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Research Article

FEASIBILITY OF ASSAM BORA RICE BASED MATRIX MICRODEVICES FOR CONTROLLED RELEASE OF WATER INSOLUBLE DRUG

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ABSTRACT

The present investigation proposed and examined the *Bora rice* of Assam in formulation of controlled release drug delivery systems being utilized as a natural mucoadhesive matrixing agent for modulation of drug release. The *Bora rice* is a festival food in Assam and is characterized by its dull milky appearance having composed of mainly amylopectin and traces of amylase; it is also known as waxy or sticky rice. In this phase of project, the controlled release microparticulate drug delivery systems were fabricated using *Bora rice* backbone along with sodium alginate and a model medicament to evaluate the potential of polymer backbone in modulation of drug release behaviour and to find out the kinetics of drug release from formulated matrix devices. The formulated drug delivery systems were characterized for particle size and size distribution, surface characteristics using SEM, drug excipient compatibility study using UV, FTIR, and DSC. The *in vitro* release of Ibuprofen was studied in USP XXIV Dissolution test apparatus (basket type). The *in vitro* dissolution profile studies for characterization of release kinetics were carried as per the guidelines provided by the Center for Drug Evaluation and research FDA for modified release dosage forms. The experimental observations have shown promising results for the pharmaceutical utility of Assam *Bora rice* as excipient in formulation of mucoadhesive controlled drug delivery systems.

Key words: Drug delivery, Pharmaceutical Excipients, *Assam Bora rice*, Biopolymer,

INTRODUCTION

The North-East India constitutes one of the 25 biodiversity hot spots across the world[1]. The biological diversity responds to a number of new, emerging concerns including thrust for the research and developments especially in the field of biotechnology, life sciences, chemical sciences, traditional phytopharmaceuticals and natural products. Biological Diversity Act 2002 is a part of the Indian attempt to make some progress and to operationalize the conservation and value addition to the natural heritage[2]. The major focus of the research carried out on the value of genetic resources has been on their use in the pharmaceutical and agricultural industries, which use genetic diversity as a source of information in their development of new products. Economists have long analyzed the research and development process as one of information utilization, application and diffusion. The concept of research and development is usually presented as a production process itself dependent upon a stock of "information" for its generation of useful innovations. The present investigation was undertaken to explore the pharmaceutical utility of *Assam Bora rice*, as the researchers from Assam Agriculture University reported that the bora rice is a variety of glutinous rice having composed of mainly amylopectin and only a traces of amylose[3]. The amylose is a

linear polymer accounts mainly for the disintegration property of starch, on the other hand amylopectin is a highly branched polymer probably responsible for retarding the degradation and release of entrapped chemical from the matrix. Using bora rice as pharmaceutical excipient is potentially interesting as it is a common food stuff and can be classified as 'GRAS' (Generally regarded as safe), which is necessary for any new excipient to be used in food or pharmaceutical for regulatory purpose[4]. It is a high cost affair the because of this there are only a handful of substances from innumerous researched materials could be scaled up for industrial use. The natural materials have been extensively used in the field of drug delivery also because they are readily available, cost-effective, eco-friendly, capable of multitude of chemical modifications, potentially degradable and compatible due to their natural origin[5]. In addition this can be a potential marketing tool in the 'herbal boom world wide', the present day consumer look for the natural ingredients in the food drug and cosmetics as they believe that anything natural will be more safe and devoid of side effects as compared to their synthetic counterparts[6].

Excipients are primarily used as diluents, binders, disintegrants, adhesives, glidants and sweeteners in conventional dosage forms like tablets and capsules. The traditional view that excipients are inert and do not exert any therapeutic or biological action or modify the biological action of the drug substance has changed and it is now recognized that excipients can potentially influence the rate and/or extent of absorption of a drug. In this connection the bora rice polysaccharide is studied for its mucoadhesive potential and property of modulation drug release from the pharmaceutical drug carrier systems.

MATERIALS AND METHODS

Materials

The *Bora rice* was procured from the local village near about Dibrugarh University and was confirmed by local people. Drug samples were obtained as gift sample from industrial sources. All other chemicals used were the analytical grade laboratory reagents and were used as such without further testing.

Methods

Preparation of microbeads

The drug loaded microbeads were prepared by the micro orifice ionotropic gelation technique in all aqueous system[7]. The carrier backbone was prepared by the pregelatinized bora rice[8] along with sodium alginate in varying ratio. Many preformulation trials were undertaken to optimize the preparation process for higher drug load and to accommodate the maximum percentage of bora rice producing beads with sufficient mechanical strength and acceptable pharmacotechnical parameters.

Drug entrapment efficiency

The amount drug entrapped in the fabricated microbeads was estimated by extracting the drug from beads and its subsequent spectrophotometric quantification. Drug entrapment efficiency was calculated using the following formula.

$$\text{Entrapment efficiency} = \frac{\text{Estimated percentage drug loading}}{\text{Theoretical percentage drug loading}} (100)$$

$$\text{Percentage drug loading} = \frac{\text{Amount of drug in microspheres}}{\text{Amount of microspheres}} (100)$$

Particle size analysis

The particle size and size distribution of the beads was studied through optical microscopy using a calibrated stage micrometer. The particle size measurements were also carried out by the phase contrast microscope (LaboMed XLR II). The effect of formulation and process parameters was observed on particle size.

Surface characteristics

Surface characteristics of the beads before and after *in vitro* drug release testing were studied by phase contrast microscope and by the SEM analysis (HITACHI, S – 3600 N, Scanning Electron Microscope).

In vitro drug release study

The *in vitro* drug release study was conducted by USP XXIV dissolution test apparatus (Campbell electronics, Mumbai) using basket type apparatus. The sample aliquots were withdrawn at predetermined intervals and were quantified spectrophotometrically to know the amount of drug released in relation to time. The study was conducted in triplicates and dissolution profiles were compared for reproducibility before they were used for modeling and characterization[9].

Assessment and comparison of dissolution profiles

The data obtained from the triplicate study was subjected to comparison for validity and reproducibility as per the SUPAC guidelines for modified release drug products provided by the Center for Drug Evaluation and research, FDA (United States, Food and Drug Administration). Similarity factor (F) factor was calculated which is a logarithmic reciprocal of square root transformation of one plus the average mean squared (average sum of squares) differences of drug percent dissolved between the two dissolution profiles over all time points[10].

$$F = 50 \text{ x } \log\left\{\left[1+(1/n)\sum_{J=1}^{n}[R_J - T_J]^2\right]^{-0.5} \text{x } 100\right\}$$

Where n is the number of dissolution time points and R_J and T_J are the dissolution values of two dissolution profiles at time t. The two dissolution profiles are considered similar when F value is in range of 50 to 100.

Modeling of drug release kinetics

The data from *in vitro* dissolution study was fitted to various mathematical models to identify the kinetics of drug release from the beads at different release environments. The best fit kinetics was identified on the basis of correlation coefficient from the line of best fit plotted as per model equation in Microsoft excel[11].

Test for mucoadhesion

The mucoadhesive potential of the prepared beads was examined using an *in vitro* wash-off test as reported by Lehr *et al.* 1992, using simulated intestinal fluid[12].

Drug excipient compatibility testing

UV spectroscopy

The UV scan was taken for pure drug sample and the drug extracted from the microbeads, and lambda max was observed. Any change in the λmax of the two or an observation of new peak will indicate the possibility of any chemical modification in the drug it provides a clue for drug-polymer backbone interaction.

FTIR spectral analysis

The FTIR spectra of drug sample, drug loaded beads, bora rice polysaccharide and placebo was recorded and was observed for any modification in reference to new peaks, or shifting of peak position that will indicate to the possibility of drug-polymer interaction.

Thermal analysis

The occurrence of drug-polymer backbone interaction was confirmed by the thermal analysis using differential scanning calorimetry (DSC). The DSC thermograms were recorded for drug sample, bora rice polysaccharide, drug loaded beads and placebo. Those were subjected to comparative observation for any new peak as an indicative of chemical interaction between the polymer backbone and entrapped medicament.

Statistical analysis

The multiple dissolution profiles were compared for significant reproducibility by similarity factor as per FDA guidelines. The statistical comparisons were made for selecting the model of best fit using regression analysis. The data in release figures and tables is represented as ± standard error of mean (SEM) unless otherwise stated.

RESULTS AND DISCUSSION

The drug loaded microcarrier systems could be prepared using bora rice backbone through an ionotropic gelation method. Several preformulation trials were undertaken for the optimization of experimental batched. Optimized beads were then coated with hydroxylpropyl methyl cellulose by solvent evaporation method in a rotary vacuum evaporator. The prepared beads were in a size range of 0.726 ± 0.008 mm to 1.16 ± 0.009mm with almost similar particle size with in a batch. Drug loaded beads have shown fairly good mucoadhesion in *in vitro* wash of test when compared with microbeads prepared with non-mucoadhesive material (Table 1). The particle size which promptly affects the drug release behaviour and extent of release duration is found to be dependent on the drug load, gel strength, precision device, stirring speed, and cross-linking agent used.

Table 1: Wash-off profile of the beads showing mucoadhesion:

S. No.	Time (hrs)	% of beads remain adhering								
		F_1	F_2	F_3	F_8	F_9	F_{13}	F_{14}	F_{15}	F_{16}
1.	01	98	96	94	90	90	96	94	94	98
2.	02	82	84	88	82	80	86	80	84	96
3.	03	78	82	80	72	70	82	70	78	86
4.	04	70	74	74	64	66	76	64	72	78
5.	05	62	64	68	56	54	68	62	62	72
6.	06	36	40	42	38	40	52	48	40	54
7.	07	34	38	40	30	28	38	30	36	40
8.	08	24	28	22	22	18	28	24	26	32

The beads forms gel when comes to the contact with simulated intestinal fluid and wash-off gradually from the mucosa. The drug release therefore seems to be primarily through diffusion through gel matrix although the erosion of matrix backbone may contribute to a little extent.

The drug release is extended up to 12 hours in dissolution testing as per USP guidelines. The initial fast release, as depicted in release profiles (Fig. 1) is probably due to fraction of drug accumulated on to the surface of microbeads that becomes available for release immediately.

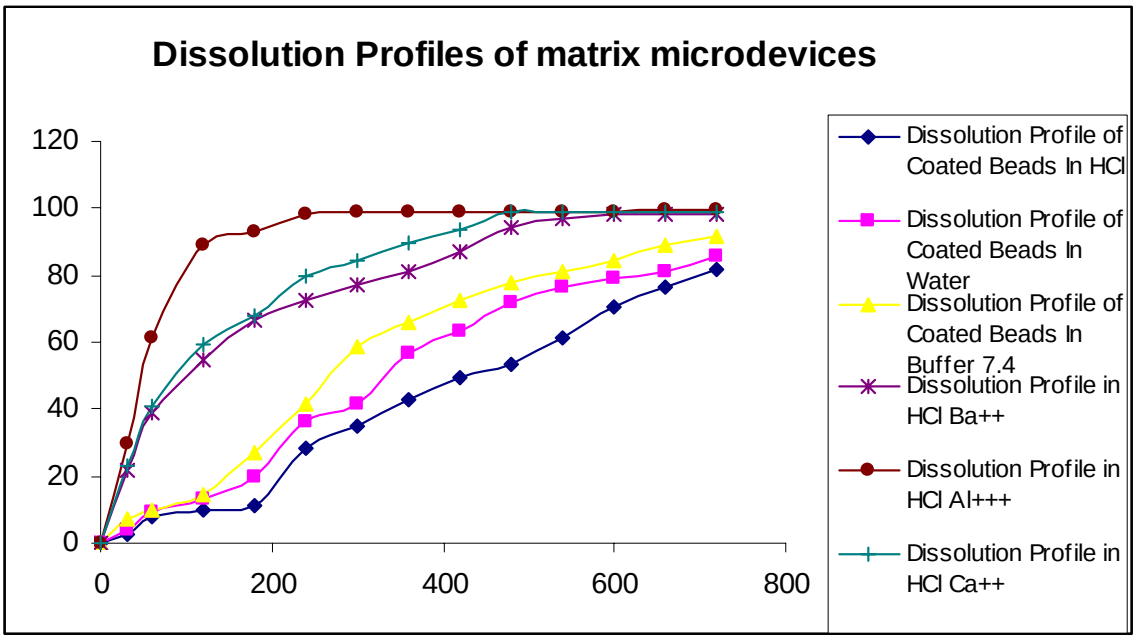

Fig. 1: Dissolution profiles of prepared microbeads

The different formulations prepared have exhibited the different release patterns at DM water, simulated gastric fluid and simulated intestinal fluid. HPMC coated beads have exhibited the comparatively much smooth and prolonged drug release than that of uncoated batches. The polymer showed high degree of swellability in alkaline medium that is a favourable property for controlled release systems for increased pay load. The fabricated polymer backbone have shown no chemical interaction with the dug in drug excipient compatibility studies therefore it can be inferred that the drug release modulation is taking place as a result of some physical entanglement only between the drug and polymer backbone. The extended drug release seems to be from the hindered diffusion of the medicament from the gel barrier of the polymer backbone and probably the inclusion of the drug into the hollow hilum of rice grain.

The preliminary studies conducted for fabrication of controlled release microcarrier systems using the ionic gelation method with model drugs of different solubility profiles have revealed that the proposed polymer holds promise for its utilization as an excipient in the formulation of controlled release drug delivery systems. Further investigation is continuing for exploring the possibility of bora rice in preparing the drug delivery devices with improved performance and economically sound methodology.

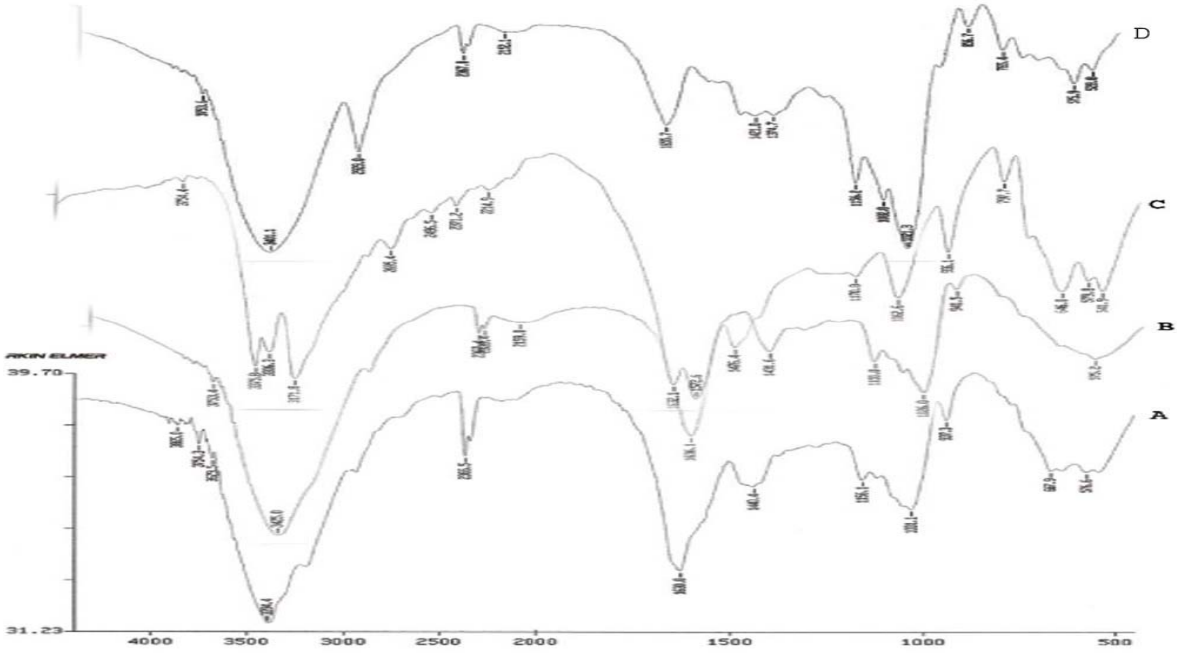

Fig. 2: FTIR Spectra of Beads: (A) Drug loaded beads (B) Placebo (C) Bora rice polysaccharide (D) Pure drug sample

CONCLUSIONS

The *Assam Bora rice*, have shown sufficient mucoadhesion and prolonged drug release with capability of further modifications in prepared microdevices to be used in the controlled drug delivery. Further it is worth full to mention here that the use of proposed biopolymer have shown good degree of binding property in preformulation study, hence it sounds the need for investigation in this area too.

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