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FORMULATION, OPTIMIZATION AND DEVELOPMENT OF ALBENDAZOLE TABLET FOR THE IMPROVEMENT OF ORAL BIOAVAILABILITY

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ABSTRACT

Albendazole is a benzimidazole carbamate with a broad anti-parasitic spectrum. Albendazole was first approved for treatment of helminth infections in sheep in 1977, and subsequently approved for human use in 1983. In general, most ascariasis, trichuriasis, enterobiasis and hookworm infections can be successfully treated with single dose Albendazole and strongyloidiasis with multiple doses of Albendazole. The increase in bioavailability is possible by in vitro drug dissolution method. The physicochemical property of most drugs that has greatest influence on their absorption characteristics from the GIT is dissolution rate. The in vivo test is extremely costly, tedious, time consuming besides exposing the healthy subject to hazards of drug. The in vitro method is inexpensive. The best available tool today which can at least quantitatively assure about the biological availability of a drug from its formulation is its in vitro dissolution test. Enhancement of bioavailability of hydrophobic drugs is one of the major challenges in drug development of the plethora of pharmaceutical technologies available to address this issue viz. micronization, the use of surfactants.

KEYWORDS: Micronization, Surfactant, superdisintegrants.

INTRODUCTION

Oral route has been the commonly adopted and most convenient route for the drug delivery. Oral route of administration has been received more attention in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for

other routes. The oral drug delivery design depends on various factors such as type of delivery system, the disease being treated, and patient, also the length of the therapy and the properties of the drug.[1]

In addition to this, oral route is preferable route because of patient acceptance, convenient to administration and cost-effective manufacturing process. Drug substances most frequently are administered orally by means of solid dosage form such as tablets and capsules.[2]

The other routes used for drug administration are parenteral route, topical route, rectal, vaginal, etc. They are commonly called as per-oral routes.[3] Generally the oral route is the choice of route for administration of the most of drugs. At least 90% of all drugs used to produce systemic effects are administered by oral route as it is safe and convenient and easy to administer by this route. Other drugs follow topical route of administration is limited in its ability to allow effective drug administration for systemic drug action. The parenteral route of administration is important in treating medical emergencies in which subject cannot swallow and in providing various types of maintenance therapy for hospitalized patients. Various solids as well as liquid dosage forms such as tablets, capsules, powders, pills, syrups, elixirs, solutions, suspensions, emulsions, etc. are administered by oral route. Amongst the various oral dosage forms, tablets are mostly acceptable and preferred by the patient. The tablet represents unit dosage form in which one usual dose of the drug has been accurately placed, but when compared with liquid oral dosage forms such as syrups, suspensions, emulsions, solutions and elixirs are contain one dose of medication in 5-30 ml. In liquid dosage form patient ask to measure his or her own medication using a teaspoon, tablespoon or other measuring device, such dosage measurements are typically in error, when drug is self-administered by the patient. Liquid oral dosage form have other disadvantages and the limitations when compared with tablets such as it is more expensive to ship, breakage and leakage during shipment, taste masking of the drug is another problem in liquid dosage form. Drugs are in general less stable in liquid form than in dry state and its expiration date tends to be shorter. Tablets offer various advantages such as the greatest dose precision and less content variability, lowest cost compare to all other dosage form, lightest and most compact of all oral dosage form, easiest and cheapest to package and ship of all dosage forms, large scale production is possible and economical, high physical & chemical stability, masks the unpleasant odor and taste of medicaments.

MATERIALS

Table 1: List of chemicals

Sr. No.	Name of the ingredient	Name of supplier
1	Maize starch BP	DFE pharma
2	Lactose Monohydrate BP	DFE pharma
3	MCC 101 BP	Chemfield cellulose pvt ltd
4	Sodium starch glycolate BP	DFE pharma
5	PVP K-30 BP	Anshul life science
6	Polysorbate 80 BP	Anshul life science
7	Aerosil BP	Gangwalchem
8	Magnesium Stearate BP	DFE pharma
9	Mannitol BP	DFE Pharma

Equipments

Table 2: List of Equipments

Sr No.	Name of equipment	Model
1	Single pan electronic balance	S. R. electronics
2	Modified physical balance	….
3	8 station tablet compression machine	Ahan
4	Hardness tester	Monsanto
5	Friability tester	Roche Friabilator
6	USP II dissolution apparatus	Electro lab
7	Double beam UV Visible spectrophotometer	Lab India Mumbai
8	Vernier caliper	Monsanto

- **Preparation of Albendazole tablets**

Sr.No.	Ingredients	Quantity in mg/tablet					
		F1	F2	F3	F4	F5	F6
1	Albendazole USP	400	400	400	400	400	400
2	PVP K 30 BP	--	--	--	--	--	32
3	Maize starch BP	25	25	25	25	25	30
4	Lactose Monohydrate BP	250.9	98.5	224.9	--	269.5	269.5
5	MCC 101 BP	98.5	250.9	124.5	87.5	80.9	26
6	Mannitol BP	--	--	--	261.9	--	--
6	Sodium starch Glycolate BP	--	--	29	--	--	45
7	PVP K 30 BP	20	20	20	20	15	10
8	Polysorbate 80 BP	--	--	--	--	05	25
9	Water	q.s	q.s	q.s	q.s	q.s	q.s
10	Sodium Lauryl Sulfate BP	18	18	18	18	18	18
11	Aerosil BP	10	10	10	9	9	9
12	Sodium Starch Glycolate BP	69.6	69.6	40.6	69.6	69.6	27.5
13	Magnesium Stearate BP	8	8	8	8	8	8
Total		**900**	**900**	**900**	**900**	**900**	**900**

- Weighing and Sifting: All the ingredient were separately weighed and sifted using mesh no. 40 Albendazole. Maize starch, microcrystalline cellulose, PVP k-30, Lactose monohydrate, Sodium Starch Glycolate, Sodium Lauryl Sulfate, sift through 30#, Aerosil and magnesium stearate pass through 60#.
- Dry Mixing: Mix the API with excipient for 15min in RMG.
- Binder Preparation: Dissolve PVP K-30 in sufficient quantity of water.
- Wet granulation: Add Binder solution in RMG with slow speed chopper and impeller and mix for 10 min to form granule.
- Drying: Dry the granule in tray drier till LOD reach below 2.0 %.
- Blending and Lubrication: the dried granule transfer into blender and add SLS, SSG and Aerosil in it and mix for 10 min. Finally add Magnesium stearate and mix for 3 minutes.
- Compression: Compress the above blend in compression machine. Use punch 19.3 X 9.4 SC.

Preformulation study of powder blends

a) Angle of repose

Angle of repose is defined as the maximum angle possible between the surface of pile of powder and horizontal plane. Angle of repose has been used as indirect method of quantifying powder flow ability. Angle of repose for blend of each formulation was determined by fixed funnel method. The fixed funnel method employs a funnel that is secured with its tip at given height, h, which was kept 2 cm, above graph paper that was placed on a flat horizontal surface. With r, being the radius of base of conical pile, angle of repose can be determined using following equation.

$\tan \theta = h/r$ 01

Where; θ = Angle of repose

r = Radius of the base

h =Height from tip of funnel to the surface of graph paper.

Table No.3 Grading of powder flow property according to angle of repose

Angle of repose	Flow Property
<25	Excellent
25 -30	Good
30 -40	Passable
> 40	Very poor

b) Bulk density

It is the ratio of mass to bulk volume. It is required to decide the appropriate packing of dosage forms. An accurately weighed 20 gm powder was allowed to flow in a fine stream into a graduated cylinder and final volume was noted. The bulk density was obtained by dividing the weight of the sample in grams by final volume in cm^3 and it was determined by equation given below

Bulk density = Mass/ Bulk volume 02

c) Tapped density

An accurately weighed 20 gm powder was allowed to flow in a fine stream into a graduated cylinder of a mechanical tapping device. The measuring cylinder was tapped for 100 times and final tapped volume was noted. The tapped density was obtained by dividing the weight of the sample in grams by final tapped volume in cm^3 and it was calculated by using equation given below,

Tapped density = Mass/ Tapped volume 03

d) Compressibility index

It is also one of the simple methods to evaluate flow property of a powder by comparing the bulk density and tapped density. The percentage compressibility of a powder is a direct measure of the potential powder arch or bridge strength and stability. It is also known as Carr's index. It can be calculated by following equation.

Carr's index = (Tapped density- bulk density/ Tapped density) X 100 ……. 04

Table No.4 Grading of compressibility of powder according to Carr's index

Carr's Index	Flow Property
5-15	Excellent
15-20	Good
20-40	Poor
>40	Very Poor

From the bulk density and tapped density data, Carr's index for powder blends of different formulations was calculated.

e) Hausner's ratio

Hausner found that the ratio of tapped density/bulk density was related to inter particle friction as such, and could be used to predict powder flow properties. He showed that the

powder with low inter particle friction had ratio of approximately 1.2, whereas more cohesive less free flowing powders have Hausner's ratio greater than 1.6. A Hausner's ratio of less than 1.25 indicates good flow properties of the powder blends or granules.

Hausner's ratio = Tapped density/ bulk density 05

Hausner's ratio for powder blends of different formulations were calculated from the equation no. 05 given above.

Calibration curve

Calibration curve in 0.1N HCL

The stock solution was prepared by dissolving 100 mg of drug in and 100 ml 0.1N HCl to get 1000 µg/ml concentration solution. From the above solution, second stock solution prepared diluting 1ml in 100 ml water to get 10 µg/ml. from this adequate aliquots were removed and diluted suitably to acquire final concentration from 1 to 10 µg/ml. All the solutions were scanned through double beam UV visible Spectrophotometer (Labindia, Mumbai) and absorbance were taken against a blank at □ max of 350 nm

Drug-excipients compatibility study

Infrared spectroscopy is one of the most powerful analytical techniques which offer the possibility of chemical identification. This technique when coupled with intensity measurements may be used for quantitative analysis. One of the most important advantages of IR over the other usual methods of structural analysis is that it provides useful information about the structure of molecule quickly without tiresome evaluation methods. The technique is based upon the simple fact that a chemical substance shows marked selective absorption in the IR region. After absorption of IR radiation the molecules of chemical substance vibrates at many rates of vibration, giving rise to close packed absorption bands, called IR absorption spectrum which may extend over wide wavelength range. Various bands will be present in IR spectrum which will correspond to the characteristic functional groups and bonds present in a chemical substance. Thus, an IR spectrum of a chemical substance is a fingerprint for its identification.

Evaluation Studies on Albendazole Tablet

a) Hardness

Tablets should be sufficiently hard to resist breaking during normal handling and yet soft enough to disintegrate properly after swallowing. The hardness of tablets measured by

Monsanto hardness tester. The hardness was measured in terms of kg/cm^2.

b) Thickness

Three tablets from each batch of formulation were collected and the thicknesses of the tablets were measured with the help of vernier caliper. The average thickness was calculated.

c) Friability

Tablet hardness is not an absolute indicator of strength, since some formulation compressed into very hard tablet tend to cap on attrition losing their crown portion. Therefore another measure of tablet strengths, its friability is often measured. The Roche friability test apparatus was used to determine the friability of the tablets. Twenty pre- weighed tablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The percentage friability was calculated according to the following formula

$$\%\text{Friability} = \frac{\text{Initial Weight- Final Weight}}{\text{Initial Weight}} \times 100$$

d) Weight Variation

The weight of tablet is measured to ensure that a tablet contain the proper amount of drug. Weight variation test was performed as per IP 2007.Twenty tablet were selected randomly and weighed. Average weight of the tablet was determined. Not more than the two of the individual weights deviate from the average weight by more than 5% percentage deviation.

Table No.5 USP standards for uniformity of weight

Sr. No.	Average weight of tablet	Percentage deviation
1	130 mg or less	±10
2	130 mg to 324mg	±7.5
3	324 mg to more	±5

e) Drug content Uniformity

Determine the absorbance of the standard solution and the test solution at the wavelength of maximum and minimum absorbance at about 308 nm and 350 nm, using 0.1N NaOH as the blank.

In-Vitro Release Studies

The United state pharmacopoeia (USP) type II dissolution apparatus was used to study the

release of drug from tablets. The dissolution medium consisted of 900 ml of 0.1N HCl. The release was performed at 37 ±0.5°C, at a rotation speed of 50 rpm. Samples (5 ML, at each time) were withdrawn at pre-determined time intervals and replaced with fresh medium. The samples were filtered through whatman filter paper no. 41 with appropriate dilutions with Sodium hydroxide and were assayed spectrophotometrically at 308-350 nm.

RESULT AND DISCUSSION

Identification of Drug Description

Albendazole is an odourless, white to off white powder.

Melting point of Albendazole

The melting point of Albendazole found to be in the range 208ºC to 210^{O}C which complies with reported value.

Calibration curve of Albendazole in 0.1N HCl

Calibration curve of Albendazole in 0.1 N HCl was found to be linear in the range of 4 to 28 µgm/ml and coefficient of correlation was found to be 0.946.

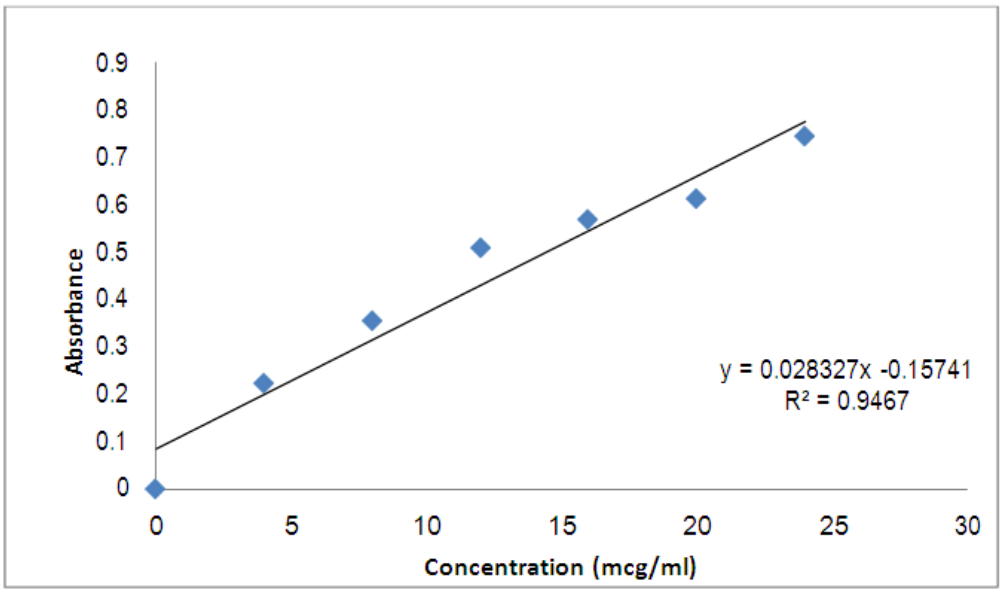
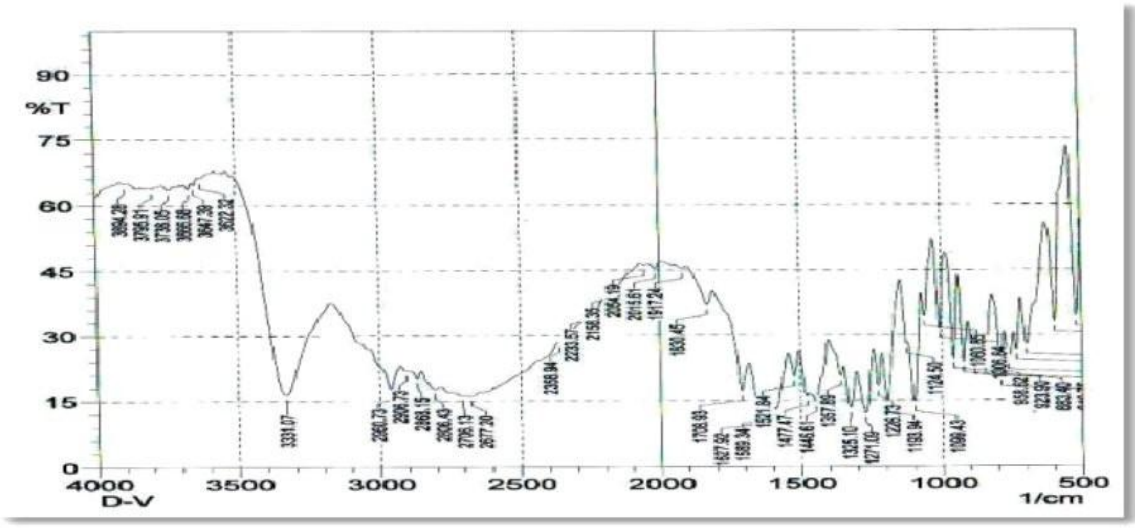


Figure: Calibration curve of Albendazole in 0.1N HCl using UV method

Fourier transform infrared spectroscopy

IR spectrum of Albendazole, was recorded on ATR Fourier Transform Infrared Spectrophotometer (MIRacle 10). From overlay IR spectra it was observed that all peaks of Albendazole are identified which was present in the standared IR spectra of Albendazole. it

proved that this albendazole was a pure compound.



Evaluation of blender blend

Evaluation parameter like angle of repose, compressibility index and Hausner's ratio of all batches.

Batch	Angle of repose (Ɵ) ±SD	BD	TD	Compressibility index	Hausner's ratio
F1	20.92±0.47	0.52	0.61	14.75	1.17
F2	26.28±1.63	0.51	0.60	15	1.17
F3	22.77±0.43	0.51	0.58	12.06	1.13
F4	23.48±0.66	0.50	0.56	10.71	1.12
F5	25.86±0.44	0.52	0.57	8.71	1.09
F6	23.21±0.24	0.52	0.60	13.33	1.15

From the above result, it can be inferred that all batches show excellent flow properties i.e. angle of repose less than 25. Compressibility of all batches found to be less than 18 indicating good compression properties. Hausner's ratio < 1.25 for all batches indicated good flow properties.

Evaluation of tablet

Tablet properties like weight variation, hardness, friability, disintegration time and drug content are given in table.

Table No.07 Evaluation parameter of Tablet

Batch	Weight (mg) ±5.0%	Hardness (kg/cm^2) ±1.0	Friability (%)	Disintegration time (min)	Drug content (%)	Thickness (mm)
F1	900.00	6	0.573	4.0 -6.0	95.13	5.6±0.2
F2	900.00	6	0.587	3.0 -5.0	96.16	5.6±0.2
F3	900.00	6	0.562	4.0 -5.0	95.14	5.6±0.2
F4	900.00	6	0.456	5.0 -6.0	96.45	5.6±0.2
F5	900.00	6	0.389	5.0 -6.0	97.46	5.6±0.2
F6	900.00	6	0.326	6.0 – 8.0	97.78	5.6±0.2

Dissolution test

The in-vitro dissolution studies were carried out using USP apparatus type II in 0.1 N HCl for 45 min (900ml) maintained at 37^0 C±2.0^0 C.

Time(min)	Drug release (Mean ±SD)					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	14.07	13.44	12.85	11.33	11.05	15.07
10	18.22	17.13	15.8	14.62	28.13	34.36
15	24.11	22.12	21.88	18.54	36.86	56.58
20	28.99	25.72	24.07	21.84	49.13	72.89
25	33.11	29.44	27.88	25.26	61.91	82.89
30	39.16	35.18	32.81	30.86	76.26	90.29
35	43.19	39.12	38.66	35.69	81.97	93.12
40	50.09	46.44	46.62	42.25	89.16	95.26
45	62.58	59.59	56.66	51.75	93.81	96.69

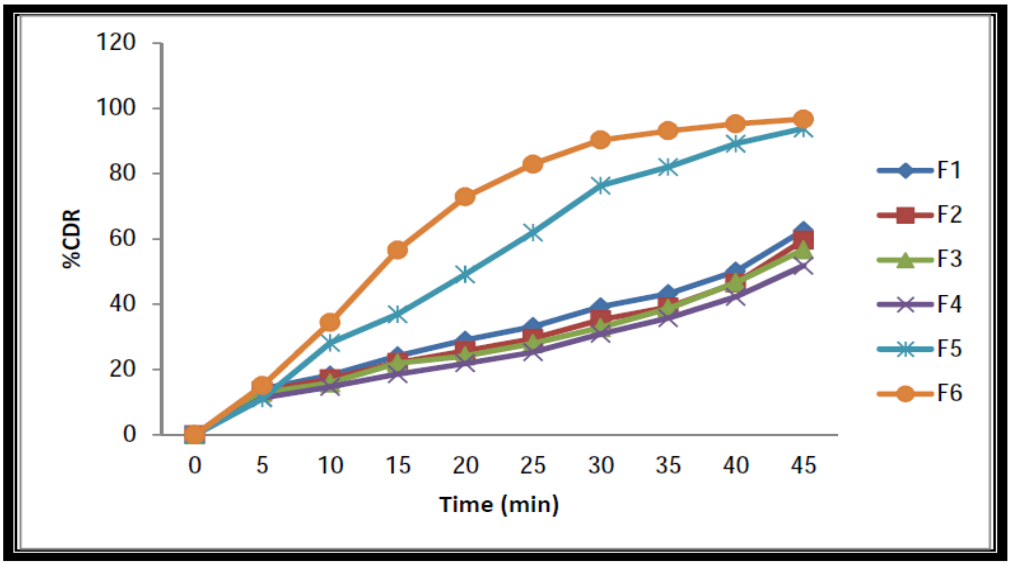


Fig: Dissolution of albendazole tablet in 0.1 N HCl

The tablet was prepared by using surfactant Sodium Lauryl Sulfate and Polysorbate 20 swelled by absorbing liquid medium and disintegrated within 10 min. 2% concentration SLS and approximately 3% concentration of Polysorbate 20 of batch F6 was show 90.29% drug release in 30 min.

CONCLUSION

The Present study was carried out to develop the Albendazole tablet by using surfactant Sodium Lauryl Sulfate and Polysorbate 20. The formulation prepared with 2% Sodium Lauryl Sulfate and approximately 3% Polysorbate 20 for improving dissolution than the available marketed tablet. It was found that the release rate was found to be influenced by the surfactant. It was concluded that the improving dissolution means improving bioavailability. Tablet of poorly soluble drug Albendazole showed enhanced dissolution which may lead to improved bioavailability and hence better patient compliance. Tablets of Albendazole can be successfully prepared by wet granulation technique using Surfactant and superdisintegrants for the better patient compliance and effective therapy. The relative efficiency of their surfactant and superdisintegrants and dissolution rate of tablet was found in order.

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