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Original Article

PREPARATION OF BUDESONIDE-PECTIN BEADS USING THE PERISTALTIC PUMP

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ABSTRACT

Objective: To formulate and evaluate budesonide-pectin beads using novel assembly with a peristaltic pump.

Methods: The prepared budesonide-pectin dispersion was added to calcium chloride solution with the help of assembly. Provided at least 2 h for hardening and dried at 60 °C for 3 h. Assembly was assembled with the use of a peristaltic pump, polymeric solution reservoir, hose, needle, magnetic stirrer, gelling bath. One side of hose was dipped in pectin solution container and another side was passed through the peristaltic pump and connected to the needle. Peristaltic pump produced pumping of pectin solution through the hose. Needles with variable diameters are available. The gelling bath was kept on magnetic stirrer to keep prepared beads in motion, which helped to provide new surface and sufficient reaction time and helped to avoid agglomeration. There were 10 different batches with different process parameters prepared. Production yield, the diameter of beads, swelling index, and *in vitro* budesonide dissolution in phosphate buffer pH 7.4 after 5 h was determined.

Results: There was a significant difference between selection of process parameter among the batches (p = 0.049, q = 6.11). As nozzle diameter was increased, percentage yield was decreased (p = 0.0038, q>5.98). However, if hardening time was decreased percentage release was increased (p = 0.0361, q>5.98).

Conclusion: The novel assembly for bead generation had developed a uniform, spherical shaped, and smooth surfaced beads.

Keywords: Beads, Micrometric properties, Peristaltic pump, Process parameters

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INTRODUCTION

Budesonide is a glucocorticoid [1]. It undergoes significant first-pass degradation (80–90%) and is rapidly and extensively bio-transformed into 6-β-hydroxy budesonide and 16-α-hydroxy prednisolone, which has no or negligible (<1/100) targeted pharma-cological action [2]. Therefore, there is a need for novel drug delivery system of it.

The basic principle for bead generation of is to convert liquid into the spherical shape. In resonance method, vibration mechanism was used. Assembly consists of liquid reservoir and nozzle. The liquid could flow through vibrating nozzle or vibration could be applied to the liquid reservoir. Scale-up of the system could be easily possible. In the jet cutting method, high pressure is applied to the liquid reservoir, resulting in a high-velocity flow of liquid through the nozzle in form of a solid-liquid jet. Rotating cutting tool made of small wires and driven by the motor is directly placed underneath of the jet flowing through the nozzle, which cuts the jet into uniform cylindrical segments. These segments convert in spherical beads due to surface tension while falling. The spherical beads are falling further down to the receiver containing cross-linking agent and a hardening agent. Each cutting event causes a cutting loss which is slugged a side where it can be gathered and recycled. This technique may be useful for various applications in biotechnology, medicine, chromatography, pharmaceutical, chemical, and food industries [3]. The basic principle of the electrostatic method is to apply an electrostatic force to form a charged stream of droplets from a nozzle tip. High voltage direct current supply is used to apply to an electrostatic potential between droplet formation device (nozzle/needle) and collecting solution. Electrostatic force induces a charge at the surface of polymer solution flowing through the needle, resulting in a decrease in surface tension and formation of small-sized droplets [4]. The basic principle of the rotary atomizer is to use rotational speed either on disc or multi-nozzle device. In case of rotating disc atomizer, the polymer solution is fed onto rotating disc whereas, in case of rotating nozzle atomizer, polymer solutions flow through the atomizer having multiple nozzles. Optimization of rotation speed is vital to formulate uniform sized spherical droplets [5]. The assembly of co-axial air stream method has two connections, one is attached to the top of the nozzle for polymer solution and another is attached to the tip of nozzle to supply air stream. The basic principle is to blow polymeric droplets from the nozzle by using co-axial air stream before they would fall into a gelling reservoir due to gravitational force [6]. These presently available methods of beads formation have technically complex procedure. Therefore, need of simply processed beads formation assembly.

The objective of the study was to formulate and evaluate budesonide-pectin beads using novel assembly with a peristaltic pump.

MATERIALS AND METHODS

Material

Budesonide was purchased from Zydus Cadila, Ahmedabad, India. Pectin was purchased from Oxford Lab., Mumbai, India. Calcium chloride was purchased from Chem. Lab. India.

Methods

Preparation of beads

Accurately weighted pectin was dissolved in the measured volume of distilled water with continues agitation to prepare 5% w/v pectin solution. To the solution, the accurately weighed budesonide was added with continuation agitation to prepare uniform dispersion and allowed to stand overnight. The 5% w/v solution of calcium chloride was prepared in distilled water. The prepared budesonide-pectin dispersion was added to calcium chloride solution with the help of assembly. Provided at least 2 h for hardening. The hardened bead was filtered and washed with fresh water. Drying was done in a tray dryer at 60 °C for 3 h. Instrumental setup of the assembly is shown in fig. 1. Assembly was assembled with the use of a peristaltic pump, polymeric solution reservoir, hose, needle, magnetic stirrer, and gelling bath. The one side of hose was dipped in pectin solution container, the side was passed through the peristaltic pump and connected to the needle.

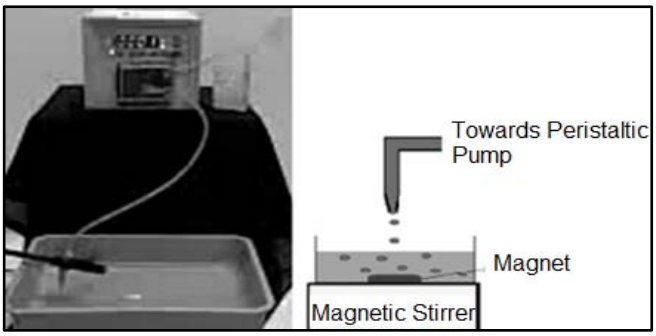

Fig. 1: A novel assembly for bead generation

A peristaltic pump is produced pumping of pectin solution through the hose. The desired size of beads was prepared by monitoring and maintaining the pumping rate of peristaltic pump depending upon the viscosity of the polymeric solution. Needles with variable diameters were available. It had chosen on the basis of the viscosity of the polymeric solution and desired size of beads. The gelling bath was kept on magnetic stirrer to keep prepared beads in motion, which helped to provide new surface and sufficient reaction time and helped to avoid agglomeration.

Evaluation of process parameters effects

There were 10 different batches with different process parameters prepared to study the effect of process parameters.

Evaluation of micrometric properties of beads

Loading amount of pectin and weight of the dried beads of each batch were accurately measured. Production yield (percentage yield) was determined as the ratio of the total mass of beads to the total mass of raw materials. The diameter of beads was measured by Digital vernier caliber (Remi equipment, India). There were 10 g of dried beads dipped in a beaker containing 100 ml of 0.1N HCl solution. The swollen beads were weighted at a specified time of 30 min. The swelling index was determined as the ratio of increase in weight of beads to initial weight of beads [7]. There was 50 mg budesonide loaded beads thoroughly crushed and placed in a volumetric flask containing 50 ml of 7.4 pH phosphate buffer for 1 h. Budesonide was completely extracted from beads to buffer solution by filtration. The sample from the solution was taken to analyze spectrophotometrically at 245 nm. The percentage budesonide loading was calculated as the ratio of actual budesonide to theoretically presence of budesonide [8]. *In vitro* budesonide dissolution in phosphate buffer pH 7.4 after 5 h was determined to calculate budesonide release profile of beads [9].

Statistical analysis

All data were represented as mean±SD of three independent experiments. One-way ANOVA (analysis of variance, Microsoft Excel® 2016, Microsoft Raymond, USA) following the Dunnett multiple comparisons test (considering critical value [q]>5.98 as significant, InStat Statistica, GraphPad Software, Inc, CA, USA) was used to show a significant difference for process parameter and evaluation results between different batches [10]. Results were considered significant at 95% of confidence level.

RESULTS

There was a significant difference between selection of process parameter among the batches (p = 0.049, q = 6.11, table 1). Moreover, there was also a significant difference among evaluated micrometric properties of different batches such as nozzle diameter was increased, percentage yield was decreased (p = 0.0038, q>5.98) and if hardening time was decreased percentage release was increased (p = 0.0361, q>5.98) (table 2).

Table 1: Process parameter optimization

Batch	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Addition rate (mL/min.)	1	1	1	1	1	1	1	1	1	Not Fixed
Stirring speed (rpm)	20	20	20	20	20	20	20	20	20	20
Drying time (h)	2	2	2	2	2	2	2	2	2	2
Drying temperature (°c)	60	60	60	60	60	60	60	60	60	60
Nozzle diameter (mm)	0.4	0.4	0.4	0.6	0.6	0.6	0.8	0.8	0.8	0.6
Hardening time (min)	10	20	30	10	20	30	10	20	30	20

All batches were prepared separately.

Table 2: Results of micrometric properties of beads

Batch	% Y	D (mm)	LOD	SI	% BL	% BR
P1	88.13±1.23	1.076±0.05	83.11±0.49	2.668±0.21	80.88±1.88	97.36±1.23
P2	86.25±1.25	1.082±0.04	82.97±0.38	2.671±0.23	87.36±1.58	97.55±1.56
P3	84.23±1.27	1.074±0.06	83.34±0.49	2.663±0.25	83.19±2.36	95.21±1.65
P4	88.61±1.31	1.098±0.07	83.46±0.28	2.661±0.19	85.23±3.27	99.51±1.69
P5	85.32±1.33	1.102±0.08	82.87±0.25	2.673±0.18	80.47±2.06	99.31±1.73
P6	84.27±1.39	1.104±0.09	83.18±0.31	2.666±0.16	82.69±2.49	97.81±1.27
P7	86.15±1.42	1.114±0.04	82.41±0.19	2.671±0.22	76.18±3.52	98.15±1.17
P8	88.19±1.43	1.108±0.03	82.36±0.13	2.672±0.29	79.41±3.71	96.76±1.19
P9	86.28±1.45	1.112±0.07	83.26±1.31	2.642±0.23	82.12±3.52	97.81±1.21
P10	70.18±1.01	1.248±0.09	80.36±1.68	2.682±0.28	70.18±4.12	96.23±1.12
*p	0.0038	0.0103	0.0026	0.0392	0.0451	0.0361
*q	>5.98	>5.98	>5.98	>5.98	>5.98	>5.98

Data were represented as mean±SD, n = 3, Y: Yield, D: Average diameter, LOD: Loss on drying, SW: Swelling Index, BL: budesonide loading, BR: budesonide release, p<0.05 and q>5.98 were considered as significant, *Overall value.

DISCUSSION

The present intention was to set up with novel assembly at laboratory scale to formulate beads. Traditionally, one of the multi-particulate dosage form (beads) is prepared by filling polymer solution in the syringe, at laboratory scale. Several difficulties arise at the time of preparation and optimization of formulation such as to obtain smaller beads with narrow size distribution, to get morphological ununiformed, tedious bulk production, and lengthy process [11]. The present process of beads formation was provided morphologically uniform, desire sized beads with narrow size distribution, and facilitate automation for bulk production.

The present work was stressed on process parameters. Process parameters had shown major influence on the physical appearance and micrometric properties (particle size, flow, and compressibility) of the prepared beads [12]. In respect to the results of process parameters, handling capacity of the assembly and primary optimization of process parameters were evaluated based on morphologic studies (appearance and shape).

CONCLUSION

The process experimental study was used novel assembly for bead generation and developed a uniform, spherical shaped, and smooth surfaced beads. With help of changes in process parameters, there could be possible to get beads with desired morphological properties. However, there is a need for modification in assembly for the scale-up process at the industrial level.

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AUTHORS CONTRIBUTION

Samir A. Atara had performed the experiment and written the manuscript for intellectual content. Moinuddin Soniwala had guided the study and collected the data.

COMPETING INTERESTS

Authors have disclosed that they have no any conflict of interest or the other interest regarding results/discussion reported in the study.

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