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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF IMIDAPRIL

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ABSTRACT

This research was to formulation and evaluation of fast dissolving tablets of Imidapril using direct compression technique (effervescent) with sodium bicarbonate, mannitol, poly vinylpyrrolidone, citric acid. Eight different formulation of Imidapril were prepared by using different ratio of NAHCO3: MANNITOL by direct compression method. The tablet was characterized by hardness, wetting time, weight variation; water Absorption Ratio, In Vitro Drug Release. All batches of fast dissolving tablets were satisfactory in terms of dissolution profile. The hardness, wetting time, water absorption ratio and wetting time were also shows the satisfactory result. The batches of all formulations, S6 batch with sodium bicarbonate: mannitol (1:3) showed more release than the other concentration and better results. The S6 batch of fast dissolving tablets was found to be 97.56 % drug release in 30 minutes. The S6 was the best of all eight formulations of Fast Dissolving Tablets of Imidapril. Bioavailability of Imidapril can be increased by formulating it as a Fast Dissolving Tablet.

Keywords: Imidapril, Fast dissolving tablet, Sodium bicarbonate, Mannitol, Citric acid.

INTRODUCTION

Fast dissolving tablets offer great advantages for the patients having difficulty in swallowing. Fast dissolving tablets are best alternate to deliver the drug having bitter taste and poor oral bioavailability.

Imidapril is an angiotensin-converting enzyme (ACE) inhibitor, used to treat hypertension and congestive heart failure. Imidapril lowers the production of angiotensin II, therefore relaxing arterial muscles while at the same time enlarging the arteries, allowing the heart to pump blood more easily, and more blood is pumped into and through larger passageways due to increasing blood flow. Imidapril have a poor bioavailability of 28%-30%, extent of absorption is not affected by the presence of food. However, the rate of absorption is reduced. Fast dissolving Tablet formulation has been widely and successfully applied to improve the dissolution, solubility, and consequently the bioavailability of poorly water-soluble drugs. Because of its poor aqueous solubility, Imidapril may pose dissolution related absorption problem. In the present study, an attempt had been made to prepare fast dissolving tablets of Imidapril in the oral cavity with enhanced dissolution rate & hence improved patient compliance using sodium bicarbonate and mannitol [1-3].

MATERIALS AND METHODS

Imidapril was received as gift sample from Torrent Pharmaceuticals Limited, Gujarat, India. Sodium bi carbonate, polyvinyl pyrrolidine, citric acid, magnesium Stearate were supplied by Central Drug House (P) Ltd., New Delhi, India and mannitol was supplied by Qualigens Fine Chemicals, Mumbai.

Calibration Curve of Imidapril in 6.8 Ph Phosphate Buffer:

Preparation of 6.8 pH phosphate buffer:

- Prepare a 0.2 M solution of potassium dihydrogen phosphate by dissolving 27.218 gm of substance in1000 ml of distilled Water.
- Prepare a 0.2 M solution of sodium hydroxide solution by dissolving 8 gm of substance in 1000 ml of distilled Water.

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➢ Take 50 ml of above prepared potassium dihydrogen phosphate solution & 22.4 ml of above prepared sodium hydroxide solution. Add both the solution & make the volume of the resultant solution 200 ml. Calibrate the solution for using pH meter & adjust the pH 6.8.

Preparation of stock solution:

Dissolve 10 mg of Imidapril in few ml of phosphate buffer by taking 100 ml volumetric flask & make up the volume 100 ml to get a solution of 100 mcg/ml concentration solutions.

Procedure:

Prepare different concentrations from 10 mcg/ml to 60 mcg/ml by diluting stock solution as for first concentration 10 mcg/ml, take 1 ml of stock solution & dilute with 10 ml of buffer solution .Similarly other concentrations are prepared. Absorbances are measured at 231nm for each concentration by using UV spectrophotometer (UV-3000, Lab India). Concentration is plotted against absorbance on a graph paper.

Formulation Development

Different batches of tablets prepared by wet granulation method. Eight different batches of tablets were prepared by taking sodium bicarbonate, polymer ratio 1:0, 1:1, 1:2, 1:3 1:4 1: of each with PVP. Thus total eight batches were prepared (Different combination shown in table 2).

Sieving

Mg. Stereate was sieved through # 60 mesh.

Granulation

All the ingredients were mixed in increasing order of weights. The bisolution of PVP in Isopropyl alcohol was used as granulating solvent. The granules were made using #40 meshes. Then granules were dried in oven at 40.

Compression

The tablets were compressed on a single punch tableting machine(Bells India Marketed and Manufactured by Meditron Ing. New Delhi) for 250mg tablet respectively.

Evaluation of Tablets

The tablets were evaluated for appearance, hardness, friability, In-vitro drug release and floating lag time and total floating time.

Bulk density

Apparent bulk density (g/ml) was determined by placing pre-sieved bulk powder blend into a graduated cylinder via a large cylinder and measuring the volume and weight "as it is.

$Pb=^{M/V}p$

Where, p b=Bulk Density"

M = Weight of sample in gm

V = Final volume of blend in cm^3

Tapped density

It was determined by placing known mass of powder in a graduated cylinder & tapping it for fixed number of taps (around 250) until the powder bed volume reached a minimum. Using the weight of the powder in the cylinder and this volume, the tapped density was computed. (Table No. 3).

Angle of repose

The angle of repose was calculated with the formulatan a =H/R, where 'a' is the angle of repose and R is the radius of the conical pile.

Tan θ= h/r

Therefore θ= Tan-1h/r

Where θ= Angle of repose

h = height of the cone

r= Radius of the cone base

Angle of Repose less than 30 ° shows the free flowing of the material

Compressibility Index

The compressibility index of the granules was determined by Carr's compressibility index.

%Carr Index= (TBD-LBD) ×100/TBD

Where, TBD= Tapped bulk density

LBD= Lowest bulk density

Hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of tablets was measured using a Monsanto hardness Tester.

Friability

It is a measure of mechanical strength of tablets. Roche Friabilator was used to determine the friability by following procedure: Preweighed tablets were placed in the Roche friabilator (Electro lab EFL Friabilator, Mumbai, India) and expressed in the percentage by using this formula.

$$\text{Friability (\%)} = \frac{\text{Initial weight} - \text{Final weight} \times 100}{\text{Initial weight}}$$

Weight variation study

With a tablet designed to contain a specific amountof drug in a specific amount of formula, the weight of a tablet being made is routinely measured to ensure that a tablet contains proper amount of drug. 20 Tablets

were taken from each batch. The tablets were weighed and applied for checking deviation from normal range as per U.S.P. standards.

Water absorption ratio and wetting time

A piece of tissue paper folded twice was placed in a petridish containing 5ml of water. A pre weighed tablet was placed on the paper and the time for complete wetting was measured which is characterized by coloring of tablet. The wetted tablet was then weighed. Water absorption. R was determined according to the following formula.

R = (Wa- Wb/ Wb) 100

Where, Wa = weight of tablet after absorption of water

Wb= weight of tablet before absorption of water

***In vitro* Dissolution studies**

In vitro dissolution studies of fast-dissolving tablets were performed by using(type 2 USP dissolution) apparatus as specified in at 50 rpm; and Sorenson's buffer (pH,6.8), 900ml, was used as dissolution medium, temperature of dissolution medium was maintained at 370 C±0.50C. Sample of dissolution medium was withdrawn at a specific time interval and was filtered. Absorption of filtered solution was checked by UV spectroscopy (Lab India Uv 3000), and drug content was determined from standard calibration curve. Dissolution rate was studied for all designed formulation [4,5].

RESULTS AND DISCUSSION

Eight formulations of Fast Dissolving Tablets of Imidapril were prepared with varying concentration of Sodium bicarbonate: Mannitol and also Citric acid, PVP were used as diluents (Table. no. 2). For each formulation, blend of drugand excipients were prepared and evaluated for various parameters as explained earlier. The powder blend was compressed using direct compression technique. Bulk density, was found in the range of (0.41-0.96 the mean was calculated. The following formula was gm/cm3) and the tapped density between (0.48-1.09 g/cm3).The compressibility index was found between (10.66-13.30) which indicates a fairly good flowbility of the powder blend. The good flowability of the powder blend was also evidenced with angle of repose in the range of (24.24-26.64) which is below 40(0) indicating good flow properties of the granules (Table no.3).

Tablets were prepared using direct compression technique. Since the powder material was free flowing, tablets were obtained of uniform weight due of uniform die fill, with acceptable weight variations as per I.P. The average weight of the prepared tablet was found 249 to 254 mg. All the tablets were exhibit in white colour, odourless, smooth surface with zero defects. A tablet requires certain amount of hardness to withstand the mechanical shocks in handling, packaging and at the time of application. The friability of all the formulation was found to be less than 1.0 %.

The hardness of the prepared tablet varied from 2.3 to 4.2 Kg/cm2 which have satisfactory strength to withstand the mechanical shocks (Table no.4).conclusion The Fast Dissolving Tablets have potential advantages over conventional dosage forms, with their improved patient compliance; convenience bioavailability and rapid onset of action had drawn the attention of many manufacturers over a decade. The preparation process of direct compression tablets includes co-grinding of all the excipients before compression, resulting the increase in the solubility due to the reduction in the effective particle size of the drug following increase in the wetting of drug by the excipients and improved dissolution of drugs. Fast Dissolving Tablet formulation obtained by some of these technologies has sufficient strength quick disintegration / dissolution in the mouth without water.

Table 1. Calibration curve in 6.8 pH phosphate buffer

S.No.	Concentration (µg/mL)	Absorbance
1	10	0.291
2	20	0.722
3	30	1.261
4	40	1.623
5	50	1.892
6	60	1.961

Table 2. Composition of Fast Dissolving Tablets of Imidapril (250 mg tablets)

Batches(mg/tablets) / Ingredients	S1	S2	S3	S4	S5	S6	S7	S8
$NaHCO_3$:Mannitol	1:0	1:1	1:2	1:3	1:4	1:5	5:1	4:1
Imidapril	20	20	20	20	20	20	20	20
$NaHCO_3$	220	100	66.6	50	40	33.3	166.6	160
Mannitol	0	100	133.3	150	160	166.6	33.3	40
Citric Acid	5	5	5	5	5	5	5	5

PVP	20	20	20	20	20	20	20	20
Talc	2	2	2	2	2	2	2	2
Mg. Stearate	2	2	2	2	2	2	2	2

Table 3. Evaluation data of Micrometric property of bulk powder blend

Different Batches / Micrometric properties	S1	S2	S3	S4	S5	S6	S7	S8
Bulk Density (gm/cm^3)	0.96	0.69	0.56	0.50	0.43	0.41	0.82	0.83
Tapped Density (gm/cm^3)	1.09	0.79	0.63	0.57	0.50	0.48	0.92	0.92
Angle of Repose	24.34	24.42	25.34	24.24	24.66	25.47	24.98	25.64
Compressibility Index (%)	11.92	12.65	10.93	13.26	12.72	13.30	10.66	12.14

Table 4. Evaluation data of compressed tablets of different formulations

Different Batches / Evaluation data	S1	S2	S3	S4	S5	S6	S7	S8
Hardness (kg/cm^2)	2.3	2.8	3.2	3.8	4.1	4.2	2.5	2.7
Friability (%)	0.51	0.43	0.41	0.42	0.43	0.42	0.43	0.47
Weight variation(mg)	251.2	252.6	250.4	250.0	254.1	253.6	249.5	250.3
Water absorption ratio	102.2	130.5	145.8	156.8	153.9	155.0	150	149.5
Wetting Time (sec)	174	165	159	152	145	143	160	155

Table 5. % Drug release of Different Batches

Batches	% Drug Release							
Time (min)	S1	S2	S3	S4	S5	S6	S7	S8
0	0	0	0	0	0	0	0	0
5	52.21	53.67	55.41	60.41	57.87	52.21	55.78	58.21
10	65.34	78.89	85.67	90.23	80.89	78.56	75.34	69.34
15	69.98	80.65	88.56	92.31	87.56	82.34	79.7	74.5
20	75.67	85.67	91.23	96.42	90.87	84.5	83.6	78.6
30	78.34	88.56	95.58	96.91	97.56	99.67	93.67	86.8

CONCLUSION

In conclusion, overall results suggest that formulation containing sodium bicarbonate and mannitol in the ratio of 1:3 (F4) shows best results in terms of percent drug release, compressibility index, and hardness and disintegration time. Thus Fast Dissolving Tablets may be developed for Imidapril, for quick onset of action without need of water for swallowing or administration, however further studies are investigations are needed to confirm the in vivo efficiency and for the development of Fast Dissolving Tablet of Imidapril Acknowledgements Authors are thankful to Principal, Professor R. Hemalatha, NKBR College of pharmacy and research centre for providing me all facilities and encouragement for successful completion of this work.

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