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Solubility enhancement and tablet formulation of Albendazole drug

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Abstract

Albendazole is belongs to BCS Class II which is use as anthelmintic treatment. Major limitation with this drug is its poor solubility. Due to poor solubility it shows poor dissolution rate which lead to poor bioavailability. There are number of methods suggested for increase the solubility of poorly water soluble drug. In this research solid dispersion method was used to improve the solubility. Carriers Hydroxy Propyl Methyl Cellulose (HPMC) and Sodium Carboxy Methyl Cellulose (Sod. CMC) were used to prepare solid dispersion. Various precompression parameters like Angle of Repose, Carr's Index were performed to check flow properties of blend. Tablets were compressed through 8 station rotator compression machine and evaluated by various tests like friability, disintegration time and hardness. Results of solubility was found that Sod. CMC shown better compare to HPMC. Angle of repose, % Carr's index and Hausner ratio comes under good to excellent flow property. All the post compression parameters also within limits. Formulation F3 shown better disintegration time (28 min.) compare to other formulation. So it could be concluded that F3 is optimized formulation.

Key words: Albendazole, BCS Classification, HPMC, Sod. CMC, Wet granulation.

Introduction

Drugs which are absorb from GI fluids have solubility and dissolution rate are rate limiting steps in bioavailabilit[1,2]. According to Biopharmaceutical Classification System (BCS) (as given in Figure-1) class II drugs have high permeability and low solubility[3,4].

Drugs exhibit poor solubility and lower bioavailability. These APIs have adequate permeability but low solubility and /or dissolution rate causes its lower bioavailability. Enhancement of drug solubility is the most challenging factor in drug discovery. There are quite a lot of techniques that can be used to increase the solubility but still it under investigation[6-8]. Albendazole is a benimidazole drug which is used in anthelmintic remedy belongs to BCS class II[9].

This work was carried out to enhance the solubility of drug using solid dispersion method and for it melting method was used. For melting methods carriers Hydroxy Propyl Methyl Cellulose (HPMC) and Sodium Carboxy Methyl Cellulose (Sod. CMC) were used and compared them. After this tablets were formulated and evaluated for various parameters.

Material and Methods

Drug Albendazole was procured from K.A Malle Pharmaceutical Ltd., Ankleshwar. Crosscarmillose, HPMC (CDH Pvt. Ltd.), Sodium CMC (Loba Chemie Pvt. Ltd.) and all other chemical, reagent, excipients were purchased from local vendor and all were analytical grade.

Figure-1: BCS Classification of Drug.

Methods: Preformulation study of drug: In preliminary study drug was tested for melting point and solubility. Melting point was determined by capillary method and qualitative method was used determination of solubility. All the parameters for solubility was referred as per Indian Pharmacopoeia (IP)[10] which are specified in Table-1.

Table-1: Solubility expression as per IP 2006.

Definition	Part of solvent required for one part of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very Slightly soluble	From 1000 to 10,000
Insoluble	More than 10,000

Preparation of Solid dispersion[7]: Solubility of drug was improved by preparation solid dispersion. Melting method was used for preparation of solid dispersion. In study two polymers HPMC and Sodium CMC was used as carrier in ratio of 1:1 and 1:2 (Drug:Polymer). In this method drug and carrier was melted upto melting point and spread on ointment plate. Sample was scrapped out after solidification of molted mass. The solid dispersion was passed through sieve no. 30 for further use of solubility determination and in tablet formulation.

Tablet formulation: Wet granulation method was used for preparation of Albendazole tablets. Three formulations with different concentration of sodium starch glycolate which was used as super disintegrating agent were prepared. Lactose granules were prepared by starch paste as binder. Sodium lauryl sulphate was added to improve the solubility. Mannitol and sod. saccharine were used as sweetening agent. Magnesium stearate was used as lubricant. The powder blend was passed through sieve no. 30. Tablet were compressed on eight station rotator compression machine (CIP Pvt Ltd.) by using 8mm punch. Tablet formulations were prepared according to Table-2.

Table-2: Different formulation of Albendazole tablet.

Ingredients (mg)	Formulation code		
	F1	F2	F3
Solid dispersion (drug+polymer)	100	100	100
Sodium starch glycolate	5	10	15
Sodium lauryl sulphate	3	3	3
Mannitol	3	3	3
Magnesium stearate	2	2	2
Sodium saccharin	1	1	1
Lactose granules	86	81	76
Total weight	200	200	200

Precompression Parameters[11]: Blend of granules was evaluated for angle of repose; bulk density; compressibility index and Hausner's ratio for flow property before compression.

Angle of repose: The fixed funnel method was used to calculate the angle of repose. The mixture was poured through a funnel that could be raised vertically to achieve the maximum cone height (h). Measured the heap's radius (r) and calculated the angle of repose using the formula provided: Angle of repose $\Theta = \tan^{-1}(2h/d)$, Where, h= pile height and, d= the diameter of the base pile.

Bulk density: The apparent bulk density (LBD) of the blend was determined by pouring it into a graduated cylinder. The bulk volume (Vo) and powder weight (M) were calculated. Bulk density= weight of powder (M)/volume of powder(Vo).

Tapped density: The measuring cylinder, which contained a known mass of blend, was tapped for a predetermined amount of time. The cylinder's minimum volume (Vt) and the weight of the powder blend (M) as measured. Tapped density was measured by as per following formula: Tapped density (TBD)= weight of powder(M)/tapped volume (Vt).

Carr's index and Hausner ratio: Carr index and Hausner ratio is frequently used in pharmaceutics as an sign of the compressibility of a powder. The Carr index is measured by given formula : Carr's index = [Bulk density-Tapped density/ tapped density] ×100, Hausner ratio = Tapped density/ Bulk density.

Post compression parameters[12,13]: Thickness and diameter: Measurement of thickness and diameter of tablets were done by using "Vernier Caliper".

Hardness test: Hardness testing is identifying the force required to break the tablets. It indicates the strength of tablets. Tablet should have sufficient hardness to withstand the mechanical stress during handling and transportation. Hardness of tablets were determined by Monsento's hardness tester.

Friability test: This quality control test was performed as per IP 2007. This test is performed to check the ability of tablets to withstand the socks during handling and transportation. This test was measured by Roche's friabilator. As per IP maximum weight loss should not be more than 1% to pass this test.

Disintegration time: DT test was performed to check the time required to disintegrate the tablets. It was also conducted according to IP 2007. Six tablets were used for test. One tablet was placed in each tube of apparatus. 37°C ±2°C temperature of distilled water was maintained throughout the test. Total time taken to complete disintegration of all six tablets was noted down. Disintegration was only considered when no mass remaining in apparatus.

Results and Discussion

Melting point of drug: Capillary method was used for determination of MP and values are given in Table-3

Table-3: Observation of Meting point.

Standard value	Observed value
210°C	208°C-210°C

Solubility study: Solubility study of albendazole drug was conducted in different solvent like water, 0.1 N HCl, strong acid and strong base. Results are given in Table-4.

Results shown that drug is insoluble in water hence it falls in Class II according to BCS Classification but in 0.1 HCl it is freely soluble.

Table-4: Results of Solubility in different solvent

Solvent	Result
Water	Insoluble
0.1N HCl	Freely soluble
Strong acid (HCl)	Very soluble
Strong base (ammonia solution)	Very soluble

Preparation of Solid dispersion: Solid dispersion of drug was prepared with two polymer carriers HPMC and Sod. CMC using melting method. These polymers were used in 1:1 and 1:2 ratio. Results are shown in Table-5.

Polymer carrier	Results with different Ratio (Drug to Polymer)	
	1:1	1:2
HPMC	Freely soluble	Freely soluble
Sod. CMC	Very soluble	Very soluble

Results show that solid dispersion with Sod. CMC has more solubility compared to HPMC and also shows that both the ratio has equal solubility. So 1:1 ration of drug to polymer was used for further preparation of solid dispersion.

Precompression parameters: All the precompression parameters shown that blend has well to excellent flow property, so it could be able to compress. Results are shown in Table-6.

Table-6: Precompression parameters of Blend.

Parameters	F1	F2	F3	Type of Flow
Angle of Repose (Θ)	19.78	21.68	21.72	Excellent
Bulk Density (gm/ml)	0.505	0.515	0.51	
Tapped Density (gm/ml)	0.56	0.57	0.565	
% Carr's index	9.8	9.64	9.73	Good
Hausner ratio	1.01	1.1	1.1	Excellent

Post compression parameters of Tablets: Evaluation or post compression parameters like diameter, thickness, hardness, friability. Disintegration time were measured and results are shown in Table-7. Results shown that all the parameter are within the limit so pass the hardness test and friability. On the basis of disintegration time it is concluded that formulation F3 taken minimum time to disintegrate so it was optimized formulation.

Table-7: Postcompression parameters of tablets.

Parameters	F1	F2	F3
Diameter (mm)	8	8	8
Thickness (mm)	3.4	3.4	3.5
Hardness Kg/cm^2	4	4	3.5
% Friability	0.50	0.97	0.99
Disintegration Time (Min.)	45	35	28

Conclusion

Solid dispersion were prepared by Sod. CMC has better solubility compare to HPMC in 1:1 ratio. From all three formulations it was concluded that formulation F3 containing 7.5% Sodium starch glycolate has found minimum disingration time (28 min).

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