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Formulation And Evaluation Of Floating Beads Of Aceclofenac Sodium For GRDDS

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ABSTRACT:

Introduction: Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. **Objective:** The main objective of this research work was to develop a novel kind of inner-porous floating beads of Aceclofenac. The beads were prepared with foam solution using poloxamer 188 as foaming agents, alginate as foaming stabilizer.. **Methods:** Preformulation studies was done to analyzed flow property of powder. Floating beads containing highly water-soluble Aceclofenac sodium were prepared by dripping method using poloxamer 188 as foaming agent and sodium alginate as foam stabilizer. Evaluation of floating beads was done by standard methods. **Results:** Percentage yield of formulation was decrease from 38.09±0.003 to 75.49±0.004 as we increase the alginate concentration. Percent Drug entrapment efficiency was increased from to 25.22±0.005 to 73.69±0.003 as the concentration of alginate increased. **Conclusion:** Best formulation (F3) was selected on the basis of entrapment efficiency, % yield and floating lag time. Formulation containing poloxamer 188 had high entrapment efficiency which might be due to high foamability and foam stability.

KEY WORDS: Pre-formulation, Aceclofenac sodium, alginate, flow property, FTIR

INTRODUCTION:

Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity.[1] To avoid this limitation, the development of oral sustained-controlled release formulations

is an attempt to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration in the systemic circulation for a long time. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinal tract (GIT).[2]

Floating drug delivery systems have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents the drug is released slowly at the desired rate from the system. This results in an increased GRT and a better control of fluctuations in plasma drug concentration. [2,3]

Controlled gastro retentive drug delivery system: Oral controlled release (CR) dosage forms (DFs) have been developed over the past three decades due to their considerable therapeutic advantages such as ease of administration, patient compliance and flexibility in formulation. [4] Gastroretention helps to provide better availability of new products with suitable therapeutic activity and substantial benefits for patients. This mode of administration would best achieve the known pharmacokinetic and Pharmacodynamics advantages of CR-DFs of these drugs. The need for gastroretentive dosage forms (GRDFs) has led to extensive efforts in both academia and industry towards the development of such drug delivery systems. [5,6]

Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) analog of Diclofenac. It is used for the relief of pain and inflammation in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.The drug inhibits synthesis of the inflammatory cytokinesinterleukin (IL)-1 and tumour necrosis fac tor and prostaglandin E2 (PGE2) production. To reduce the dosing frequency and adverse effect during prolong treatment, it is needed to formulate aceclofenac in long acting dosage form. [2,7]

Material and Methods:

Aceclofenac Sodium pure drug obtained as gift sample from SGPTC Pvt. Ltd. foaming agents such as Sodium Alginate and Poloxamer 188 was procured from BASF Mumbai.

Methods:

Melting point: Melting point was determined by capillary fusion method. [8]

Partition coefficient ($P_{o/w}$): The partition coefficient of Drug was determined in n-octanol/distilled water at room temperature (25± 2ºC). [9]

$$P_{o/w} = (C_{octanol} / C_{aqueous})$$

Characterization of Aceclofenac: [10, 11]

The drug substance was characterized for following parameters.

Determination of Solubility:

It is an essential and extensively utilized pre-formulation parameter. [22] The solubility of drug was determined as per BCS classification system. [23] The solubility was checked in 250 ml different medium and water. The solubility of drug in different solvents like water, 0.1N HCl, and phosphate buffer pH 6.8 was determined by using standard procedure.

Infrared spectrum:

The infrared spectrum of pure drug and with excipients was carried out using potassium bromide disk method. The samples were prepared on KBr-press and over wave number range of 4000 to 400cm $^{-1}$ it was scanned.

Preparation of Alginate/Poloxamer floating beads dripping Method:

Sodium Alginate was dissolved in double distilled water at a concentration of 1.0 % (w/v), poloxamer 188 was then added into sodium alginate solution while stirring at 2600 rpm held by mechanical stirrer (REMI Mumbai) equipped with three blade propeller, at room temperature. The whole system was stirred for 20 minutes to completely form the foam solution. Aceclofenac sodium (30 mg) was added into foam solution under vigorous stirring condition continuously. The foam solution was pumped using a syringe into 2 % CaCl 2 (100 ml). The distance between the edge of the needle and the surface of the CaCl 2 medium was about 10 cm. The beads formed were left in the solution with gentle stirring for 10 min at room temperature to be cured. [12,13]

Table: 1 Composition of different formulations

S. No.	Formulation Code	Drug (mg)	Sodium alginate (%w/v)	Poloxamer 188 (mg)	Calcium Chloride (%)w/v
1.	F1	100	1%	300	2
2.	F2	100	2%	300	2
3.	F3	100	3%	300	2
4.	F4	100	4%	300	2
5	F5	100	5%	300	2

Evaluation of floating bead of Aceclofenac sodium:

Determination of Percentage Yield and Drug Entrapment:

The prepared floating beads were collected and weighed. The measured weight was divided by the total weight of all the excipients and drug. The % yield was calculated using following formula: **% yield = Total bead weight/Total weight of all excipients.**

***In –vitro* Floating study:**

Beads 10 mg of each batch were placed in 10 ml water of 0.1NHCl agitated at 100 rpm and temperature was maintained at 37±2□C. The number of sinking beads was observed visually at different time interval.

F (%) = NF/NT×100

Where: F= Floating percent, NF = Number of floating beads, NT = Total number of beads

RESULTS AND DISCUSSION:

7.1 Pre-formulation study

7.1.2 Melting point determination

The melting point was observed with the capillary fusion method.

Table 2: Standard and observed melting point of Aceclofenac sodium

Observed melting point	Reported melting point
150-155°C	150-153°C

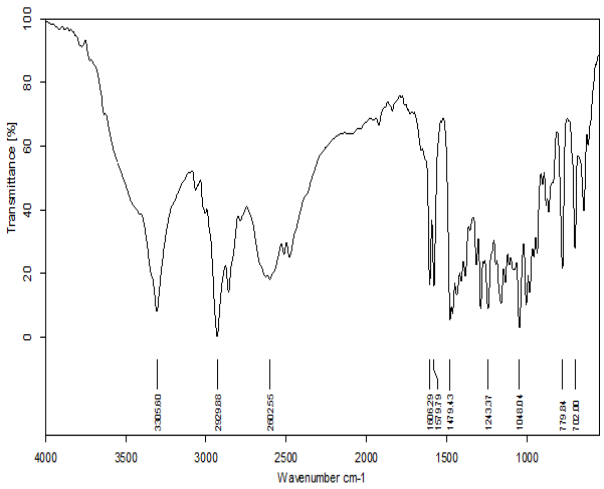
Partition coefficient:

Table 3: Determination of partition coefficient

Partition coefficient of drug	Solvent system	Log p Values
Aceclofenac sodium	n-octanol: water	1.087±0.003

Discussion: The partition coefficient of Aceclofenac sodium in n-octanol: water was found to be 1.087 this indicates that the drug is lipophillic in nature.

Characterization of Aceclofenac sodium by FT-IR spectroscopy:



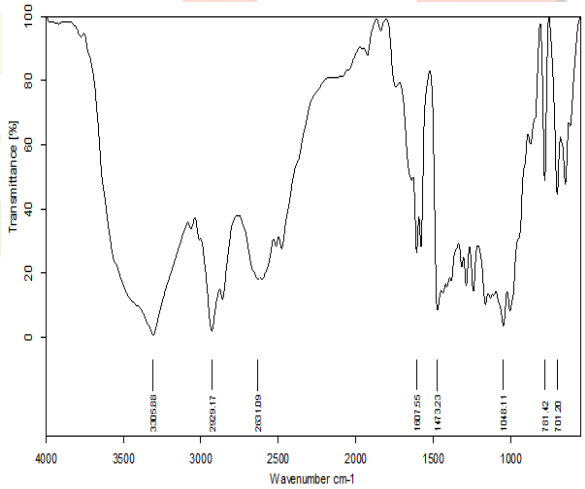


Fig 1: FTIR of aceclofenac sodium Fig2: FTIR of physical mixture of drug+polymer

Evaluation of floating bead of Aceclofenac sodium

Percentage Drug Entrapment, Percentage Yield of different formulations.

Five different concentrations of sodium alginate were examined namely: 1, 2, 3, 4& 5% (calcium chloride 1% as a cross linking agent at 2600 rpm). Percentage yield of formulation was decrease from 38.09±0.003 to 75.49±0.004 as we increase the alginate concentration. Percent Drug entrapment efficiency was increased from to 25.22±0.005 to 73.69±0.003 as the concentration of alginate increased. This may be attributed to the greater

availability of active calcium-binding sites in the polymeric chains and, consequently, the greater degree of cross linking as the quantity of sodium alginate increased. A sufficient quantity of Poloxamer and alginate solution was needed for maximum loading capacity, and its corresponding encapsulation efficiency can also be improved.

Table 4: Percentage drug entrapment and percentage yield of F1-F6

S. No.	Formulation code	%Yield	%Drug entrapment
1	F1	38.09±0.003	25.22±0.005
2	F2	45.02±0.006	35.42±0.002
3	F3	64.52±0.005	73.69±0.003
4	F4	75.49±0.004	71.69±0.001
5	F5	56.14±0.005	69.56±0.005

Poloxamer is a non-ionic surfactant it was responsible for foam production. When we added alginate in Poloxamer solution, strength of alginate Poloxamer solution was increase. Addition of some polymers to formable formulations can lead to an increase of foam stability due to formation surfactant–polymer complex through interactions between polymer and surfactant. Thus, as we increase concentration of sodium alginate upto an optimum level of 3%, percentage drug entrapment was increase.

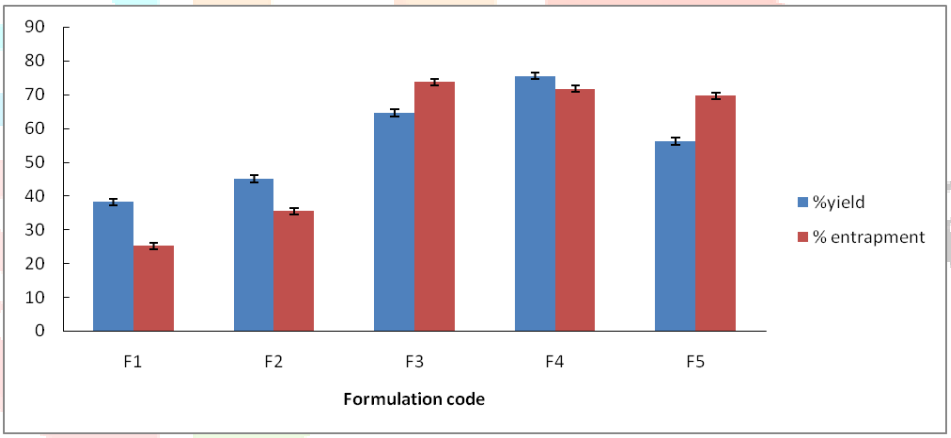


Fig 3: %Yield and drug entrapment of different formulation

***In vitro* floating study:**

The beads can float on the surface of simulated gastric fluid (SGF) at the beginning of the experiment. As time passed on, the beads could absorb water and sink in water or disintegrated. It is the most important factors challenging the floating ability of these beads. The beads are floating because of their low density than SGF. When water penetrating into the beads and take the place of gas, the density of the beads became bigger than that of SGF, then the beads will sink. If the beads were disintegrated, the fragment will disperse in the SGF.

Table 5: Floating lag time and floating time of different Poloxamer- alginate floating bead formulation

S.No	Formulation Code	Time (hrs)	Percent Floating (%)							
			0	1	2	3	4	5	6	7
1	F1		100	100	100	100	100	100	100	100
2	F2		10	100	100	100	100	100	100	100
3	F3		100	100	100	100	100	100	100	100
4	F4		100	100	100	100	100	100	100	100
5	F5		100	80	90	100	100	100	100	100

***In vitro* drug release study:**

Performing drug release study using the paddle method only is equally unacceptable for floating dosage forms because only a proportion of the dosage form is exposed to the media. In addition, the placement of the beads is not consistent and hence results are not reproducible. The presence of the mesh, as used for the current work, ensured that the full surface area of the beads was exposed to the dissolution medium and the paddle ensured sufficient agitation of the medium for drug dispersion. Previous studies have shown that the mesh and paddle method provides more reproducible and reliable dissolution profiles compared to other conventional methods.

Table 6: Percentage drug release of F3 Batch

Sr.no.	Time (hours)	%Drug Release of F3 Batch
1	0	0±0
2	1	17.31±0.29
3	2	28.8±0.34
4	3	42.51±0.51
5	4	48.88±0.77
6	5	57.75±0.94
7	6	65.76±0.86
8	7	73.9±0.54
9	8	79.8±0.21
10	9	85.72±0.27
11	10	90.11±0.19
12	11	92.62±0.15
13	24	93.71±0.21

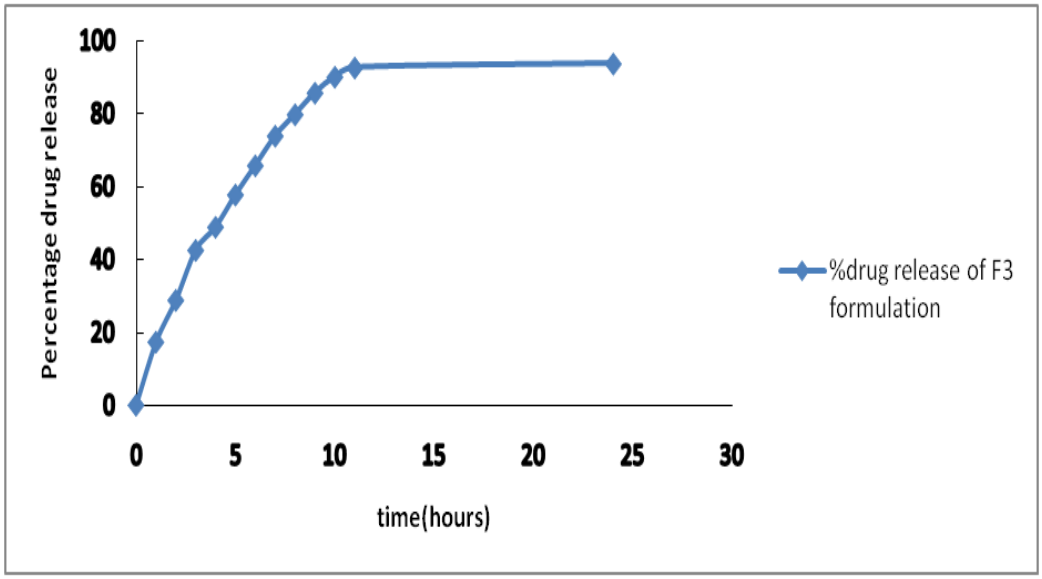


Fig 4: Percentage drug release of F3 formulation

Conclusion:

Gastroretentive formulation in the form of beads was developed to a satisfactory level in terms of drug release and floating ability and to be used as an alternative to conventional dosage forms. Initially collection of theoretical and technical data was done. Melting point determination of Aceclofenac sodium confirmed that no impurity was present in the drug as melting point was 150- 153°C which was similar as reported in literature. FT-IR analysis of drug confirmed the authentication of Aceclofenac sodium. [14]

Firstly, five formulations (F1-F5) of floating beads of Aceclofenac sodium was prepared using different concentration of sodium alginate concentration. Best formulation (F3) was selected on the basis of entrapment efficiency, % yield and floating lag time. % Entrapment efficiency of all formulation was found in range of 25.22±0.005 to 73.69±0.003. Formulation containing poloxamer 188 had high entrapment efficiency which might be due to high foamability and foam stability. The highest percentage yield was found in the range of 38.09±0.003 to 75.49±0.004. The beads floated for prolonged time over the surface of dissolution medium without the apparent gravity. Drug release from the beads sustained upto 24 hrs. The cumulative % drug release of Aceclofenac sodium was found to be 93.71±0.21. [15,16]

CONFLICT OF INTEREST:

No conflicts of interest are mentioned by the researchers.

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