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Research Article

Formulation, Development and In-Vitro studies of Sotalol - Gastro Retentive Floating tablets

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ABSTRACT

In the "present research work gastro retentive floating matrix formulation of Sotalol" by "using various hydrophilic polymers. "Among all the formulations" the formulations prepared by using Xanthan gum were "unable to produce desired drug release, they were unable to" retard "drug release up to 12" hours. The formulations prepared with Methocel K15 M retarded the drug "release up to 12 hours" in the concentration of 75 mg (ST3).The "formulations prepared with xanthan gum" were "unable to retarded the drug "release for more than 12 hours. Hence they were not considered".

Keywords: Sotalol, Guar gum, Xanthum gum, HPMC K15 M and Floating tablets

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CONTENTS

1. Introduction

Floating systems or dynamically controlled systems are low density systems that have sufficiently buoyancy to flow over the gastric contents and remain "buoyant in the stomach without affecting the gastric emptying rate "for a prolonged period of" time. This result is an increased gastric retention time and a better control of the fluctuations in plasma drug concentration. The ultimate goal of any drug delivery is Effective disease / disorder management, minimum side effects and greater patient compliance in the cost effective manner. More than 50% of the drug delivery systems available in the market are oral drug delivery systems. Controlled release drug delivery systems (CRDDS) provide drug release at a predetermined, predictable, and controlled rate. Controlled release drug delivery system is capable of achieving the benefits like maintenance of optimum therapeutic drug concentration in blood with predictable and reproducible release rates for extended time period, enhancement of "activity of duration for short" half-life drugs, elimination of side effects, "reducing frequency of dosing and" wastage of

drugs, optimized "therapy and better patient compliances. The" controlled "gastric retention of solid dosage" forms may be achieved by mucoadhesive systems that causes bioadhesion to stomach mucosa, floating systems, swelling and expanding systems, modified-shape systems, high density systems and other delayed gastric emptying devices. Gastro "retentive dosage form can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs". Prolonged "gastric retention improves bioavailability, reduces drug waste, and" improves solubility of drugs that are "less soluble in a high pH environment. Gastro retention helps to provide better" availability of new products with suitable therapeutic activity and substantial benefits for patients.

Drug name : SOTALOL
Category : Antiarrhythmic agents
CAS NO : 3930-20-9
Structure :

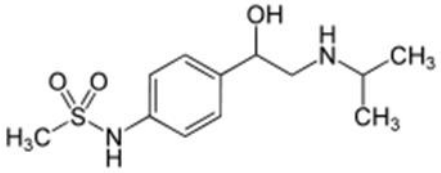

Fig.1

Half-life:
Mean elimination half-life is 12 hours. Impaired renal function in geriatric patients can increase the terminal elimination half-life.

Locust bean gum
Nonproprietary names: carob gum, carob bean gum, carobin, E410
Chemical Formula: $C_{27}H_{42}NO_2$ Cl
Structural Formula

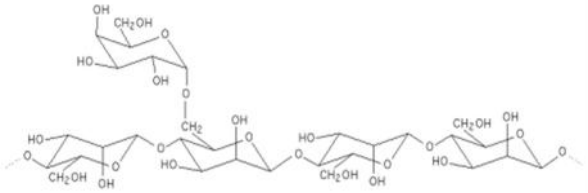

Fig.2

Structure of locust bean gum
Molecular weight: approximately 50,000-3,000,000
Functional categories: Locust bean gum can be used in gels, creams and lotions in hair and skin care applications. Thickening, Texture modifier, Stabilizer, Gel strengthener.

Sodium Bicarbonate
Non-proprietary names: BP/EP: sodium bicarbonate
Synonym: Baking soda, e-500, and monosodium carbonate.
Chemical name: carbonic acid, monosodium salt, monosodium carbonate.
Empirical formula: NaHCO3
Molecular weight: 84.01
Category: alkalizing agent, therapeutic agent

2. Methodology

Analytical method development:
"Determination of absorption maxima:
A "solution containing the concentration 10 µg/ ml drug was prepared in 0.1NHCl UV spectrum was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400.

Preparation" calibration curve:
100mg of Sotalol pure "drug was dissolved in" 100ml" of "0.1N HCl (stock solution) 10ml of "solution was taken and make" up with100ml of 0.1N HCl (100µg/ml).From "this 10ml was taken and" make "up with 100 ml of"0.1N HCl (10µg/ml). The above solution "was subsequently diluted with 0.1N HCl to obtain" series of dilutions Containing 0.5,1, 1.5, 2 and 2.5µg/ml of Sotalol per ml "of solution. The absorbance of the above dilutions was measured" at 266 nm by using UV-Spectrophotometer "taking 0.1N HCl as blank. Then a graph was plotted by" taking "Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from "the "square of correlation coefficient (R2)"which determined by least-square linear regression analysis.

Formulation development "of Tablets:
Optimization of Sodium bicarbonate concentration:
"Sodium bicarbonate was employed as" effervescent "gas generating agent. It helps the formulation to float. Various concentrations of sodium bicarbonate were employed; floating lag time and floating duration were observed. Based on that the concentration of sodium bicarbonate was finalized and" preceded for further formulations.

Evaluation of post compression parameters for prepared Tablets
The designed compression "tablets were studied for their physicochemical properties like weight variation, hardness", thickness, friability and drug content.

In vitro Buoyancy studies:
The in "vitro buoyancy was determined by floating lag" time, and total floating time. (As "per the method described by" Rosa et al) The tablets were placed in a 100ml beaker containing 0.1N HCl. The time required for the "tablet to rise to the" surface "and float was determined as" floating "lag time (FLT) and duration of time the tablet constantly floats" on the dissolution medium was noted "as Total Floating Time respectively" (TFT).

***In vitro* drug release studies**
Dissolution" parameters:
"Apparatus--USP-II, Paddle Method
Dissolution Medium -- 0.1 N HCl"
RPM --75
Sampling intervals (hrs)-- "0.5,1,2,3,4,5,6,7,8,10,11,12
Temperature --37°c $\pm$ 0.5°c
As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

3. Results and Discussion

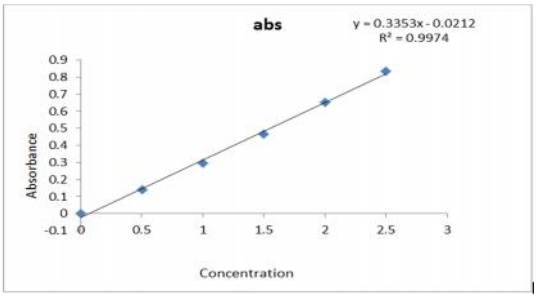

Figure 3: Standard graph of Sotalol in 0.1N HCl

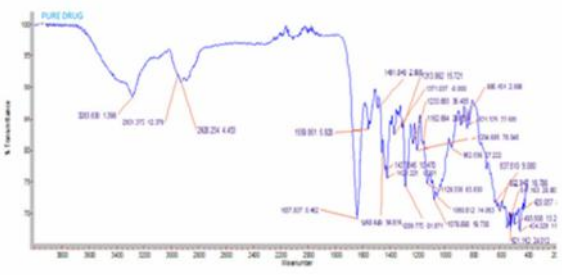

Figure 4: FT-TR Spectrum of Sotalol pure drug

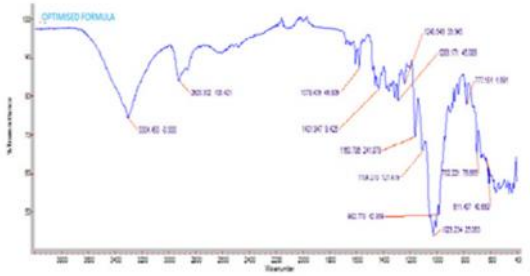

Figure 5: FT-IR Spectrum of Optimized Formulation

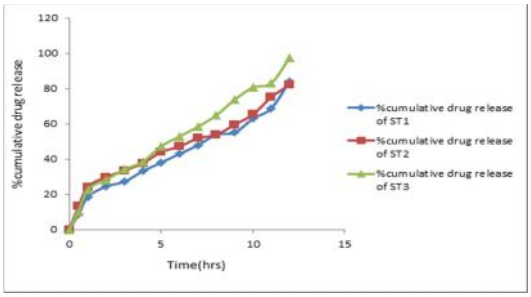

Fig 6: Dissolution profile of Sotalol floating tablets (ST1, ST2, ST3)

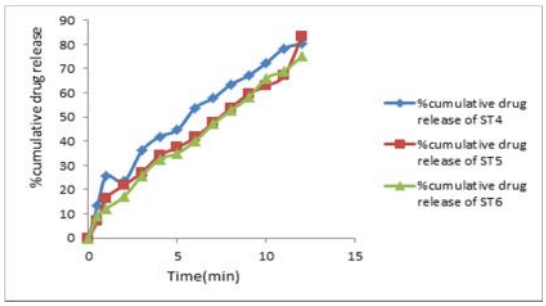

Fig 7: Dissolution profile of Sotalol floating tablets (ST4, ST5, ST6).

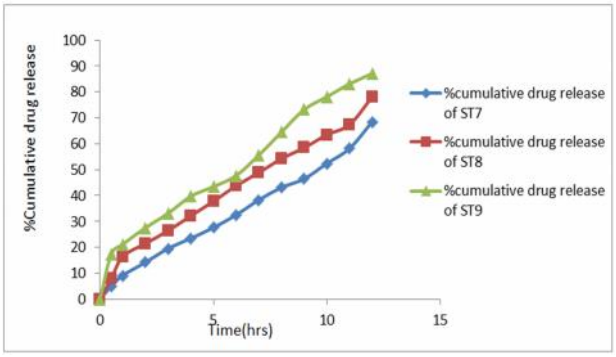

Fig 8: Dissolution profile of Sotalol floating tablets (ST7, ST8, ST9)

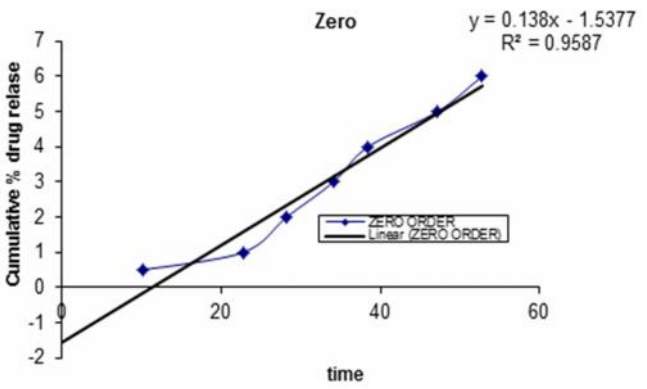

Fig 9: Zero order release kinetics

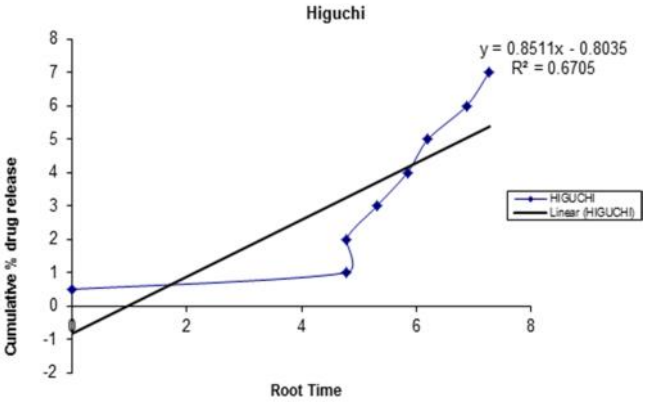

Fig 10: Higuchi release kinetic

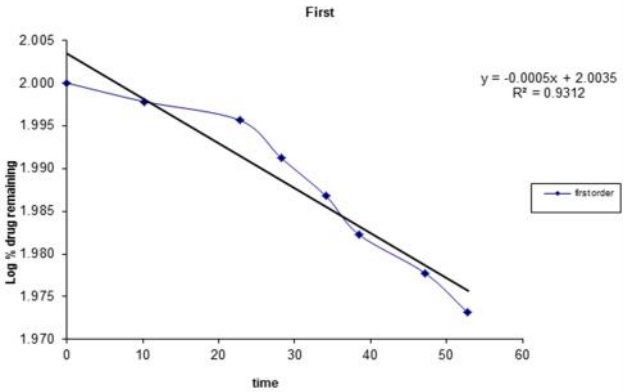

Fig 11: First order release kinetics

Table 1: Formulation composition for floating tablets

Formulation No.	Sotalol	Methocel K 4 M	Locust Bean Gum	Xanthan gum	$NaHCO_3$	Mag. Stearate	"Talc	MCC pH 102
ST1"	80	40	-----	-----	40	5	5	QS
ST2	80	60	-----	-----	40	5	5	QS
ST3	80	80	-----	-----	40	5	5	QS
ST4	80	-----	40	-----	40	5	5	QS
ST5	80	-----	60	-----	40	5	5	QS
ST6	80	-----	80	-----	40	5	5	QS
ST7	80	-----	-----	40	40	5	5	QS
ST8	80	-----	-----	60	40	5	5	QS
ST9	80	-----	-----	80	40	5	5	QS

Table 2: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
ST1	25.01	0.48	0.54	15.21	0.87
ST2	25.8	0.57	0.63	17.87	0.95
ST3	23.74	0.53	0.69	16.11	0.63
ST4	24.33	0.55	0.65	17.76	1.13
ST5	25.24	0.55	0.66	17.92	1.45
ST6	28.12	0.57	0.67	16.65	1.07
ST7	26.08	0.56	0.68	17.43	0.78
ST8	24.12	0.47	0.56	15.97	1.17
ST9	25.45	0.53	0.63	16.54	1.19

Table 3: Dissolution Data of Sotalol Tablets Prepared With Methocel K 4MIn Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED		
	ST1	ST2	ST3
0.5	8.77	13.14	10.21
1	18.51	24.16	22.8
2	24.4	29.77	28.21
3	27.14	33.47	34.11
4	33.11	37.64	38.45
5	37.97	43.97	47.21
6	42.97	47.12	52.77
7	47.79	51.77	58.34
8	53.77	53.74	64.77
9	54.94	59.44	73.64
10	62.87	65.32	80.54
11	68.77	75.11	83.11
12	84.22	82.21	97.45

4. Conclusion

In the present research work gastro retentive floating matrix formulation of Sotalol by using various hydrophilic polymers. Among all the formulations the formulations prepared with HPMC K15 M retarded the drug release up to 12 hours in the concentration of 75 mg (ST3).The formulations prepared by using Xanthan gum were unable to produce desired drug release, they were unable to retard drug release up to 12 hours. The formulations prepared with Locust bean gum were also retarded the drug release for more than 12 hours. Hence they were not considered. The optimized formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed peppas mechanism of drug release.

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