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Formulation and Evaluation of Sustained Release Insitu Floating Gel of Salbutamol

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ABSTRACT

The objective of the present study was to formulate and evaluate a sustained release *in- situ* floating gel of salbutamol. Salbutamol (BCS class I drug) is a beta 2 adrenergic receptor. Sodium alginate based salbutamol floating *in-situ* gels were prepared by dissolving sodium alginate in distilled water, to which varying concentrations of viscosity enhancing polymer, HPMC K05, drug, and gas-forming agent (s) as calcium carbonate and sodium bicarbonate were added and dissolved by stirring. Prepared formulae were evaluated for viscosity, floating behavior, drug content and *in-vitro* drug release behavior. Formulation variables such as the type and concentration of viscosity enhancing polymer, the concentration of gas-forming agents affected the formulation viscosity, floating behavior and *in-vitro* drug release. The formulation was optimized on basis of *in vitro* drug release. The result indicates that formulation F4 for salbutamol *in situ* gel achieved a sustained release of drug for 8 hrs. The prepared *in-situ* gel formulations of salbutamol could float in the gastric conditions and release the drug in sustained manner for 8 hrs.

KEY WORDS: Floating drug delivery system, Salbutamol, HPMCK05, *In situ* gel, Sustained manner.

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INTRODUCTION:

Floating drug delivery system (FDDS)[1] is a novel approach to achieve gastric retention to obtain sufficient drug bioavailability. The gel formed from *In situ* gelling system, being lighter than gastric fluids, floats over the stomach contents or adhere to gastric mucosa due to presence of bio adhesive nature of polymer and produce gastric retention of dosage form and increase gastric residence time resulting in prolonged drug delivery in gastrointestinal tract. After the drug is released, the residual system is emptied from the stomach. *In situ* gelling system is a novel approach in the FDDS.[2]

In-situ gels which when administered are in solution form, but as it comes in contact with gastric fluids, it forms gels. The phase transition of *in-situ* gels[3] may be attributed to one or combination of different stimuli like ionic interaction/pH change/ temperature modulation and solvent exchange. Over the past few years, the development of floating *in situ* gel systems[4] has received considerable attention, mainly because of the advantages shown by these systems such as the ease of administration along with the ability of providing controlled and prolonged action compared to conventional drug delivery systems. These factors led to reduced frequency of administration and therefore improved patient compliance and comfort. Such gel conversions is due to one or more mechanisms such as physiological stimuli (e. g., temperature and pH), physical changes in biomaterials (e. g., diffusion of solvent and swelling), and chemical reactions (e. g., enzymatic, ionic and photo-initiated polymerization). [5]

MATERIALS AND METHODS

Materials used in the formulation are Salbutamol (Hetero drugs), Sodium alginate(SDFCL), HPMC K05(Loba Chemi Pvt Ltd), HPMC K10(Loba Chemi Pvt Ltd), HPMC K100(Loba Chemi Pvt Ltd), Sodium bicarbonate(Merk Specialities Pvt Ltd),Calcium carbonate(Merk Specialities Pvt Ltd).

Preparation of *In Situ* Gel

Sodium alginate was dissolved in water (75%) and heated at 60°c.The above solution was cool down to 40°C.Then the above solution is taken in mortar and pestle and triturated [6]. Required quantity of Drug, HPMC, Sodium bicarbonate, calcium carbonate are added to the above solution and mix well then make up to 50ml with water

Evaluation

pH: pH of prepared *in situ* gel is measured with pH meter.

Rheological studies:

The viscosity measurements are carried out using Brookfield viscometer. The *in-situ* gel formulations are placed in the sample tube. The samples are analyzed at 37±0.5°c by a circulating

bath connected to the viscometer adaptor prior to each measurement .The angular velocity of the spindle is increased to 1 to 4 and the viscosity of the formulation are measured.

Drug content estimation:

The drug content estimation is carried out by diluting 5 ml of prepared formulation in 100 ml of distilled water and analyzed using UV- visible spectrophotometer at appropriate wave length.

Dissolution rate studies:

The dissolution rate testing of different salbutamol formulations was studied using USP XXII dissolution rate testing apparatus, (paddle type). The paddle was rotated at a speed of 50 rpm and the dissolution fluid (900 ml 0.1N HCL) was maintained at a temperature of $37.5^0 \pm 0.5\ ^0C$. At specific time intervals a 5 ml aliquot of dissolved medium was withdrawn and was replaced with fresh quantity of dissolution medium. The samples were suitably diluted with dissolution medium and assayed for salbutamol content by measuring the absorbance at 276 nm using U.V Spectrophotometer[7]. The percent of salbutamol dissolved at various time intervals was calculated and plotted against time. The results are given in table. Graphical plots of percentage dissolved versus time were drawn.

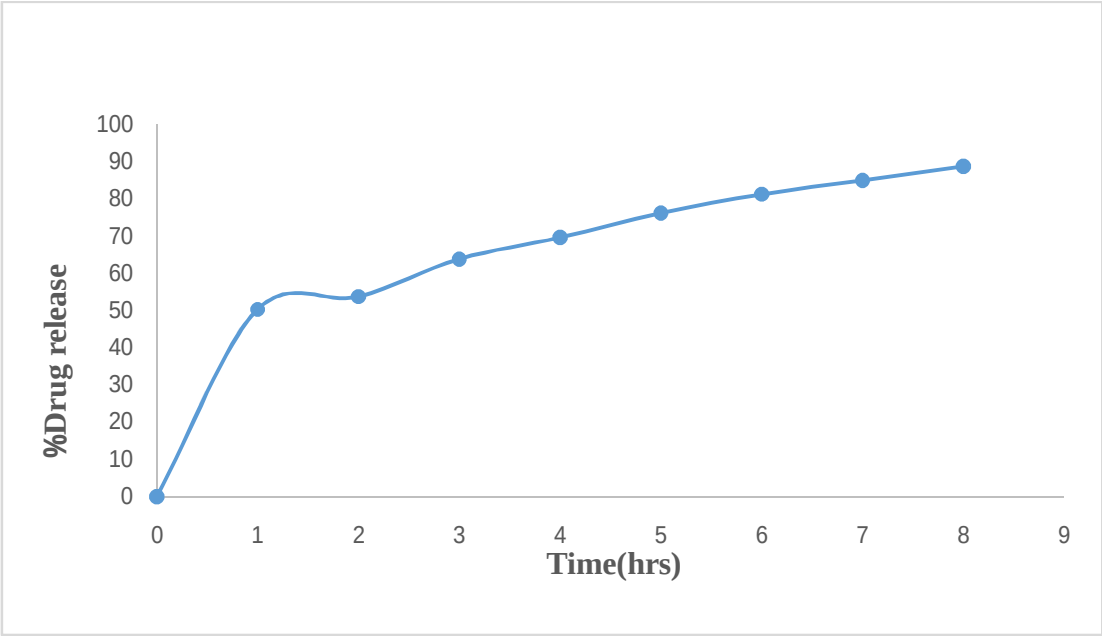
Table No: 1 Formula for *In Situ* Gel

S.NO	INGREDIENTS	F1	F2	F3	F4	F5	F6	F7
1	SALBUTAMOL	8mg	8mg	8mg	8mg	8mg	8mg	8mg
2	SODIUM ALGINATE	1g	1g	1g	1g	1g	1g	1g
3	HPMC K05	-	0.5g	0.2g	0.8g	-	-	-
4	HPMC K10	0.2g	-	-	-	0.5g	-	-
5	HPMC K100	-	-	-	-	-	0.5g	0.2g
6	SODIUM BICARBONATE	0.25g	0.25g	0.25g	0.25g	0.25g	0.25g	0.25g
7	CALCIUM CARBONATE	0.75g	0.75g	0.75g	0.75g	0.75g	0.75g	0.75g
8	DISTILLED WATER(Q.S)	50ml	50ml	50ml	50ml	50ml	50ml	50ml

RESULTS

Table no: 2 Dissolution data of salbutamol in situ Gel (F4):

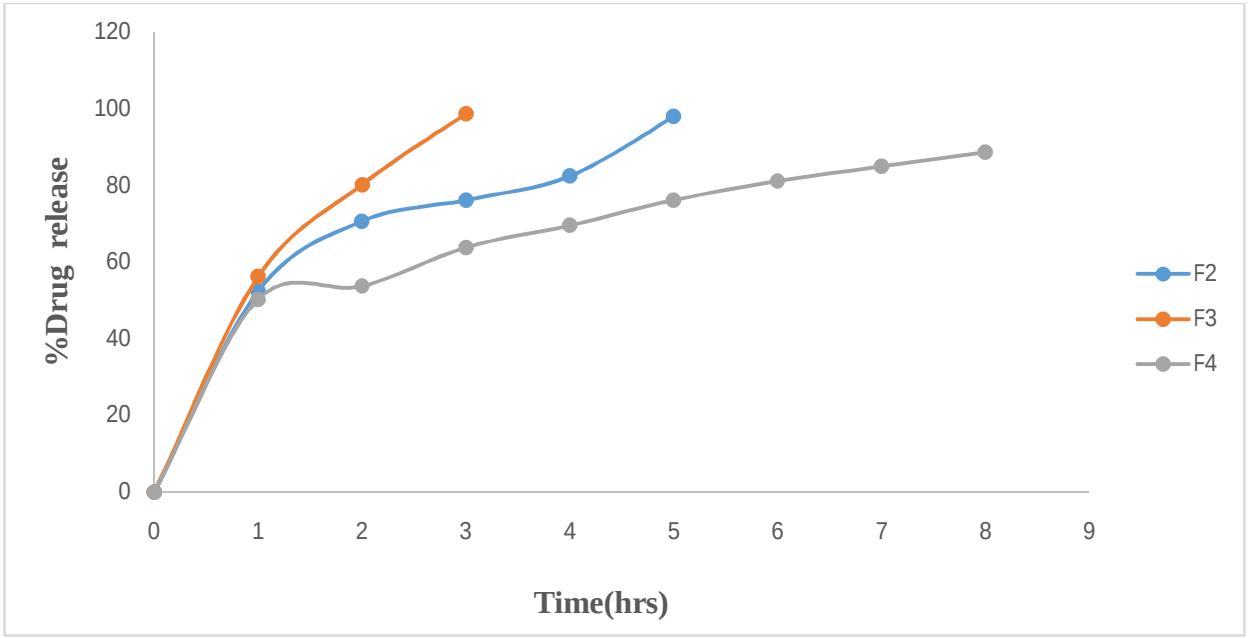
Dissolution data of formulation – F4					
S. NO	Time in hrs	Percent Amount dissolved			
		Trail-1	Trail-II	Trail-III	Average % dissolved
1.	1	50.6	50.4	50	50.3%
2.	2	54.4	53.9	52.8	53.75%
3.	3	64.2	63.8	63.9	63.87%
4.	4	69.6	69	70.4	69.62%
5.	5	75.6	76	77	76.25%
6.	6	80.8	81	82	81.25%
7.	7	85	84	86	85%
8.	8	87.9	89.3	88.7	88.75%



Graph 1 Dissolution profile for optimized formulae(F4)

Table No: 3 Comparative Dissolution data of Salbutamol in situ gels – F2, F3, F4.

S. NO	Time in Hrs	Average percent amount dissolved		
		Formula- 2	Formula – 3	Formula– 4
1.	1	52.5%	56.25%	50.3%
2.	2	70.75%	80.25%	53.75%
3.	3	76.25%	98.75%	63.87%
4.	4	82.5%		69.62%
5.	5	98.1%		76.25%
6.	6			81.25%
7.	7			85%
8.	8			88.75%



Graph 2 Comparative Dissolution profile of salbutamol in situ gel

Table No: 4 EVALUATION TESTS:

S.NO	PARAMETER	RESULT
1	Dissolution time	8 hours of drug release
2	pH	9.5
3	Drug content	8mg of drug in 5 ml of solution
4. Rheological studies:		
Viscosity (Cp)	**Torque (%)**	**RPM**
3260	81.5	30

Table No: 5 DISCUSSION FOR ALL IN-SITU FORMULAE

S.NO	FORMULAE	RESULT
1	F1, F5	HPMC(K10)dosage form was slightly viscous and the drug release was not satisfactory
2	F6, F7	HPMC(K100)dosage form was highly viscous in nature so dissolution studies are difficult to carryout
3	F2	HPMC(K05)Drug was released for 5 hours
4	F3	HPMC(KO5)Drug was released for 3 hours
5	F4	Sustain drug release was obtained with the help of HPMC(K05) of 0.8g.Immediately solution gets converted into gel and it was floated for 8 hours and the drug releases for 8 hours

CONCLUSION

- In the present study, various *in situ* gelling liquid oral formulations of Salbutamol were prepared. The study has shown that by modifying parameters like the type and concentration of viscosity enhancing polymer, concentration of gas generating agent, the release can be modulated to the desired rate.
- These formulae were used for preparing *in situ* floating gel systems of salbutamol. All the prepared formula was tested for floating and release time by dissolution testing procedure in 0.1N HCL.
- The best product that releases the drug for 8hrs consists of polymer of HPMC K05 (0.8g).
- By observing various evaluation parameters for the studied formulations, it can be stated that incorporation of sodium bicarbonate is used for the floating time and variation in concentration of sodium alginate influences viscosity and HPMC is used to release the drug in a sustained manner from *in situ* gel.
- The prepared floating *in situ* gel of Salbutamol has the feasibility of sustaining the drug release while remaining in the stomach.

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