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 16α-hydroxy prednisolone, which has no or negligible (<1/100) targeted pharmacological 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. 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.

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 continuous 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 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 nozzle. 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.

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
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 caliper (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 = 0.038, 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 | 0.4 | 0.6 | 0.6 | 0.6 | 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 | 1.07±0.05 | 83.11±0.49 | 2.668±0.21 | 80.98±1.88 | 97.36±1.23 |
| P2    | 86.25±1.25 | 1.08±0.04 | 82.97±0.38 | 2.671±0.23 | 87.36±1.58 | 97.55±1.56 |
| P3    | 84.23±1.27 | 1.07±0.06 | 83.34±0.49 | 2.663±0.25 | 83.19±2.36 | 95.21±1.65 |
| P4    | 88.61±1.31 | 1.09±0.07 | 83.46±0.28 | 2.661±0.19 | 85.23±3.27 | 99.51±1.69 |
| P5    | 85.32±1.32 | 1.10±0.08 | 82.97±0.25 | 2.673±0.18 | 80.47±2.06 | 99.31±1.73 |
| P6    | 84.27±1.39 | 1.10±0.09 | 83.18±0.31 | 2.666±0.16 | 82.69±2.49 | 97.81±1.27 |
| P7    | 86.15±1.42 | 1.11±0.04 | 82.41±0.19 | 2.671±0.22 | 76.18±3.52 | 98.15±1.17 |
| P8    | 88.19±1.43 | 1.10±0.03 | 82.36±0.13 | 2.672±0.29 | 79.41±3.71 | 96.76±1.19 |
| P9    | 86.28±1.45 | 1.12±0.07 | 83.26±1.31 | 2.642±0.23 | 82.12±3.52 | 97.81±1.21 |
| P10   | 70.18±1.01 | 1.24±0.09 | 80.36±1.68 | 2.682±0.28 | 70.18±4.12 | 96.23±1.12 |

| ‘q’ | >5.98 | >5.98 | >5.98 | >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 multiparticulate 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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