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Research Article

DEVELOPMENT AND EVALUATION OF METFORMIN LOADED ALGINATE BEADS USING *PHASEOLUS VULGARIS* BIOPOLYMER

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ABSTRACT

Metformin hydrochloride is oral antidiabetic drug belonging to the biguanide class of drugs. Metformin hydrochloride is used to treat non-insulin dependent diabetes mellitus (NIDDM-Type II diabetes), alone or in combination with other hypoglycaemic agents. It is also used in the treatment of polycystic ovary syndrome. The objective of the study was to prepare the sodium alginate beads of antidiabetic drug Metformin hydrochloride to provide sustained release effect. Five batches (F1-F5) were formulated by using varying concentration of drug and polymer. In this method drugs were blended with biopolymer and sodium alginate in different ratio (1:1, 1:2, 1:3, 1:4 and 1:5) and calcium chloride was used as a cross-linking agent. Metformin loaded Alginate beads were formulated by ionotropic gelation and prepared beads were evaluated with respect to its particle size, surface characteristics, entrapment effiency, swelling index, loss on drying, total moisture content and in-vitro release of drug.

From the above investigation it was found that the biopolymer will serve as a better alternative to develop the alginate bead.

Keywords: Hypogycaemic agent, ionotropic gelation, biopolymer, entrapment efficiency.

1. INTRODUCTION

Polymers are the substance, containing large number of structural unit joined by the same type of linkage. Natural polymers were generally obtained from gummy exudates and fibres. The Use of natural polymers for pharmaceutical applications is attractive because they are economical, readily available and non-toxic.The pulp of *Phaseolus vulgaris*are termed as an excellent remedy against cancer, heart, diabetes, bladder dysfunctions. Oral route is a common or sutable for a drug delivery. Oral hypoglycaemics should be used to supplement dietary management and not to replace it. Metformin hydrochloride is oral antidiabetic drug belonging to the biguanide class of drugs.Metformin hydrochloride is used to treat non-insulin dependent diabetes mellitus (NIDDM-Type II diabetes), alone or combination with other hypoglycaemic agents.

The gastrointestinal tolerance of metformin is poorer. Metformin hydrochloride is a BCS class II drug which is highly soluble with low permeability,the absorption is limited by the permeation rate.Sodium alginate is capable of forminggels by the action of calcium ion and provide sustained action for a long period of time.The aim of this study controlled release rate and increase buoyancy time.

2. MATERIAL AND METHOD

2.1. MATERIAL

Metformin were obtained as gift samples from Accacia Biotech Laboratories Ltd. All other reagents used were analytical grade.

2.2. METHOD

2.2.1. ISOLATION OF BIOPOLYMER

The pulp of the *Phaseolus vulgaris*collected in a beaker.Then the distilled waterwas added in a beaker and stirred on magnetic stirrer for 1 hrs to form slurry.

The slurry was filtered by the musclin cloth and filtrate was centrifuged at 3000 rpm for 15 minutes .Suparnatent solution was collected, treated with Acetone to extract the biomaterial.The solution kept in refrigerator overnight so that most of the undissolved

portion was settled down in precipitate form. The precipitate was washed repeatedly with acetone and dried in desiccator. Powdered bio polymer passed through sieve number 80 and stored in air tight container for future use.

2.2.2. Characterization of Biopolymer

The biopolymer obtained from the pulp of *Phaseolus vulgaris* was characterized for their physicochemical and phytochemical properties.

A. Physicochemical characterization

The isolated biopolymer was evaluated for physicochemical properties such as solubility behavior, organoleptic evaluation (colour, odour, taste and shape Appearance), melting point, flow properties, density behavior.

B. Phytochemical characterization

Biopolymer obtained from the pulp of *Phaseolus vulgaris* was evaluated for phytochemical properties like test for alkaloids, test for carbohydrates, test for proteins, test for saponins test for flavonoid, test for tannin and test for mucilage.

2.2.3. Spectrophotometric determination of Metformin hydrochloride

Calibration curve of Metformin hydrochloride was prepared in methanol. Stock solution of Metformin hydrochloride (100µg/ml) was prepared. Aliquot from stock solution obtained was then serially diluted with methanol to get final concentrations in the range of(2-14 µg/ml). The absorbance value of the resultant solutions were measured using methanol as blank at 232nm.

The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

2.2.4. Preparation of Polymer Drug Solution

Weighedaccurate quantity of Sodium alginate and biopolymer was taken in a mortar and pestle and made into a homogenousdispersion by addition of required quantity of water. The drug was added to form a polymerdrug solution and mixed thoroughly. Different combinations of biopolymer were used to get various proportions ofbeads. For combination of biopolymer, biopolymers are added in the different ratios of (1:1-1:5) and mixed without any lumps formation.Then Metformin hydrochloride(100 mg) was dispersed in the polymer mixture.

2.2.5. Preparation of Calcium Chloride Solution

10% Calcium Chloride solution was prepared by mixing 10 g of Calcium Chloride in 100ml of water.

2.2.6. Preparations of Metformin loaded alginate beads

Sodium alginate and biopolymer solutions of different concentrations were prepared by dissolving required amount of alginate in 100 ml of deionized water under gentle agitation. Metforminhydrochloride were dispersed in alginate solution under constant stirring foruniform mixing.

The dispersion was sonicated for 30 minutes to remove air bubbles. The resultant dispersion was droped through a syringe needle into 100 ml of 10 % (w/v) calcium chloride solution at room temperature. Then the beads formed were allowed to remain in the stirred solution for 15 min. The beads were filtered andsubsequently oven-dried at 50-60°C for 2-3 hours.

EVALUATION OF BEADS

a) Swelling Index

Metformin hydrochloride alginate beads were soaked in 0.1N Hcl, and pH 6.8 phosphate Buffer. After 24 hrs, the alginate beads were removed from their media's and excess water is removed and their weights are measured again. Swelling index was calculated using the formula:

$$\text{Swelling index} = \frac{\text{Weight of wet beads - weight of dry beads}}{\text{Weight of dry beads}} \times 100$$

b) Drug content

100 mg alginate beads crushed and dissolved in 100 ml distilled water. This solution was shaken then kept for 24 hrs. After 24 hrs the solution was filtered. The filtrate of Metformin alginate beads was analyzed using a SHIMADZU UV 1800 - spectrophotometer at 232 nm. The percent drug content is calculated using following formula.

% Drug content = Actual drug content/ Theoretical drug content × 100

c) Moisture content

Metformin loaded alginate beads weighed and kept in a desiccators containing calcium chloride at room temperature for 24 hrs. Thenbeads are weighed again after a specified time interval until they show a constant weight. The percent moisture content is calculated using following formula.

$$\% \text{ Moisture content} = \frac{\text{Initial weight - Final weight}}{\text{Final weight}} \times 100$$

d) Moisture Uptake

Weighed Metformin loaded alginate beads and kept in a desiccator at room temperature for 24 hrs. Then taken out alginate beads and exposed in a room temperature.Thenbeads are weighed again after a specified time interval until they show a constant weight. The percent moisture content is calculated using following formula.

$$\% \text{ Moisture Uptake} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

e) In Vitro Release Studies

The in-vitro release beads were performed using USP type II dissolution test apparatus in 900 ml of medium (0.1M hydrochloric acid) for the first 2 hrs and then in pH 6.8 phosphate buffer at temperature 37 ± 0.5°C and stirring rate of 50 rpm for the rest 8 hrs. A 5 ml sample of the solution was removed from the apparatus after different time intervals. The volume of each sample was replaced with the same volume of Phosphate buffer (pH6.8) to maintain the sink conditions. The released amount of Metformin alginate beads was analyzed using a SHIMADZU UV 1800 - spectrophotometer at 232 nm.

EVALUATION OF BEADS

3. RESULT AND DISCUSSION

3.1. Characterization of Biopolymer

A. Physicochemical Characterization

Table 1: Solubility profile of Biopolymer

Solvent	Solubility Behavior
Cold Water	Sparingly soluble
Warm Water	Soluble forming a viscous colloidal solution
Methanol	Insoluble
Ethanol	Insoluble
Acetone	Insoluble

Table 2: Organoleptic evaluation of Biopolymer

PARAMETERS	BIOPOLYMER (*Phaseolus vulgaris*)
Colour	White brownish
Odour	Odourless
Taste	Tasteless
Shape	Irregular
Appearance	Amorphous

Table 3: Characterization of isolated biopolymer powder

PROPERTY	RESULT
Bulk density (g/cc)	0.61 g/cm3
Tapped Density (g/cc)	0.75g/cm3
Angle Of Repose (°)	28.36
Housner's ratio	1.22
Carr's Indix	18.6

Table 4: Phytochemical characterization of isolated biopolymer powder

PROPERTY	RESULT
Alkaloid	-
Carbohydrate	-
Saponin	-
Proteins	-
Flavonoid	-
Mucilage	+
Tannin	-

3.2. Spectrophotometric determination of Metformin hydrochloride

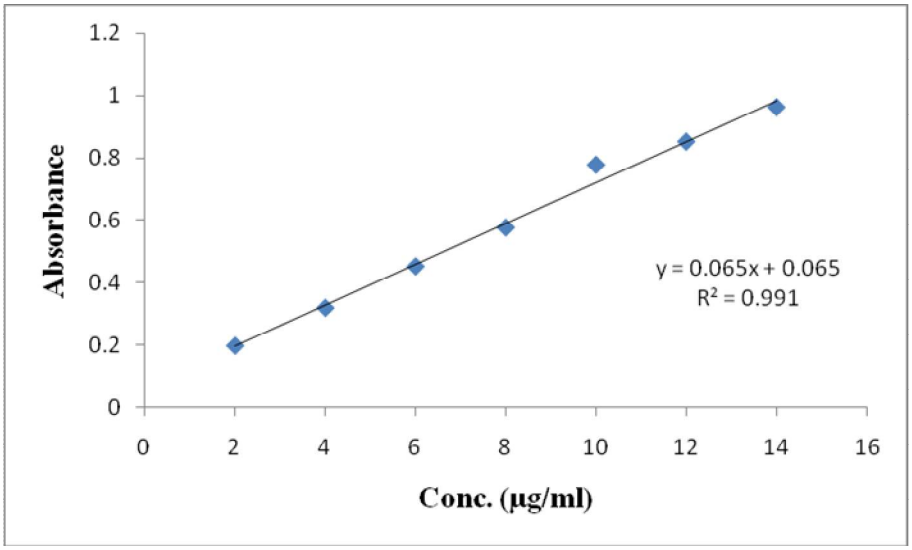

Fig. 1: Calibration Curve of Metformin hydrochloridein HCl

3.3. Preparartion of alginate beads using biopolymer *Phaseolus vulgaris*

Table 5: Composition of alginate beads using biopolymer *Phaseolus vulgaris*

Formulation code	Drug (mg)	Sodium alginate (mg)	CaCl2 solution (%)	BioPolymer (mg)
F1	100	100	10	100
F2	100	150	10	200
F3	100	200	10	300
F4	100	250	10	400
F5	100	300	10	500

Table 6: Evaluation parameter of biopolymeric alginate beads

Formulation code	Swelling index	%Drug content	%Moisture content	%Moisture uptake	Invitro drug release
F1	0.81	88.25	12.28	10.58	82%
F2	0.85	81.98	14.55	18.49	89 %
F3	0.75	78.11	13.58	13.74	75%
F4	0.90	69.76	16.45	15.83	78%
F5	0.79	71.51	22.08	20.71	85 %

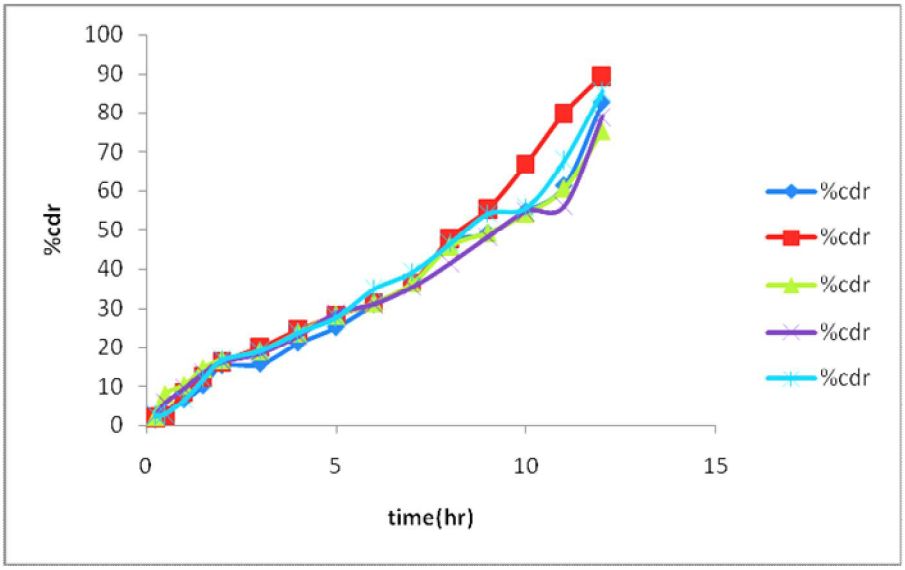

Fig. 2: Cumulative Drug Release of alginate beads

4. RESULT

The present study indicates that formation of completely aqueous environment avoiding the use of organic solvents to minimize the curing time of alginate beads leads to enhance drug entrapment efficiency in comparison to previous works and the biopolymer serves as a better alternative excipient for the development of dosages forms.

5. CONCLUSION

This study investigated that Metformin loaded alginate beads were prepared successfully by using the combination of biopolymer*Phaseolus vulgaris*, sodium alginate, calcium chloride in different ratios (1:1-1:5), It was observed that the concentration of the biopolymer can be control the drug release properties of the alginate beads. Formulations F2 showed better rate of release.Thus, Metformin loaded alginate beads could be developed for controlled drug delivery.

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