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DEVELOPMENT OF CLARITHROMYCIN GASTRORETENTIVE MICROSPHERES

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ABSTRACT

Gastroretentive microspheres of clarithromycin were prepared on the principle of cation induced gelification using sodium alginate and pectin. These microspheres were investigated for micromeritic properties, drug entrapment, mucoadhesion and drug release properties. Microspheres were found to be discrete, spherical and free flowing. Microspheres were found to adhere to gastric mucosa with high affinity and showed controlled drug release.

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INTRODUCTION:

H. pylorus infects approximately 50% of the adult formulation; is associated with a wide range of upper gastrointestinal diseases like peptic ulcer and gastric cancer. The widely used drugs for the eradication of *H. pylori* failed to treat the disease fully, might be due to the fact that the drug does not remain in the stomach for long period and do not attain minimum inhibitory concentration in the gastric mucosa. Stomach specific drug delivery systems can prolong the residence time of drug in the stomach, thereby continuously release the drug in the infected area. Mucoadhesive dosage forms have been widely used for site-specific targeting for both local and systemic drug delivery and have also been beneficial for the treatment of *H. pylori* infection. Mucoadhesion involves strong interaction between polymer and mucus lining of the tissue which increases contact time, permits localization, and prolongs drug absorption.

MATERIALS AND METHODS:

Clarithromycin (CLA) was obtained from Alkem labs. (Daman, India) as gift sample. Sodium Alginate and Pectin were procurred of Loba chemie Pvt. Ltd., Mumbai brand (LR grade).

Preparation of Microspheres

Microspheres were prepared employing method of Rajaonarivony *et al.* with some modification on the principle of cation-induced gelification. Aqueous dispersions of sodium alginate and Pectin were prepared in varying ratio of 1:1, 2:1, 3:1, 2:1, 2:2, 2:3, 3:1, 3:2, 3:3 respectively with proper mixing on magnetic stirrer. Clarithromycin 250 mg was added in polymeric dispersion with continuous stirring for 5 minutes. Calcium chloride (1 mL, 18 mmol L^{-1}) was added into 20 mL of the above drug polymer dispersion followed by stirring for 30-45 minutes. The microspheres so prepared were collected by decantation technique, washed repeatedly with deionized water and dried at 45^0C for 12 hr[1].

Characterization of Microspheres

Surface morphology of the microspheres was done using scanning electron microscopy (SEM) (Joel 6100, Japan). All microsphere formulations were sprinkled on a double adhesive tape, which was previously stuck to an aluminum stub. The stubs were coated with gold up to a thickness of about 300 Å under an argon atmosphere using a gold sputter module in a high-vacuum evaporator. Prepared samples were randomly scanned and photomicrographs were obtained using electron microscope. Compressibility and flow properties were then determined.

Drug Entrapment Study

Hundred milligrams of the microparticles were placed in 100 mL of phosphate buffer (pH 7.4) and allowed to disintegrate completely for 4 hr. The drug concentration in the buffer was analyzed at 353 nm using UV-visible spectrophotometer (Shimadzu 1800) and percent drug entrapment was calculated [2].

$$\% \text{ Drug entrapment} = \frac{\text{Calculated drug content}}{\text{Theoretical drug content}} \times 100$$

Percent mucoadhesion

The mucoadhesive properties of the mucoadhesive microspheres were evaluated by in vitro wash-off test

[3].A 1x1 cm piece of stomach mucosa was mounted on to a glass slide with cyanoacrylate glue and rinsed with 0.1N HCL. Fifty microspheres were spread on to it and kept in USP tablet disintegrating test apparatus containing the 900 ml of 0.1N HCL at 37± 0.5°C. Number of microspheres still adhering to tissue were calculated after 30 min, 1 hr and at the hourly intervals up to 6 hr. The studies were carried out in triplicate.

$$\% \text{ Mucoadhesion} = \frac{\text{No.of microspheres adhered at the end of 6th Hour}}{no.of\ microspheres\ spread} \times 100$$

Dissolution Study

The release rate of clarithromycin microspheres was determined in a USP XXIII paddle type 2 dissolution apparatus. Weighed quantity of microspheres equivalent to 100 mg of clarithromycin was filled into a hard gelatin capsule (#2) and placed in the paddle of dissolution apparatus. The dissolution medium (900 mL) of SGF (pH 1.2) was used as dissolution medium. The dissolution fluid was maintained at 37±0.5 ^{0}C and rotation speed of 100 rpm. The sample of 5 mL was withdrawn at the intervals 30 min of and was filtered through 0.25 µm membrane filter. The volume of the dissolution fluid was maintained by adding 5 ml of fresh dissolution fluid after each withdrawal. Samples were analyzed at 353 nm^2.

Statistical analysis

In vitro drug release of CLA from CLAP3b was statistically treated by one-way analysis of variance, ANOVA followed by Dunnet's test where P<0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Microspheres were prepared by cation-induced controlled gelification of the polymer. The particle size, compressibility index, and angle of repose of the prepared microspheres was found in the range of 106 ±2.13to 180±0.78, 15.26±0.56 to 21.22±0.78, 23.67±0.04 to 27.78±0.03. The particles were found to be discrete, spherical and free flowing. The entrapment effieciency and percent mucoadhesion were found to be in the range of 70.25±0.02 to 62.24±0.02 and 40.1±1.2 to 80.4±3.9 respectively. The formulation CLA3b is opted as best formulation as it has optimum micromeritic properties, maximum entrapment efficiency and percent mucoadhesion.

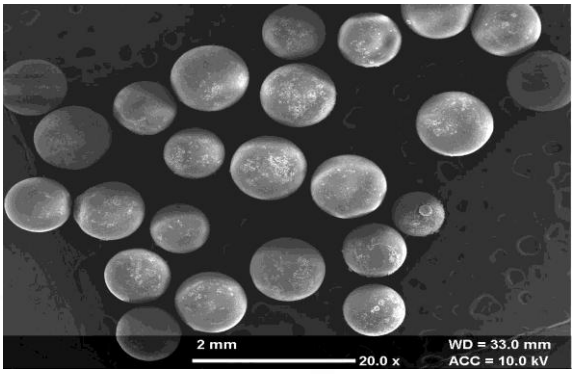

Figure 1: SEM Photograph of formulation CLA3b

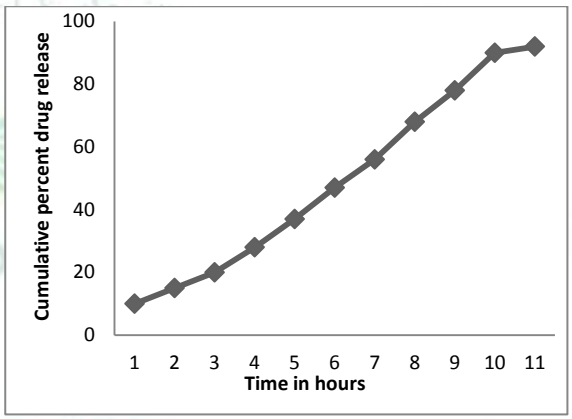

Figure 2: Cumulative % drug release profile of CLA3b in simulated gastric fluid (pH 1.2) at 37°C ± 0.5°C.

Table 1: Micromeritic properties, (%) drug entrapment and (%) mucoadhesion of the microspheres

Formulation code	Sodium alginate : pectin Ratio	Average Particle size (µm)	Compresibi-lity index (%)	Angle of repose in degree (^{o})	Drug Entrapment (%)	Mucoadhesion (%)
CLA 1a	1:1	110±2.13	21.22±0.78	26.27±0.02	62.24±0.02	40.1±1.2
CLA1b	1:2	108±1.43	19.67±0.79	27.78±0.03	65.67±0.04	45.2±0.01
CLA1c	1:3	106±2.13	17.78±0.56	27.98±0.02	62.57±0.02	50.2±0.06
CLA2a	2:1	144±0.34	17.56±0.57	25.98±0.04	67.46±0.01	50.4±0.04
CLA2b	2:2	140±0.27	15.34±0.47	25.45±0.05	69.36±0.03	55.4±1.4
CLA2c	2:3	139±0.45	15.26±0.56	24.67±0.03	66.58±0.02	65.5±0.08
CLA3a	3:1	180±0.78	15.45±0.37	23.67±0.04	65.45±0.04	65.6±0.09
CLA3b	3:2	179±0.68	16.67±0.25	25.01±0.06	70.25±0.02	80.4±3.9
CLA3c	3:3	175±0.86	17.62±0.47	26.24±0.04	64.25±0.02	75.3±0.06

CONCLUSION:

Gastroretentive Clarithromycin microspheres were successfully prepared with significantly enhanced mucoadhesiveness and controlled release. Such developed formulations could be furthers subjected for *in vivo* studies in future.

REFERENCES:

1. Rajaonarivony M, Vauthier C, Couarraze G, Development of a new drug carrier made from sodium alginate, JPS, 1993, 82, 912–917.
2. Tripathi GK, Formulation and evaluation pH stimuli sensitive multiparticulate delivery system of Clarithromycin for the treatment Of *Helicobacter pylori*, IJPTR, 2013, 5, 7-16.
3. Lehr CM, Bouwstra JA, Schacht EH, Junginger HE, *In vitro* evaluation of mucoadhesive properties of chitosan and some other polymers, IJP, 1992, 78, 43-48.