tube method and it was found to be 208 0C. This value is same as that of literature value.

Table 17:Solubility:

The slope	= 0.035
The intercept	= 0.001
The correlation coefficient	= 0.997

The Albendazole is freely soluble in formic acid, sparingly soluble in dimethylformamide, slightly soluble in chloroform, very slightly soluble in methanol, insoluble in solutions of alkalis..

UV Scanning:

observed that the drug was shown maxima at 291 nm in phosphate buffers pH 6.8.

Standard calibration curve of Albendazole :

Standard solution:

Weight of Albendazole taken = 10mg, Volume made up to 100 ml Concentration of standard solution = 100 µg/ml.

Working standard solution:

From Standard Stock Solution 0.5 ml, 1.0 ml, 1.5 ml, 2.0 ml and 2.5 ml were with drawn and Volume made up to 10 ml. Concentration of working standard solution 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml and 25µg/ml respectively. From the standard curve of Albendazole, it was observed that the drug obeys beer's law in concentration range of 5-25 µg/ml in phosphate buffer pH 6.8. The linear regression equation generated was used for the calculation of amount of drug.

The linear regression analysis for standard curve:

For standard curve in phosphate buffer pH 6.8 the linear regression analysis was done on Absorbance data points. The results are as follows;

Compatibility study of Pure Drug and polymers:

The infrared spectral analysis of the procured Albendazole was carried out. Sample was compared with the reference standard IR spectrum of Albendazole. The IR spectrum was measured in the solid state as potassium bromide dispersion. The IR spectrum of Albendazole is presented and Observed peaks a these peaks are similar to reported peaks of Albendazole. Physical mixture of drug and polymer was characterized by FTIR spectral analysis for any physical as well as chemical alteration of the drug characteristics. From the results, it was concluded that there was no interference in the functional

groups as the principle peaks of the Albendazole were found to be unaltered in the spectra of the drug-polymer physical mixture.

Pre-compression parameters:

Powder ready for compression containing drug and various excipients were subjected for pre-compression parameters (Micromeritic properties) to study the flow properties of granules, to achieve uniformity of tablet weight. Angle of Repose, Loose Bulk Density, Tapped Bulk Density and Carr's Compressibility Index:

Angle of repose (θ):

The values were found to be in the range of 26o 50'and 35o'. All the formulations prepared by both the methods showed the angle of repose less than 350, which reveals good flow property.

Bulk density:

Bulk density for all the formulations batches varied from 0.333gm/cm3 to 0.411gm/cm3. The result lies within the acceptable range and this result helps in calculating the percent Compressibility of the powder. In optimized batch the bulk density should within limit so depending upon that, we can conclude that formulation have good flow property.

Tapped density:

Tapped density for all the formulation batches varies from 0.368gm/cm3 to 0.482gm/cm3. The values obtained lies within the acceptable range and not large differences found between tapped densities. This result helps in calculating the % compressibility of powder. In optimized batch the tapped density should within limit so depending upon that, we can conclude that formulation have good flow property.

Carr's consolidation index:

The results of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 8.33 to 15.08. The directly compressible granulations had shown excellent compressibility index values up to 15% result in good to excellent flow properties.

Hausner's ratio:

The Hausner's ratio for all the formulation batches lies within the range of 1.08 to 1.18. The values obtained lies within the acceptable range and not large difference found. All formulation was shows good flow abilities. In optimized batch the hausner's ratio should be within limit i.e. below 1.18 so depending upon that, we can conclude that formulation has good flow property.

Formulation design:

The present study was carried out to develop Albendazole mouth dissolving tablets in order to improve patient compliance and also to prepare used-friendly formulation.

In this case, nine formulations of mouth dissolving tablets were prepared using superdisintegrants such as microcrystalline cellulose, sodium starch glycolate, crospovidone, croscarmellose sodium in different ratio.

Post compression parameters:

The tablets prepared by direct compression technique was subjected for evaluation according to various official specifications and other parameters like, shape, thickness, hardness, friability, weight variation, in-vitro disintegration time, wetting time, water absorption ratio, drug content, in-vitro dissolution studies, model fitting of release profile, for tablets formulated by direct compression method and stability studies.

Shape, Diameter and color of tablets:

Formulations prepared, were randomly picked from each batch examined under lens for shape and in presence of light for colour. Tablets showed 12mm diameter, flat, circular shape in white colour.

Thickness:

Thickness of the tablets was measured by vernier caliper by picking tablets randomly from all the batches. The mean thickness was (n=3) almost uniform in all the formulations and values ranged from 4.86 mm to 5 mm. The standard deviation values indicated that all the formulations were within the range.

Hardness:

The hardness of all the tablets prepared by direct compression method was maintained within the 2.50 kg/cm2 to 3.30 kg/cm2.The hardness values ranged from 2.50 kg/cm2 to 3.30 kg/cm2 for formulations were almost uniform.

Friability test:

They were found to be well within the approved range (<1%) in all designed formulations. The formulations F4 showed slightly higher than the other. The values were found to be within the limit. Thus tablets possess good mechanical strength.

Weight variation test:

All the tablets passed weight variation test as the average percentage weight variation was within the pharmacopoeial limits of 5%. It was found to be 697 mg to 702 mg. The weight of all the tablets was found to be uniform with low standard deviation.

Wetting Time:

This experiment mimics the action of saliva in contact with the tablet to illustrate the water uptake and subsequent wetting of tablet. Wetting time is closely related to the inner structure of the tablet.

Water absorption ratio:

Water absorption ratio, which is important criteria for understanding the capacity of disintegrants to swell in

presence of little amount of water. It was found to be in the range of 61.89% to 85.71%.

Drug Content:

The drug content uniformity was performed for all the nine formulations and Three trials from each batch were analyzed spectrophotometrically. The average value and standard deviations of all the formulations were calculated. The drugs content of the tablets were found to be between 95.07% to 98.12% of Albendazole

***In-vitro* Dispersion Time:**

The in-vitro dispersion time of tablets were found to be between 35-57 seconds of Albendazole.

***In-vitro* Disintegration Time:**

The internal structure of tablets that is pore size distribution, water penetration into tablet and swelling of disintegration ingredients are suggested to be the mechanism of disintegration. which was determined as per Indian Pharmacopoeial specifications for all the developed formulations. All the formulations showed disintegration time less than 60 seconds. Formulations F5 showed rapid disintegration compared to other formulations.

***In-vitro* Dissolution Study:**

All the nine formulations were subjected for in-vitro dissolution studies using USP type 2 Dissolution test apparatus (USP XXIIII). The dissolution medium 6.8 pH buffer was used to study the drug release. The samples were withdrawn at different intervals of time and analyzed at 291 nm using UV spectrophotometer. Cumulative percentage drug release was calculated on the basis of amount of Albendazole present in the respective formulations. The data obtained in the in-vitro release for formulations prepared by direct compression technique. The plots of cumulative percentage of Albendazole released as a function of time (t) for formulations prepared by direct compression technique.

All the formulations showed rapid % drug release (86.85% - 97.06%). Formulations F1, F2, F3, F4, F5 F6, F7, F8 and F9 showed 86.85%, 89.21%, 89.93%, 91.98%, 97.06%, 96.61%, 93.26, 92.49%, 94.54% of drug release respectively. But the rapid drug dissolution was noticed in F5 formulation compared to other formulations, which releases at the end of 40 minutes. The fast dissolution might be due to quick disintegration of the tablets to form particles and rapid absorption will take place.

Stability studies:

Stability studies of optimized formulation F5:

Stability studies for the developed formulations were carried out by storing the selected formulations at 40∟C/75% RH up to one month. The formulation F5 was selected on the basis of their high cumulative percentage drug release, and also results of in-vitro disintegration time, wetting time. After one month, the tablets were analyzed for the colour, hardness, drug content uniformity and cumulative % drug released, in-vitro disintegration time. These formulations showed no significant changes in the values. The data obtained are tabulated in Table no.6.9. From the obtained data of tablet evaluation parameters indicated that stable formulations can be developed using direct compression method.

CONCLUSION:

Preformulation studies of Albendazole were performed; the FT-IR analysis revealed that the superdisintegrants and excipients used were compatible with Albendazole Mouth dissolving tablets of Albendazole prepared by direct compression technique using different superdisintegrants, namely croscarmellose sodium, crospovidone and sodium starch glycolate. Apart from all the batches the F5 batch has optimized formulation showed rapid disintegration and maximum drug release (97.06 %) at the end of 40 min. Thus, the present study was achieved the target by formulating Mouth dissolving tablets of Albendazole.

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