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Preparation and evaluation calcium alginate beads of Diclofenac and Glycyrrhiza glabra

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ABSTRACT:
The present study deals with the formulation of sustain release calcium alginate beads containing diclofenac and glycyrrhiza glabra by ionotropic gelation method at various concentration of sodium alginate and calcium chloride. The diclofenac shows the anti-inflammatory activity but can cause the gastric irritation / ulceration because of this glycyrrhiza glabra is used which shows the anti-irritant activity. The prepared beads were free flowing by showing acceptable results in bulk density, tapped density, angle of repose, carr's index and Hausner ratio. the prepared beads are brown in colour. The drug loaded beads showed 89-94 % drug entrapment efficiency for Diclofenac and 68-78% for glycyrrhiza glabra. In vitro drug release study of these alginate beads indicated controlled release for Diclofenac sodium 89-98 % release and for Glycyrrhiza glabra 38-64% release at the end of 5 hrs.

I. INTRODUCTION

Inflammation is localised protective response elicited by injury or destruction of tissues, which serves to destroy, dilute both the injurious agent and the injured tissue [6]. Non-steroidal anti-inflammatory drugs such as diclofenac is used for inflammation [2]. Diclofenac is used commonly to treat mild to moderate postoperative or post-traumatic pain, when inflammation is also present. It is available as a sodium or potassium salt. Diclofenac is believed to work by decreasing the production of prostaglandins, like other drugs in this class. But have side effect such as gastric ulceration.[1] To reduce the side effect glycyrrhiza glabra is used. Glycyrrhiza glabra, a flowering plant of the bean family Fabaceae, from the root of which a sweet, aromatic flavouring can be extracted. Liquorice is common name of Glycyrrhiza glabra. The extracts from the root of the plant can be referred to as liquorice, sweet root, and glycyrrhiza extract.[8] It is reported to have antiviral, anticancer, anti-ulcer. In study of microbeads of Glycyrrhiza glabra the microbeads are prepared to aim the stomach specific drug delivery which is useful in treatment of gastric ulceration [4]. In some study shown that, the Glycyrrhiza glabra increases the absorption of Diclofenac**[7]**

Calcium alginate beads were prepared of diclofenac and glycyrrhiza glabra. Alginate beads gives sustained release which is also helpful in reducing the side effect of diclofenac. The ionotropic gelation technique is used to make alginate beads.

Objective:
1. To prepare the alginate beads of different concentration of sodium alginate and calcium chloride.
2.To prepare the alginate beads of Diclofenac which gives the anti-inflammatory activity and Glycyrrhiza glabra which gives anti irritant activity which helps to reduce the ulceration and irritation caused by Diclofenac.
3. To evaluate microbeads for the following parameters like Bulk density, tapped density, Flow properties, drug loading and entrapment efficiency, In vitro drug release study.

Methods and materials
Materials:
Diclofenac (free sample from murlikrishna pharma pvt ltd)
Glycyrrhiza glabra powder extract (Purchased from India Mart)
Sodium alginate
Calcium chloride

Method:
Construction of calibration curve:
Calibration curve of Diclofenac and Glycyrrhiza glabra was constructed in phosphate buffer PH 7.4 using UV spectrophotometer.

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Preparation of alginate beads:

The calcium alginate microbeads were prepared by ionotropic gelation technique. In the present work four sets of microbeads were formulated by using sodium alginate and calcium chloride in different proportions. The detailed composition of the various formulation batches (F1-F4) was mentioned in table no. 2.

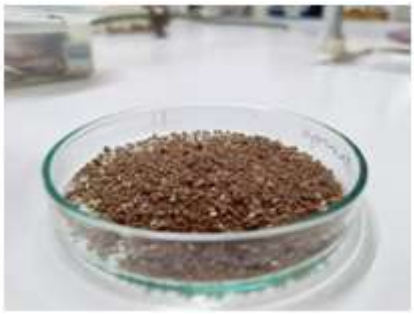
Table no. 1 Composition details of formulation

Formulation	Sodium alginate	Calcium chloride
F1	2%	1%
F2	2%	2%
F3	3%	1%
F4	3%	2%

In first set of two batches of drug loaded microbeads were prepared. (F1 and F2). In this 50 ml of sodium alginate solution of 2% w/v was prepared in this weighed amount of 100 mg Diclofenac and 10mg of Glycyrrhiza glabra were added and uniformly dispersed using mechanical stirrer. This solution is dropped using the syringe in calcium chloride solution of 100 ml. Then formed beads were separated by filtration and then dried at 60^0 C for 2 hrs.

In next two batches (F3 and F4), the 50 ml of sodium alginate of 3% w/v were prepared and Diclofenac and Glycyrrhiza glabra were dispersed uniformly using mechanical stirrer. Then this solution is dropped by using syringe in calcium chloride solution of 100 ml. then it filtered out and dried at 60^0 C for 2hrs.

Before drying



After drying

Evaluation parameter:

Determination of bulk and tapped density:

The bulk density and tapped density of prepared microbeads was determined using bulk density apparatus.

Determination of flow properties:

The flow properties of drug-loaded microbeads were investigated by measuring the angle of repose using funnel method. Depend upon these values we can assume the flow properties of the microbeads

Determination of drug content:

About 50 mg of microbeads were weighed and added to 50 ml of phosphate buffer (pH 7.4). The resulting mixture was agitated on mechanical shaker for 24 hrs, then solution was filtered and the drug content was estimated at respective wavelengths by using UV spectrophotometer.

Determination of drug loading and entrapment efficiency:

Accurately weighed 50mg of drug-loaded microbeads were suspended in 100ml of phosphate buffer pH 7.4±0.4. The resulting solution was kept for 24 h. Next day it was stirred for 5 min and filtered. Then analysed using UV spectrometer at respective wavelength. and calculate using following formula:

Drug loading= amount of drug in beads/ amount of bead taken *100

Entrapment efficiency= practical drug / theoretical drug *100

In vitro Drug Release Study:

In vitro Drug release studies were carried out in a USP XIII rotating basket apparatus containing 900ml of phosphate buffer pH 7.4 at 37^0C. Hard gelatine capsule filled with microbeads were placed in basket rotated at a constant speed of 50 RPM. Aliquots of sample were withdrawn after

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predetermined periods and replenished immediately withthe same volume of fresh medium Aliquots. Then analysed using UV spectrophotometer. (Model – shimadzu 1800)

FTIR

IR spectrometer, suggest that the drug and polymer are compatible and free from chemical interactions. IR interpretation of both the drug was performed.IR spectrophotometer used is Bruker FTIR alpha spectrometer

II. RESULT

Calibration curve:

Calibration curve of Diclofenac and Glycyrrhiza glabra was constructed in phosphate buffer PH 7.4 using UV spectrophotometer.

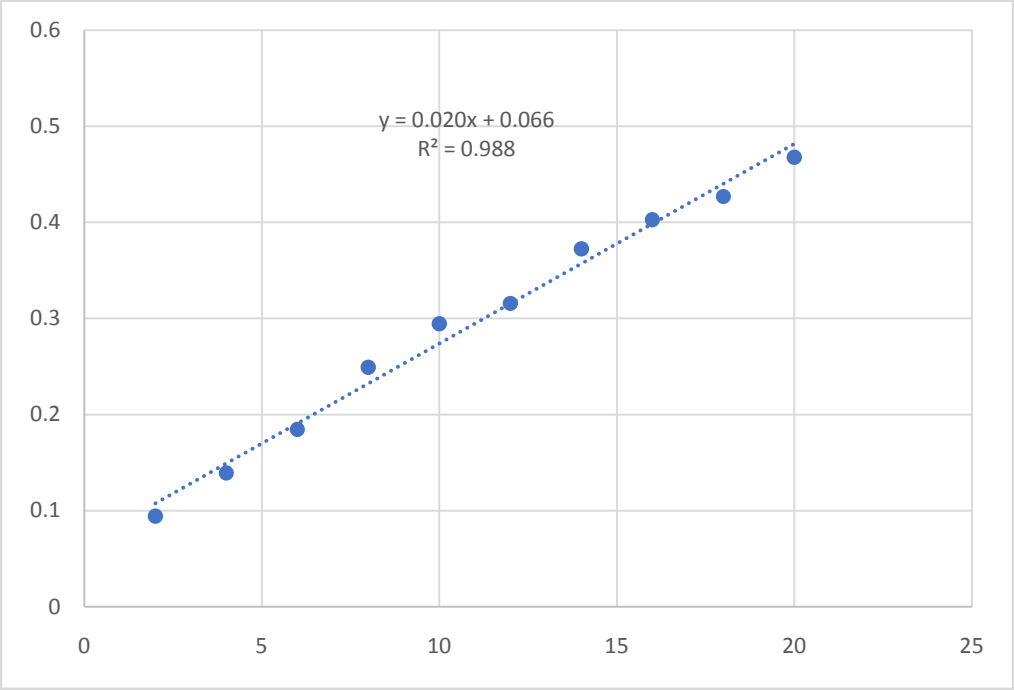

Fig. 1 Calibration curve of Diclofenac

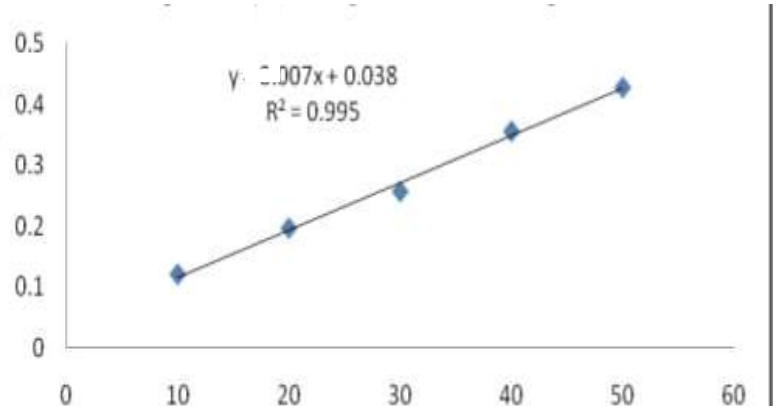

Fig. 2 Calibration curve of Glycyrrhiza glabra

FTIR spectrophotometer

IR interpretation of both the drug was performed.IR spectrophotometer used is Bruker FTIR alpha spectrometer.

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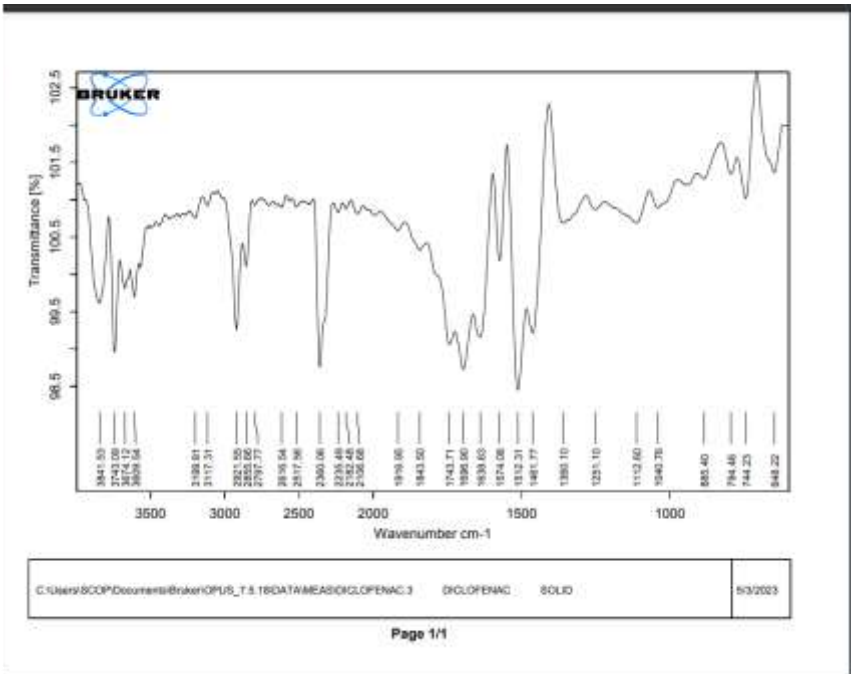

Fig.3 FTIR interpretation of Diclofenac

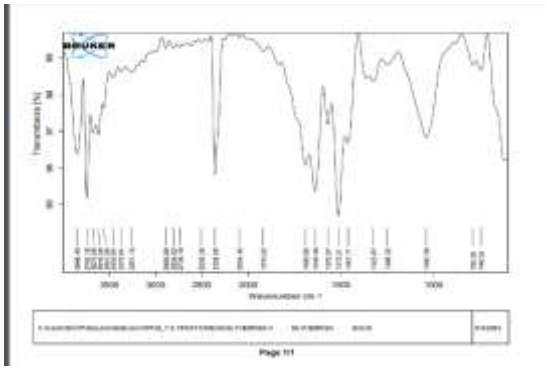

Fig. 4 FTIR interpretation of Glycyrrhiza glabra

Bulk and tapped density and flow properties:
The flow properties of drug-loaded microbeads were investigated by measuring the angle of repose using funnel method. Depend upon these values we can assume the flow properties of the microbeads.

Table no. 2 Flow properties

Formulation	Bulk density	Tapped density	Angle of repose	Carr's index	Hausner' ratio
F1	0.7692	0.8	19.48^0	12.5	1.14
F2	1.13	1.23	20.04^0	8.13	1.08
F3	0.93	1.07	23.8^0	13.08	1.15

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F4	0.68	0.755	21.6^0	9.33	1.10

Drug content and entrapment efficiency:

Table no. 3 Characterization of formulation

formulation	Drug in mg /50 mg of microbead of diclofenac	Drug in mg/50 mg of microbeads of g glabra	Entrapment efficiency of Diclofenac	Entrapment efficiency of Glycyrrhiza glabra
F1	0.0124	0.00221	89.2%	60.4%
F2	0.0144	0.00369	90.5%	77.2%
F3	0.0255	0.00636	92.86%	72.2%
F4	0.0155	0.00358	94.2%	78.6%

In vitro study:

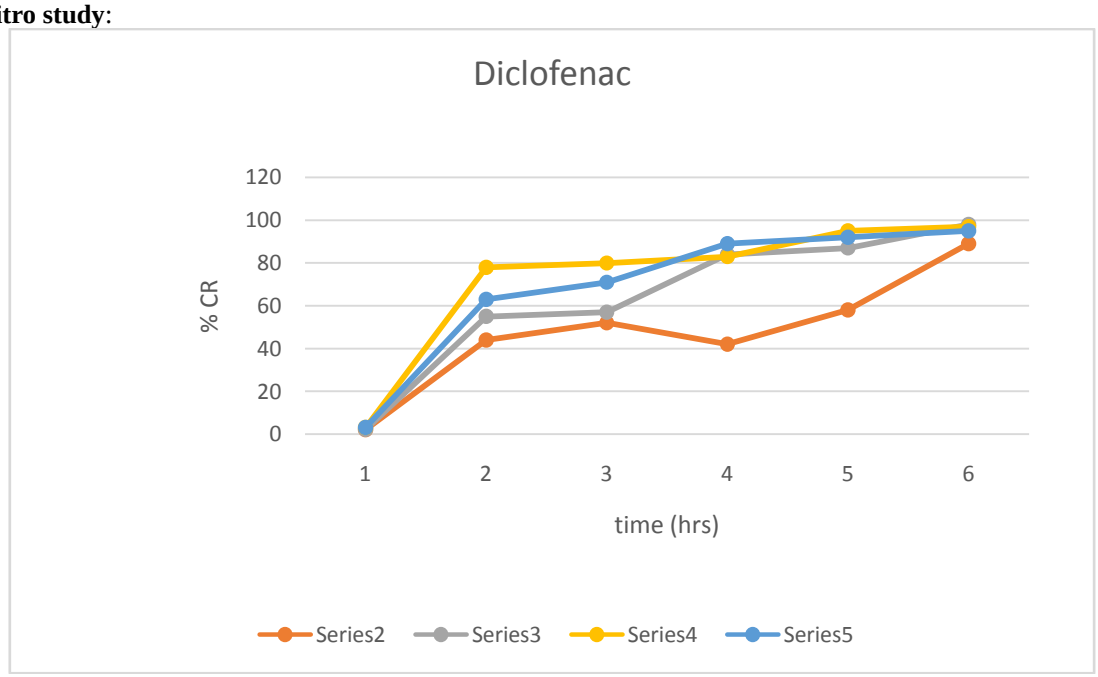

Fig.5 Cumulative percentage release of diclofenac

Table no 4 Diclofenac dissolution percentage:

time	2:1 (F1)	2:2 (F2)	3:1 (F3)	3:2 (F4)
1	44%	55%	78%	63%
2	52%	57%	80%	71%

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3	42%	84%	83%	89%
4	58%	87%	95%	92%
5	89%	98%	97%	95%

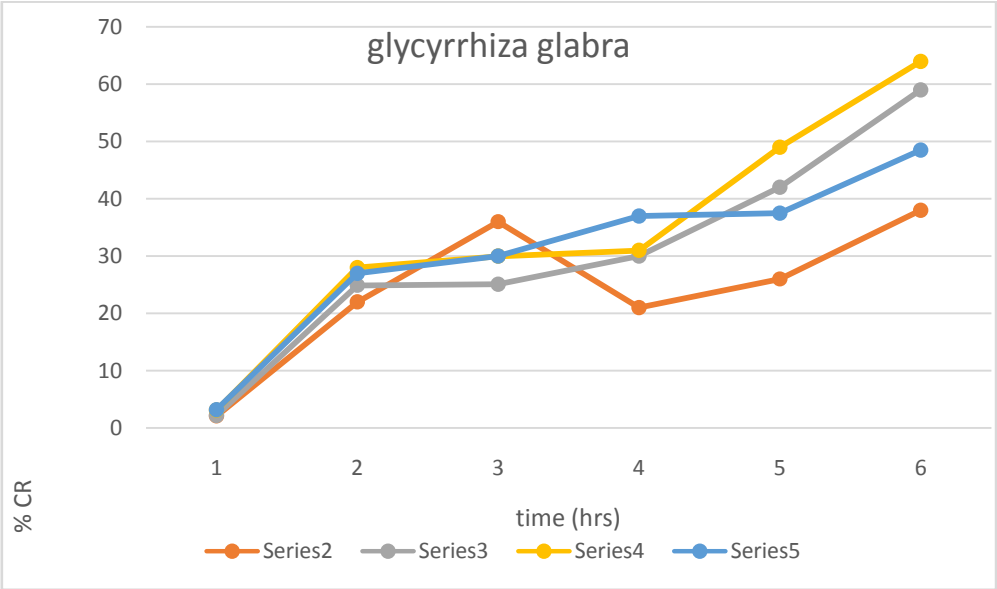

Fig. 6 Cumulative release of glycyerhiza glabra

time (hrs)	2:1 (F1)	2:2 (F2)	3:1 (F3)	3:2 (F4)
1	22%	24.9%	28%	27%
2	36%	25.1%	30%	30%
3	21%	30%	31%	37%
4	26%	42%	49%	37.5%
5	38%	59%	64%	48.5%

Table no. 5 Glycyrrhiza glabra dissolution percentage

Primary test of Glycyrrhiza glabra:

Test	Standard	Observation
Solubility	Soluble in water	Soluble in water
PH	4.1-6.8	6
Melting point	209-215℃	210℃

Table no. 6 primary test

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III. DISCUSSION:

Inflammation is localised protective response elicited by injury or destruction of tissues, which serves to destroy, dilute both the injurious agent and the injured tissue.

Diclofenac acts as an anti-inflammatory drug but it causes gastric irritation and ulceration. For this reason, Glycyrrhiza glabra is used in combination with Diclofenac that acts as anti-irritant. The calcium alginate beads of the above combination were formed to treat inflammation.

The calibration curve for Diclofenac and Glycyrrhiza glabra was constructed in phosphate buffer PH 7.4 using UV spectrophotometer. Diclofenac regression value is 0.98 and g. glabra regression value is 0.99 and used in standard in vitro calculation.

The colour of alginate beads is brown. The alginate beads flow properties were calculated by angle of repose method. the alginate beads are free flowing. Acceptable range of angle of repose was found to be 20 – 30. All the formulations showed an acceptable range of bulk density and tapped density.

The drug loaded beads showed 89-94 % drug entrapment efficiency for Diclofenac and 68-78% for Glycyrrhiza glabra. Drug entrapment efficiency of microbeads increases with increasing in the concentration of sodium alginate. In vitro drug release study of these alginate beads indicated controlled release for Diclofenac sodium 89-98 % release and for Glycyrrhiza glabra 38-64% release at the end of 5 hrs

IV. CONCLUSION:

The alginate beads of Diclofenac and Glycyrrhiza glabra is prepared by ionotropic gelation technique. the formulation F3 shows best result in In vitro studies with 97% release of Diclofenac and 64% release of glycyrrhiza glabra. Entrapment efficiency of formulation F3 is 92% for diclofenac and 72% for Glycyrrhiza glabra.

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