Beads of gellan gum and gellan gum/pectin: comparative study of mucoadhesional and dissolution properties

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ABSTRACT SUMMARY
In the present work, gellan gum and pectin, two natural polysaccharides with mucoadhesive properties, were used to prepare beads through ionotropic gelation technique. Aluminium chloride was used as crosslinking agent, ketoprofen (KP) as model drug and the mucoadhesiveness and dissolution profile were evaluated.

INTRODUCTION
Multiparticulate systems, such as beads, present several advantages compared to single unit dosage forms, such as more predictable gastric emptying time, a more uniform distribution over a larger area of the gastrointestinal tract (GIT) and a reduced risk of mucosa irritation due to drug accumulation¹.

Gellan gum is an anionic polysaccharide with gelling properties and mucoadhesive ability what makes it a promising material for pharmaceutical application in controlled drug delivery systems²-⁶. Its use have been exploited in nasal delivery systems⁷, ocular⁸, and in several sites of oral route³, ⁹, ¹⁰. Pectin is a natural polysaccharide with a well-known mucoadhesive propertie. Numerous works have studied its use in colon-specific and controlled drug delivery systems¹¹-¹³. Recently it has been used in tissue engineering¹⁴, gene targeting¹⁵ and in wound healing¹⁶. In acid pHs pectin has the ability to remain as aggregates of macromolecules and can resist to enzymes like amylase and proteases, being digested specifically in the colon¹¹.

Mucoadhesive drug delivery systems adhere to the mucus layer present in the GIT mucosa, remaining for longer periods and in a closer contact with the site of absorption thus drug bioavailability can be improved¹⁷.

EXPERIMENTAL METHODS

Beads preparation
Aqueous dispersions of gellan gum (2%) or gellan gum:pectin (4%, 1:1) containing KP (1%) was dripped into Al³⁺ solution 3% or 5%, using syringe and flat-tipped needles (23G). Crosslinking reaction was kept by additional 20 minutes for strengthening of the beads. After, beads were separated by filtration, washed with distilled water and dried at room temperature until constant weight (3% of humidity) and kept in a desiccator.

In vitro mucoadhesion
The mucoadhesiveness of beads was analyzed by in vitro adsorption of mucin. Beads were dispersed in mucin solutions (50, 100, 150 e 200 µg/ml) and incubated in thermostatic bath at 37°C for 1 h. Then, the dispersions were centrifuged at 3000 rpm (2 min). The supernatant was used to quantify the free mucin content by colorimetric assay using a Lowry protein assay modified by Peterson in a spectrophotometer UV-Vis at 749 nm.

In vitro drug release
This analysis was performed on a Hanson Dissolution Test Station SR8-Plus (Chastworth – USA) equipped with USP apparatus 1 (basket) at 50 rpm. The experiment was conducted using media with different pH values at 37°C: simulated gastric media (900 mL of 0.1N HCl pH 1.2 with sodium lauryl sulfate 0.75%) during 120 minutes and simulated enteric medium (900 mL of phosphate buffer pH 7.4) during 270 minutes. At appropriate time intervals, aliquots of 3 ml were withdrawn and immediately replaced with fresh dissolution media. The amount of drug release was quantified using a UV-Vis spectrophotometer at 258 nm and 260 nm, for gastric and enteric media, respectively.
RESULTS AND DISCUSSION

The amount of adsorbed mucin increased with increasing mucin concentration for all beads. However, the amount of adsorbed mucin was not influenced by polymers (p>0.05). The high values of adsorbed mucin evidence the high mucoadhesiveness of the beads.

![Figure 1](image1.png)

**Figure 1** - Relation between the amount of mucin added and the mucin adsorbed on different beads.

Approximately 72% of free KP was dissolved in acid pH and dissolution was completed in phosphate buffer (pH 7.4) after 180 minutes (Fig. 2). Beads containing only gellan gum (G2%-A13% and G2%-Al5%), released 42 and 45% of the drug after 120 min (pH 1.2), respectively.

![Figure 2](image2.png)

**Figure 2** – *In vitro* release profile of ketoprofen free and from beads in simulated gastric and enteric media.

KP release profile from gellan gum/pectin beads evidenced the significant decrease of release rates in acid media, releasing only 33 and 19% for beads GP4%-A13% and GP4%-Al5%, respectively. For all beads, the drug release was completed in pH 7.4, after 240 min. The presence of pectin decreased the drug release in acid media (about 2.4 times).

CONCLUSION

All beads presented high mucoadhesive ability. The drug dissolution rates from beads were decreased and a pH-dependent drug release behavior was observed. The presence of pectin contributed to reduction of drug release rates.

REFERENCES


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