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Research Article

PLANTAGO OVATA SEEDS AND BHRINGARAJ LEAVES AS SUPERDISINTEGRANTS: FORMULATION AND EVALUATION OF SOTALOL HYDROCHLORIDE ORODISPERSIBLE TABLETS

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ABSTRACT

other superdisintegrants natural origin is preferred because they are comparatively cheaper, abundantly available, non-irritating and nontoxic in nature. An attempt has been made for the development of orodispersible tablets of the Sotalol hydrochloride, using different concentrations of natural superdisintegrating agents like plantago ovata mucilage, Bhringaraj powder, synthetic and semi synthetic superdisintegrants like cross povidone and croscarmellose sodium by direct compression method. Disintegration time and drug release were taken as the basis to optimize the orodispersible tablet. All the tablets were Prepared & evaluated for various parameters like hardness, weight variation, friability, thickness, disintegration time wetting time and dissolution time. Among all the formulations, formulation containing 5% w/w of natural superdisintegrant (Plantago ovata mucilage) was found to be shown faster and high drug dissolution.

Keywords: Sotalol hydrochloride, orodispersible tablet, Plantago ovata, Bhringaraj powder.

INTRODUCTION

Sotalol Hydrochloride is an anti arrhythmic drug. It falls into the class of Beta blockers (and class II anti arrhythmic agents) because of its primary action on the β-adrenergic receptors in the heart. In addition to its actions on the beta receptors in the heart, Sotalol Hydrochloride inhibits the inward potassium ion channels of the heart. Fast onset of action is a major concern in the treatment of hypertension. Thus the purpose of this research is to formulate and evaluate orodispersible tablets of Sotalol Hydrochloride for rapid dissolution of drug and absorption, which may produce the rapid onset of action in the treatment of arrhythmias.

Orodispersible tablets are those solid dosage forms when put on the tongue, disintegrate or dissolve instantaneously, releasing the drug within a few seconds without the need of water[1]. These dosage forms provide fast onset of action, patient compliance, and good chemical stability. Orodispersible tablets are also known as "Mouth dissolving tablets", "Orally disintegrating tablets"," Melt- in- mouth"," Fast dissolving drug delivery", " Rapimelts tablets", "Porous tablets", Quick dissolving tablets" etc. Orodispersible tablets allows high drug loading and no chewing is needed. In conventional dosage from there is delay in disintegration and therefore dissolution, while ODTs rapidly disintegrates in oral cavity and thus dissolution is fast. Due to disintegration of ODTs in mouth absorption starts at mouth then pharynx and oesophagus. Various approaches to formulate ODTs are lyophilisation, moulding, spray drying, sublimation, direct compression and mass extrusion.

Mucilage of natural origin is preferred over semi synthetic and synthetic substances because they are comparatively cheaper, abundantly available, non irritating and non toxic in nature. An attempt has been made for the development of fast dissolving tablets of the Sotalol hydrochloride, using different concentrations of natural superdisintegrating agents like plantago ovate mucilage and Bhringaraj powder.

The present study focuses on comparison between natural super disintegrants and synthetic superdisintegrants in the formulation of orodispersible drug delivery system to study the effect of functionality differences of

synthetic superdisintegrants and natural super disintegrants on the tablet properties.

MATERIALS AND METHODS

MATERIALS

Sotalol hydrochlorides, Croscarmellose sodium, Crospovidone, Micro crystalline cellulose, Mannitol are obtained from Natco Pharma Ltd, Hyderabad as a gift sample. Iso propyl alcohol, Magnesium stearate and Talc are purchased from S.D. Fine chem., Mumbai. Plantago Ovata seeds and Brhingaraj powder are obtained from local market.

FORMULATION STUDIES

Extraction of mucilage from seeds of Plantago ovata[2]

10 grams of Plantago ovata seeds were soaked in 2 litres of distilled water for 48 hours and boiled for 2 hrs. The mucilage released into the water was squeezed out and separated from seeds with the help of the muslin cloth. The mucilage was collected and precipitated using 3 times of 95% ethanol. Collected mucilage was dried in the oven at 50-55°. Dried mucilage was scraped and powdered using pestle and mortar. Powder was sieved using mesh no#60.

Preparation of Treated Bhringraj powder[3]

The leaves of *E.alba* were collected from medicinal garden of Bapatla College of Pharmacy. Mumbai, India. The whole plant and leaves of *E.alba* were authenticated from pharmacognosy Department of Bapatla College of Pharmacy. Leaves were separated and subjected to shade drying at room temperature. The dried leaves were subjected to size reduction to a coarse powder with the help of grinder. 10 grams of powder was weighed and added in distilled water (100ml). Agitation is done continuously by a stirrer for one day to swell. The swollen contents are dried on a tray for 3 days at room temperature. The dried powders were grinded by mortar and pestle. The powder was finally re-sieved (100 mesh) and stored in airtight container at 25^0C.

Micromeritic properties of the blend[4]

a) Bulk density

Blend was weighed and transferred to a measuring cylinder. Then bulk volume was noted. Bulk density was calculated by using the following formula.

$$\textbf{Bulk density} = \frac{Massofthepowder}{Bulkvolume}$$

b) Tapped density

Blend was weighed, transferred to a measuring cylinder and subjected to 100 tapings. Then volume was noted as tapped volume. Tapped density was measured by using the following formula

$$\textbf{Tapped density} = \frac{Massofthepowder}{Tappedvolume}$$

c) Carr's index

Carr's index was calculated by using the following formula

$$\textbf{Carr's index} = \frac{Tappeddensity - Bulkdensity}{Tappeddensity} \times 100$$

d) Hausner's ratio

Hausner's ratio was calculated by using the following formula

$$\textbf{Hausner's ratio} = \frac{Tappeddensity}{Bulkdensity}$$

e) Angle of repose

Required quantity of blend was taken and poured into a hollow cylinder which was placed on a graph sheet. Then the cylinder was slowly lifted. Then height and diameter of the heap formed were noted down. The angle of repose (θ) was calculated by the formula

$$\textbf{Angle of repose, } \theta = \textbf{Tan}^{-1}\frac{h}{r}$$

Preparation of Sotalol hydrochloride tablets

Tablets were made from blends by direct compression method. All the ingredients (shown in Table-1) were passed through mesh no. 80. All the ingredients were co ground in a mortar with pestle. The resulting blend was lubricated with magnesium stearate and compressed into tablets using the Cadmach single punch (round shaped, 7mm thick) machine.

Evaluation of Sotalol hydrochloride tablets

a) Weight variation test[5]

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

b) Drug content

Twenty tablets were powdered, and 80 mg equivalent weight of Sotalol hydrochloride in tablet powder was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 5 ml methanol was added and shaken for 10 min. Then, the volume was made up to 100 ml with 0.1N Hydrochloric acid. The solution in the volumetric flask was filtered, diluted suitably and analyzed spectrophotometrically at 230 nm.

c) Disintegration Time[6]

The disintegration time was determined in distilled water at 37±0.5^{0}C using disintegration test apparatus USP ED-2L (Electro lab, Mumbai).

d) Friability[7]

Roche friabilator was used to determine the friability. Pre weighed tablets were placed in friabilator and rotated at a speed of 25 rpm for 4 minutes or up to 100 revolutions. The tablets are dropped from a distance of 6 inches in each revolution. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

$$\%\,\text{friability} = \frac{\text{Weight before friabilation} - \text{Weight after friabilation}}{\text{Weight before friabilation}} \text{X}\,100$$

e)Hardness[8]

Hardness of the tablet was determined using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning threaded bolts until the tablet fractured. Then the final reading was recorded. The hardness was computed by deducting the initial pressure from the final pressure.

f) Wetting Time[9]

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a Petri dish with a 10 cm diameter. 10 mL of water-containing amaranth (a water soluble dye) is added to Petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

g) In vitro dispersion time[10]

Tablet was added to 10 ml of phosphate buffer solution pH 6.8 (pH of saliva) at 37± 0.5°C. Time required for complete dispersion of tablet was measured.

h) Fineness of dispersion[11]

This test was performed by placing two tablets in 100 ml of water and stirring it gently, until the tablets get completely disintegrated. Then the dispersion is passed through a sieve screen with a nominal mesh aperture of 710 μm.

i) Dissolution studies[12]

Dissolution studies for Sotalol hydrochloride fast dissolving tablets were performed in 0.1N Hydrochloric acid using USP dissolution test apparatus (Electrolab, Mumbai, India) with a paddle stirrer. The paddles were allowed to rotate at speed of 100 rpm. The dissolution medium was maintained at a temperature of 37±0.5 ^{O}C and samples were withdrawn at an interval of every 5 min the volume of the withdrawn samples were replaced by fresh dissolution medium in order to kept the volume of the dissolution medium as constant. The withdrawn samples were filtered and absorbance was measured at absorption maxima of 230nm using UV-visible spectrophotometer.

k) In-vitro dissolution kinetic studies[13]

The drug release data were plotted and tested with zero order (cumulative % drug released Vs time), First order (Log % remained Vs time). The in vitro dissolution kinetic parameters, dissolution rate constants (K), correlation coefficient (r), the time (t_{50}) for 50 % drug released (half-life) and dissolution efficiency [D.E] were calculated. From the slopes of linear plots, the dissolution rates were calculated.

RESULTS AND DISCUSSION

Micrometric properties

Micromeritic properties of the blends were studied and results were shown in Table- 2.All the blends exhibited good flow properties and are found to be suitable for direct compression.

Influence of different synthetic superdisintegrants on Sotalol hydrochloride orodispersible tablets

To study the influence of superdisintegrants on the performance of sotalol hydrochloride, a set of two formulations (F_1 and F_2) were prepared using two superdisintegrants *viz*, Croscarmellose sodium (5%) and Crospovidone (5%) respectively. The formulated tablets were subjected to various quality control tests and the results were shown in Table-3 .All the tablets complied with the pharmacopoeial standards. The dissolution data was presented in Table-4 and Figureure-1. The *In-vitro* dissolution kinetics was presented in Table-5. The dissolution rate followed first-order kinetics (Figure-2) as the graphs drawn between log % drug unreleased Vs time were found to be linear. The dissolution rate of sotalol hydrochloride was found to be effected by nature of the superdisintegrant used in the preparation of

tablets. Based on the dissolution rate, superdisintegrants can be rated as Croscarmellose sodium < Crospovidone. The formulation prepared with Crospovidone was offered relatively rapid release of sotalol hydrochloride when compared with Croscaramellose sodium.

Influence of natural superdisintegrants on sotalol hydrochloride orodispersible tablets

To study the influence of natural superdisintegrants on the performance of sotalol hydrochloride, a set of two formulations (F_3 and F_4) were prepared using two natural superdisintegrants *viz*, *plantago ovata* mucilage (5%) and treated Bhringraj powder (5%) respectively. The formulated tablets were subjected to various quality control tests and the results were shown in Table-3. All the tablets complied with the pharmacopoeial standards. The dissolution data was presented in Table-4 and Figureure-3. The *In-vitro* dissolution kinetics was presented in Table-5. The dissolution rate followed first-order kinetics (Figure-4) as the graphs drawn between log % drug unreleased Vs time were found to be linear. The dissolution rate of sotalol hydrochloride was found to be effected by nature of the natural superdisintegrant used in the preparation of tablets. Based on the dissolution rate, superdisintegrants can be rated as Treated Bhringraj powder < *plantago ovata* mucilage. The formulation prepared with *plantago ovata* mucilage was offered relatively rapid release of sotalol hydrochloride when compared with Treated Bhringraj powder.

Comparison of dissolution data of tablets containing synthetic superdisintegrants and natural superdisintegrants

The tablets with synthetic superdisintegrants shown maximum release for 20 minutes where as the sotalol hydrochloride tablets containing natural superdisintegrants showed the maximum release for 15 minutes.

CONCLUSION

All the blends exhibited good flow properties and suited for direct compression. The formulation prepared with 5%w/w of Crospovidone was offered relatively rapid release of sotalol hydrochloride when compared with 5%w/w of Croscarmellose sodium.

Dissolution rate of sotalol hydrochloride influenced by type of synthetic superdisintegrants employed and type of natural superdisintegrants employed. The formulations prepared with natural superdisintegrants were found to be fast releasing than the tablets formulated with synthetic superdisintegrants. The formulation prepared with *plantago ovate* mucilage was offered relatively rapid release of sotalol hydrochloride when compared with Treated Bhringraj powder.

Table 1: Composition of ingredients for Sotalol hydrochloride orodispersible tablets(In mg)

Ingredients	F_1	F_2	F_3	F_4
Sotalol hydrochloride	80	80	80	80
Crospovidone	10	-	-	-
Croscarmellose sodium(CCS)		10	-	-
plantago ovata mucilage			10	
Treated Bhringraj powder				10
(CP+CCS)	-			
Mannitol	55	55	55	55
MCC	47	47	47	47
Talc	4	4	4	4
Mg stearate	4	4	4	4
Total weight	200	200	200	200

Table 2: Micrometric properties for formulation blends

Formulation code	Bulk density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr's index (%)	Hausner's ratio	Angle of repose (°)
F_1	0.531	0.608	12.66	1.145	29.1
F_2	0.512	0.609	15.92	1.189	27.6
F_3	0.514	0.611	15.87	1.188	27.3
F_4	0.511	0.603	15.25	1.180	27

Table 3: Physical parameters of Sotalol hydrochloride orodispersible tablets

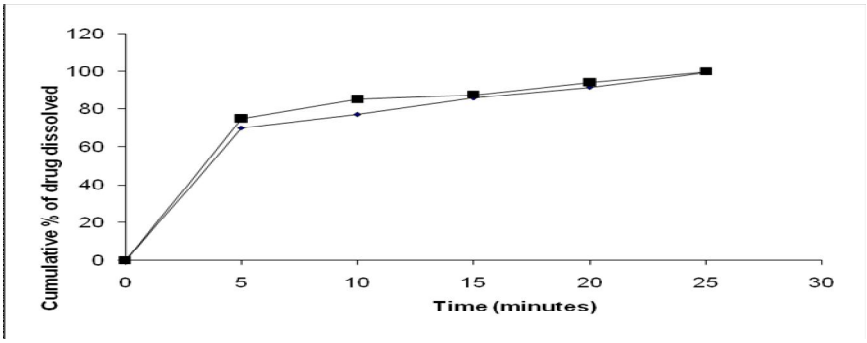
S.No.	Parameters	F_1	F_2	F3	F4
1	Average weight (mg)	199±0.1	199±0.2	201±0.2	198±0.1
2	Drug content (%)	99.6	99.7	99.48	99.47
3	Disintegration time (sec)	145	134	127	136
4	Friability (%)	0.32	0 .29	0.33	0.32
5	Hardness(kg/sqcm)	4.2	4.1	4.1	4.2
6	Wetting time (sec)	127	119	108	117
7	*In-vitro* dispersion time SEC)	234	213	223	232
8	Fineness of dispersion	pass	pass	pass	pass

Table 4: *In-vitro* dissolution data of sotalol hydrochloride orodispersible tablets

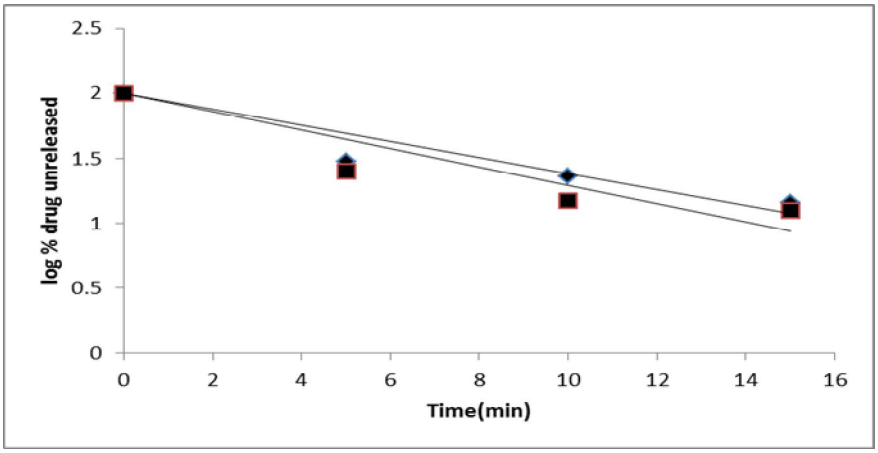
S.No.	Sampling time (min)	Amount of drug released ($\overline{X}$ ± S.D.)			
		F_1	F_2	F_3	F4
1	0	0	0	0	0
2	5	69.93	74.9	86.18	80.54
3	10	77.09	85.01	93.65	85.05
4	15	85.64	87.51	98	94.77
5	20	91.52	94.09	-	-
6	25	99.25	99.79	-	-

Table 5: *In-vitro* dissolution kinetics of sotalol hydrochloride orodispersible tablets

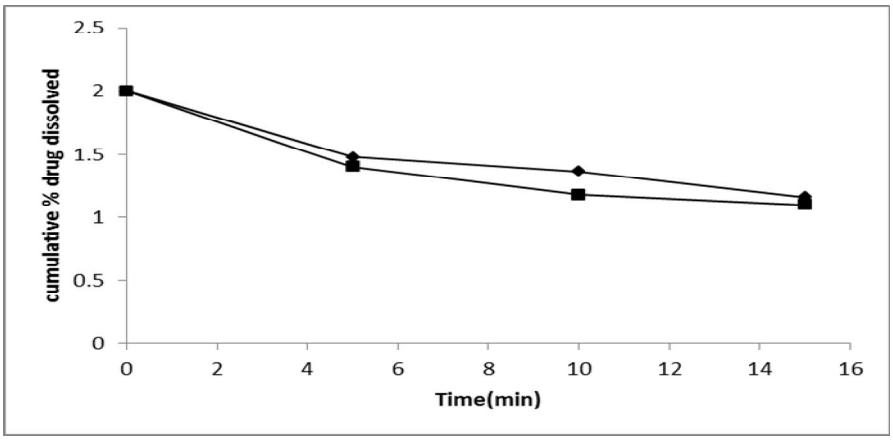
S.No.	Formulation	T_{50} (min)	T_{90} (min)	DE_{15} (%)	K (min^{-1})	Correlation coefficient values	
						Zero Order	First order
1	F_1	4.3	14.3	63.28	0.161	0.6716	0.9982
2	F_2	3.5	11.8	70.02	0.195	0.6805	0.9901
3	F_3	2.6	8.7	78.06	0.266	0.7591	0.9926
4	F_4	3.4	11.3	75.82	0.201	0.7792	0.9929



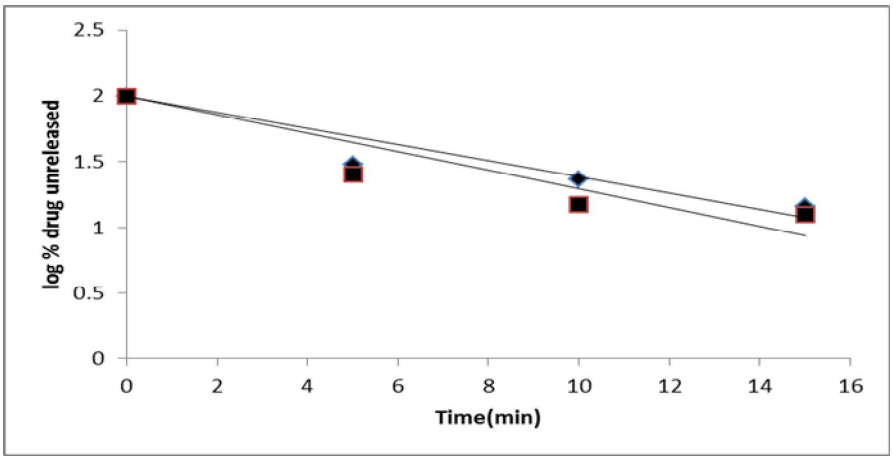
(♦) F_1 - Tablets prepared with5% Croscaramellose sodium
(■) F_2 - Tablets prepared with 5% Crospovidone
Fig. 1: *In-vitro* dissolution profile of sotalol hydrochloride orodispersible tablets formulated with different superdisintegrants



(♦) F_1 - Tablets prepared with5% Croscaramellose sodium
(■) F_2 - Tablets prepared with 5% Crospovidone
Fig. 2: First order plots of sotalol hydrochloride fast dissolving tablets formulated with different synthetic superdisintegrants



(♦) F_3 - Tablets prepared with 5% Plantago ovate mucilage
(■) F_4 - Tablets prepared with 5% Bhringaraj powder
Fig. 3: *In-vitro* dissolution profile of sotalol hydrochloride orodispersible tablets formulated with natural superdisintegrants



(♦) F_3 - Tablets prepared with 5% Plantago ovate mucilage
(■) F_4 - Tablets prepared with 5% Bhringaraj powder
Fig. 4: First order plots of sotalol hydrochloride fast dissolving tablets formulated with different natural superdisintegrants

REFERENCES

1. Suresh Bandari. Orodispersible tablets: An over view. Asian J Pharm. 2008;1:1-5.
2. Gokul Ghenge, Pande SD, Anwar Ahmad, Lalit Jejurkar and Tushar Birari. Development and Characterization of Fast Disintegrating Tablet of Amlodipine besylate using Mucilage of Plantago ovata as a Natural Superdisintegrant. International Journal of PharmTech Research. 2011;3(2): 938-945.
3. Sai Kishore V and Sudheshnababu S. Natural Superdisintegrants: Changed Scenario and Latest Advances. Research J. Pharma. Dosage Forms and Tech. 2012;4(2):53-57.
4. Martin A and Swarbrick J. Physical pharmacy, 3rd edition, Mumbai: Varghese publishing house, 1993;444-447.
5. Indian pharmacopoeia. Monographs on dosage forms. The Indian pharmacopoeia commission, Ghaziabad. 2007;3:182-183
6. Indian pharmacopoeia. Monographs on dosage forms. The Indian pharmacopoeia commission, Ghaziabad. 2007;3:177-178.
7. Indian pharmacopoeia. Monographs on dosage forms. The Indian pharmacopoeia commission, Ghaziabad. 2007;3:183-184.
8. USP 27/NF 22, Asian edition, General test procedures, U.S. Pharmacopoeial convention, Rockville MD. 2000;1677-1678.
9. Battue SK, Repay MA, Maunder S and Rio M Y. Formulation and evaluation of rapidly disintegrating tablet Fenoverine tablets: Effect of superdisintegrants. Drug Dev Ind Pharm. 2007; 33:1225-1232.
10. Sunada H, Yonezawa Y, Danjo K, Otsuka A and Iida K. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem Pharm Bull (Tokyo). 1996;44: 2121-2127.
11. Shashank C, Vipin Kumar A and Sunil Singh. Impact of superdisintegrants on the release of orodispersible tablets of losartan potassium: A comparative analysis. Der Pharmacia Lettre. 2012;4(6):1768-1776.
12. Suhas MK, Vinodh SM and Ketan BR. Formulation and evaluation of mouth dissolving tablets of losartan potassium by direct compression techniques. Int J Res Pharm Sci. 2010;1(3):290-295.
13. Suresh B, Rajendra kumar M, Ramesh G and Madhusudan Rao Y. Orodispersible tablets: An overview. Asian journal of pharmaceutics. 2008;2(1):2-11.