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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLET OF BENDROFLUMETHIAZIDE

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ABSTRACT

In the present research work, mouth dissolving tablets of bendroflumethiazide were prepared by direct compression method with a view to enhance patient compliance. Mouth dissolving tablets have many numbers of advantages over the conventional tablets like rapid disintegration, faster dissolution, Ease of administration and quick onset of action etc. Two super-disintegrants, viz., croscarmellose sodium and sodium starch glycolate in different ratios with microcrystalline cellulose along with mannitol to enhance mouth feel. Many pharmaceutical dosages are administered in the form of pills, granules, powders, and liquids. Generally, a pill is designed for swallowing intact or chewing to deliver a precise dosage of medication to patients. The drug and excipient interaction study was carried out by taking Infrared Spectrum of Pure drug and optimized formulation (B2). There was no change in the prominent functional groups of indicating drug is in intact form. The prepared batches of tablets were evaluated for hardness, friability, drug content, wetting time, water absorption ratio, disintegration time and dissolution study.

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INTRODUCTION

The most commonly used dosage form for pharmaceutical preparations is currently the tablet, available in various forms and administered orally. The advantages of this dosage form are manifold: tablets are cost effective to manufacture, convenient to dispense and store, easy for the patient to administer and they provide a versatile means of delivering the drug. Release of drug from the tablet can be controlled by altering the design and content of the formulation. Also, since this is a dry dosage form, tablets provide a supportive environment for drug stability and generally have a relatively long shelf life (Bharat Parashar *et al*., 2012). The properties of the tablet (e.g. mechanical strength, disintegration time and drug release characteristics) are affected by both the properties of the constituent materials and the manufacturing process. Excipients such as diluents, binders and lubricants are generally needed in a formulation in order to facilitate the manufacturing process, but also to ensure that the resulting tablets have the desired properties. For instance, tablets should be sufficiently strong to withstand handling during manufacturing and usage, but should also disintegrate and release the drug in a predictable and reproducible manner (Rudnic, ?). Drug Delivery Systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation and are moving rapidly. Drug delivery systems are becoming increasingly sophisticated as scientists acquire a better understanding of the physicochemical parameters pertinent to their performance (Chein, 1992). Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because of low cost of therapy, ease of administration, self-medication, leading to high levels of patient compliance. Tablets and capsules are the most popular dosage forms [(4)]. It is a tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 15 second to 3min.

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Most of the MDTs include certain super disintegrates and taste masking agents [5].Require no water for oral administration. Have a pleasing mouth feel. Have an acceptable taste masking property. Be harder and less friable. Leave minimal or no residue in mouth after administration (Ashish *et al*., 2011).

MATERIALS AND METHODS

Materials

Bendroflumethiazide was received gift sample from Ipca Laboaratories Ltd. Sejavata. Microcrystalline cellulose was obtained as a gift sample from Lupin Pharmaceuticals, Aurangabad. Sodium starch glycolate, sodium saccharine, Mannitol &Talc from SD fine chemicals, Mumbai. All other chemicals and reagents of analytical grade were used.

Method

Preparation of Bendroflumethiazide MDT by Direct Compression Method: Mouth dissolving tabletsof Bendroflumethiazide were prepared by direct compression. All the ingredients were passed through 60- mesh separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 100mg using 6mm round flat punches on 8-station rotary tablet machine (karnavati mini press-2). A batch of 50 tablets of each formulation was prepared for all the designed formulations.

Formulation of Mouth Dissolving Tablets: All ingredients are in mg.

RESULTS AND DISCUSSION

Pre-formulation Study

Physical Characteristic of Bendroflumethiazide

Melting point: Melting point of Bendroflumethiazidewas found at 222°C while as per standard literature, it was reported to be 221-223°C. So it can be concluded that Bendroflumethiazideis in a pure state.

Identification and characterization of Bendroflumethiazide by FT-IR absorption spectroscopy

FT-IR spectra of Bendroflumethiazide: The FTIR spectra of Bendroflumethiazide was taken by using the ATR method. The scanning range was 650 to 4000 cm^{-1}.The major peaks in the recorded spectra were compared with standard frequencies. The scanning range was 650 to 4000 cm^{-1}.The major peaks in the recorded spectra were compared with standard frequencies.

Analytical Methodology

U.V Spectrophotometric Analysis

Determination of λ_{max} and calibration curve of Bendroflumethiazide in methanol

Determination of λ_{max} of pure Bendroflumethiazide in methanol: The UV spectrum obtained was shown in figure no 12. The wavelength of maximum absorbance (λ_{max}) was found to be 273 nm.

Construction of Calibrate of Bendroflumethiazide in methanol

The absorbance value obtained for various concentrations were shown in table no 16. The absorbance obtained was in range of 0.3-1.4. Using absorbance-concentration data, Beer- lambert's graph was plotted and is shown in figure no 13. The calibration curve of Bendroflumethiazide in methanol was found to be linear in the range of 2-10 µg/mL and coefficient of regression (R^2) was found 0.9993.

Result of pre-compression parameter

- Angle of repose for all batches was found in the range of 23.74-29.24^0.The angle of repose was within the range of25-30 showed the good flow property. All the Mouth dissolving tablets were found to be elegant without any chipping, capping and sticking.
- Bulk density and Tapped density for all batches was found in the range of 0.41-0.50gm/cm^3 and 0.47-0.62 gm/cm^3 respectively.
- Carr's index was found in the range of 12.76-19.35%.The value ranges up to 20 % showed that good to excellent flow property.
- Hausner's ratio was found in the range of 1.14-1.27.Indicating good flow property

Post-compression parameter

- Hardness for all batches was found in the range of 2.9-3.2 kg/cm^2.The tablets of the batch B_2 showed hardness of 2.9 kg/cm^2
- Thickness for all batches was found in the range of 4.03-4.05 mm.
- Weight Variation for all batches was found in the range 100mg.All the formulation pass the test as average percent weight deviation was found less than 10%.
- Friability for all batches was found in the range 0.35-0.55%.The results suggest that the friability will with stand the rigors which occurred during packing, transportation and shipping etc. because of friability was less than 1%.
- Disintegration time for all batches was found in the range 52-80 sec. It was concluded that, by the addition by increasing in concentration of Super disintigrants significantly decrease the disintegration time.
- Water absorption ratio for all batches found in the range 49.23-70.29%
- Drug content for all batches found in the range 97.77-100.6%. The results of all batches were showed that there was uniform distribution of the drug throughout the batch. The tablets of the batch B_2 showed drug content of 99.07%.
- Wetting time for all batches found in the range 92-102 sec. wetting time is closely related to inner structure of tablet, which facilitate faster dispersion in mouth.

In vitro dissolution studies: Tablets of batch B1 to B6 was evaluated for *in-vitro* drug release the result was showed that the *in-vitro* drug release of tablet was found in the range of 55.20 to 99.02.

Table 1. Formula for preparation of MDT

Sr. No.	Ingredients	B_1	B_2	B_3	B_4	B_5	B_6
1	Bendroflumethiazide	10	10	10	10	10	10
2	Croscarmellose sodium	10	15	20	-	-	-
3	Sodium starch glycolate	-	-	-	10	15	20
4	Microcrystalline cellulose	60	60	60	60	60	60
5	Sodium saccharine	1%	1%	1%	1%	1%	1%
6	Magnesium Stearate	1%	1%	1%	1%	1%	1%
7	Talc	2%	2%	2%	2%	2%	2%
8	Mannitol	16	11	6	16	11	6
	TOTAL	100	100	100	100	100	100

All ingredients are in mg.

Table No. 2. Physical Characteristic of Bendroflumethiazide

Sr. No.	Test	Observation	Inference
1	Color	White	Complies to BP
2	Odor	Odorless or almost odorless	Complies to BP
3	Surface Nature	Crystalline Powder	Complies to BP

Table No. 3. Melting point of Bendroflumethiazide

Sr. No.	Standard M.P. (°C)	Observed M.P. (°C)	Mean (°C)
1	221-223	223	222
2		222	
3		221	

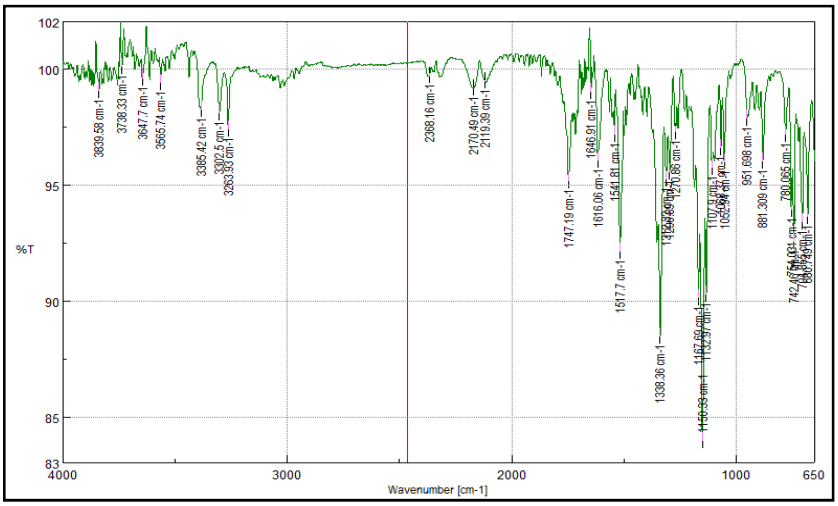

Figure No. 1. FT-IR Spectra of Bendroflumethiazide

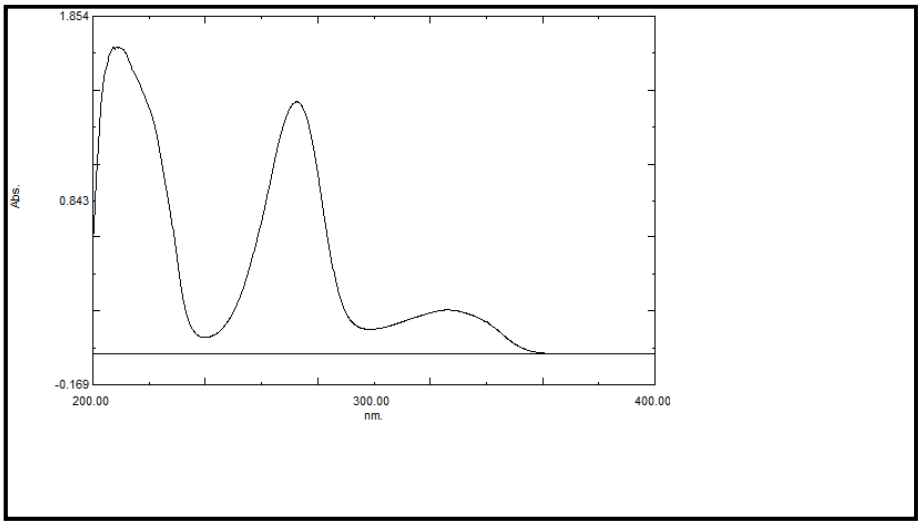

Figure No.2.λ_{max}bendroflumethiazide 10 µg/mL in methanol

Table No. 4. Absorbance and conc. data of Bendroflumethiazide in methanol (at 273 nm)

Sr. No.	Conc. (µg/mL)	Absorbance
1	2	0.31
2	4	0.577
3	6	0.887
4	8	1.19
5	10	1.46
R^2		0.9993

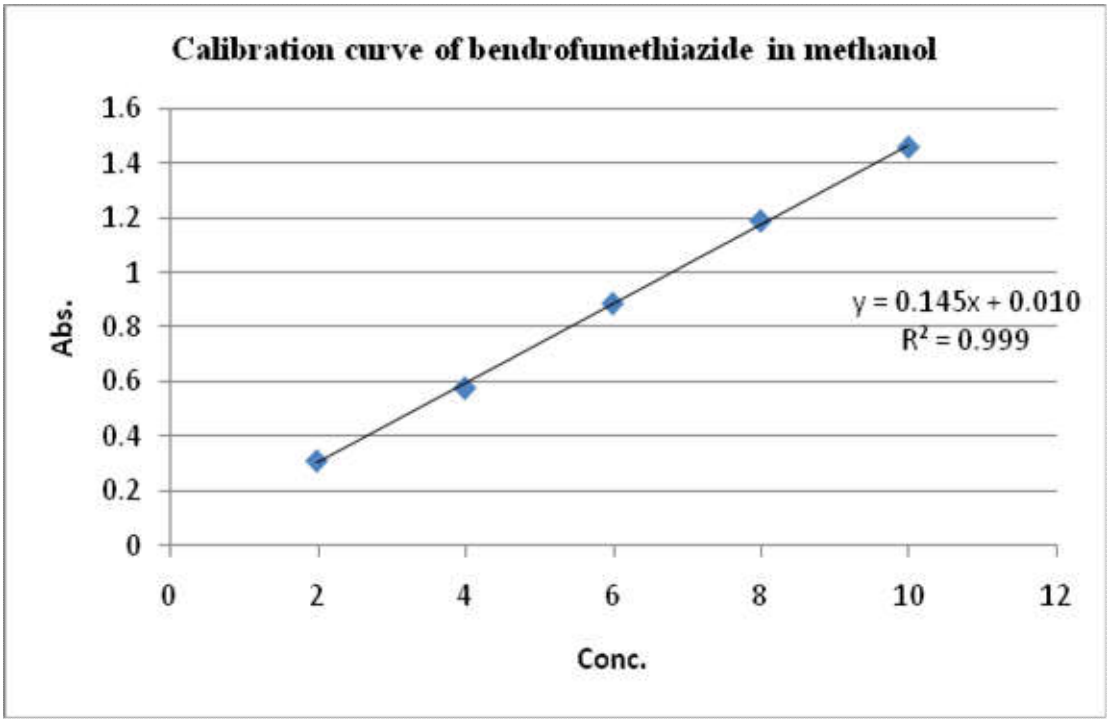

Figure No. 3. Calibration curve of Bendroflumethiazide in methanol

Table No. 5. Calibration data of Bendroflumethiazide in methanol

Sr. No.	λ_{max} (nm)	Solvent	Conc. range (µg/mL)	Regression equation	Regression coefficient (R^2)
1	273	Methanol	2-10	y = 0.1457x + 0.0109	0.9993

Table No. 6. Result of powder blend

Formulation Code	Angle of repose (0)	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr's Index %	Hausner Ratio
B_1	23.74±0.14	0.41±0.18	0.47±0.89	12.76±0.15	1.14±0.08
B_2	29.24±0.4	0.42±0.45	0.50±0.76	16.01±074	1.19±0.10
B_3	27.47±.19	0.45±0.13	0.5±0.14	18.18±0.62	1.22±0.11
B_4	25.64±0.82	0.50±0.13	0.62±0.19	19.35±0.11	1.24±0.19
B_5	27.02±0.34	0.43±0.17	0.55±0.4	17.80±0.65	1.27±0.79
B_6	26.10±0.2	0.50±0.17	0.62±0.16	19.35±0.18	1.24±0.06

*All values are expressed as mean ± standard deviation,n=3

Table No. 7. Evaluation data of the prepared Bendroflumethiazide MDT

Batch Code	Hardness (kg/cm^2)	Thicknes s(mm)	Wt. Variation (mg)	% Friability	Disinti-gration time (sec)	Water absorption ratio (%)	Drug content (%)	Wetting time (sec)
B_1	3.03±0.09	4.05±0.2	99.4±1.4	0.35	60±2.4	67.63±1.4	98.20±0.17	92±1.05
B_2	2.9±0.02	4.03±0.1	101.5±0.75	0.39	55±1.5	66±2.0	99.07±0.15	90±2.03
B_3	3.03±0.03	4.04±0.3	100.6±0.23	0.55	52±2.9	70.29±1.6	97.77±0.12	98±2.1
B_4	3.06±0.04	4.03±0.1	100.2±0.1	0.49	80±1.1	50.49±1.4	100.6±0.10	100±1.2
B_5	3.2±0.29	4.04±0.3	100.5±0.78	0.50	70±1.9	50.25±1.8	98.59±0.35	95±1.3
B_6	3.2±0.17	4.03±0.1	100.4±0.95	0.49	65±1.5	49.23±1.1	98.77±0.15	102±2.0

All values are expressed as mean± standard deviation, n=3

Table No. 8. % cumulative drug release of MDT

Time in min	% Cumulative Drug Release					
	B_1	B_2	B_3	B_4	B_5	B_6
0	0	0	0	0	0	0
2	65.29±0.19	66.04±0.69	62.52±1.29	55.20±1.63	55.60±2.35	62.66±1.54
4	76.16±3.36	75.20±0.16	78.16±1.27	65.12±0.69	70.66±2.34	74.13±1.64
6	85.63±2.14	85.52±0.36	86.25±2.14	78.88±0.16	87.37±1.56	88.88±1.36
8	95.33±2.19	95.00±1.32	92.58±0.19	89.89±1.34	92.52±0.19	95.45±1.33
10	97.37±1.36	99.02±0.65	97.06±0.51	98.79±0.51	95.52±0.19	96.12±1.32

All values are expressed as mean ± standard deviation, n=3

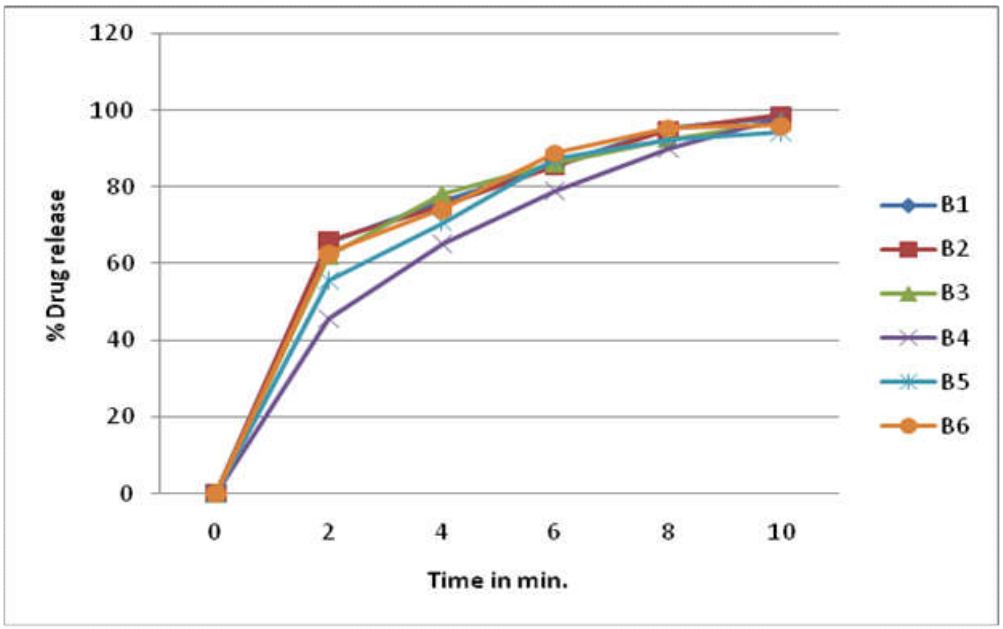

Figure No. 5. Graph for% cumulative drug release of MDT

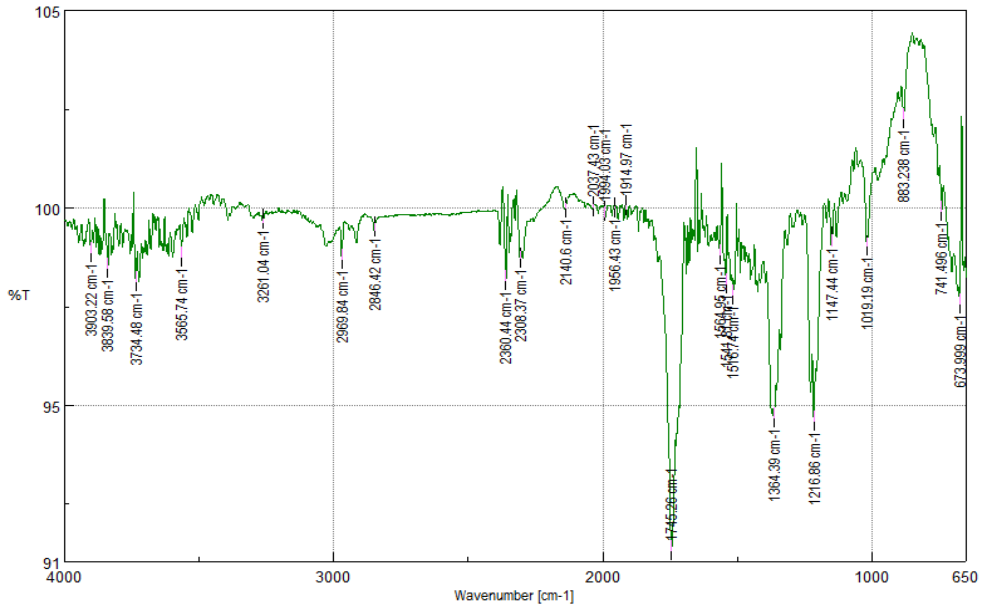

Figure No. 6. FTIR Spectra of selected batch (B_2)

It was concluded that by the addition by increasing in concentration of superdisintegrants significantly increase the % drug release.

FT-IR spectra of selected batch (B_2): IR Spectral analysis suggests that the characteristic peaks of the pure drug Bendroflumethiazide exist in the Spectra of Formulation prepared indicting the intactness of the drug is in intimate contact with the additives. It has not undergone any chemical interaction with the excipients used in the development of Bendroflumethiazide mouth dissolving tablets.

Conclusion

The concepts of formulating Mouth dissolving tablets of offers a suitable and practical approach in serving desired objectives of faster disintegration and dissolution characteristics. In the present work, Mouth dissolving tablets of Bendroflumethiazide were prepared by Direct Compression Technique using croscarmellose sodium, sodium starch glycolate as Super disintegrants. All the Mouth dissolving tablets of Bendroflumethiazide prepared were subjected to drug content Uniformity, weight variation, hardness, thickness, friability, wetting time, water absorption ratio, disintegration, dissolution studies.

- The result of angle of repose of all batches was found in the range of 23.74-29.24^0 indicating good flowing characteristics of granules.
- The result of bulk density of all batches was found in the range of 0.41-0.50gm/cm^3. The result of tap density was found in the range of 0.47-0.62 gm/cm^3.
- The result of car's index of all batches was found in the range of 12.76-19.35%.
- The result of hausner's ratio of all batches was found in the range of 1.14-1.27. Indicating good flow property.
- Hardness of the tablet of every batch was in the range of 2.9-3.2 kg/cm^2.
- Friability of all the tablets was found in the range of 0.35-0.55%. The results suggest that the friability will withstand the rigors which occurred during packing, transportation and shipping.
- Weight Variation for all batches was found in the range 99.4-101.05 mg ±7.5.
- The result of water absorption ratio of all batches was found in the range of 49.23-70.29%.
- The result of wetting time of all batches was found in the range of 92-102 sec. wetting time is closely related to inner structure of tablet, which facilitate faster dispersion in mouth.
- The result of *in-vitro* disintegration time of all batches was found in the range of 52-80 sec. It was concluded that, by the addition by increasing in concentration of Super-disintigrants significantly decrease the disintegration time.
- The results of *in-vitro* drug release of batch B_1 to B_6 was found in the range of 55.20-99.02%.
- IR Spectral analysis suggests that the characteristic peaks of the pure drug Bendroflumethiazide exist in the Spectra of Formulation prepared indicting the intactness of the drug is in intimate contact with the additives. It has not undergone any chemical interaction with the excipients used in the development of Bendroflumethiazide Mouth dissolving tablets.
- Finally, we can conclude that, among various formulations prepared, the mouth dissolving tablets of batch B_2 prepared by using Croscarmellose sodium (B_2), have a friability 0.39 % , hardness 2.9 Kg/cm^2, drug content 99.07 % ,disintegrated rapidly in 55 sec and gave highest dissolution of Bendroflumethiazide 99.02 % in 10 min.

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