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EFFECT OF IBUPROFEN AND IBUPROFEN INCORPORATED BIODEGRADABLE ALGINATE BEADS ON GASTRIC AND DUODENAL MUCOSA (A COMPARATIVE HISTOLOGICAL STUDY) Sema Çalis¹, Betül Arica¹, Pergin Atilla²,Tugba Durlu³,Nur Çakar², A.Atilla Hincal¹

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ABSTRACT SUMMARY:

In this study, the effect of ibuprofen, which is a widely used Non Steroidal AntiInflammatory Drug, was evaluated on gastric and duodenal mucosa when administered in 0.5% CMC and in alginate beads. Erosive effect of ibuprofen on gastric mucosa seemed to dissappear when administered as alginate beads.

INTRODUCTION:

well known Ibuprofen is a nonsteroidal antiinflammatory drug and is the first phenylalkanoic acid approved by the FDA for general analgesic use. The most frequent adverse effects occuring with ibuprofen are gastrointestinal disturbances, peptic ulseration and gastrointestinal bleeding.(1,2) The formulation of ibuprofen as a controlled release dosage form of microspheres seems to be an important approach to overcome the potential problems in gastrointestinal (GI) tract so to achieve a reduction of the NSAID's adverse effects.(3,4) Therefore, the purpose of this study was to evaluate the effect of ibuprofen on gastric and duodenal mucosa of animals when administered in 0.5% CMC and also in alginate beads.

EXPERIMENTAL

Pharmacology:

All procedures used in this in vivo study were approved by Hacettepe University Ethics Committee (2001/78-4). Locally bred female albino mice weighing 22±2 g were used. The animals were housed in groups of six and acclimatized to laboratory conditions for at least 2 days before the experiments, with food and water at libitum. 24 hours before the experiment, the food was withdrawn but free access to water was allowed. Ibuprofen (100 mg/kg), alginate bead including ibuprofen were suspended in 0.5% carboxymethyl cellulose (CMC). Compounds were given orally to mice in groups of six. The animals were sacrified 7 h after the oral administration and their stomachs and intestines were removed. After macroscopic examinations, the specimens were put into 10% formalin solution for microscopic examinations.

Histology:

After removal of the stomachs and duodenums of the rats, the tissues were placed in 10% buffered formaldehyde solution and fixed for 72 hours. Afterwards tissues were processed according to routine light microscope technique. First they were dehydrated in ascending degrees of ethyl alcohol (70,80,90,96,100), then cleared in xylene and embedded in paraffine. 5 μ m paraffine sections were cut and stained with hematoxylene-eosine, examined and photographed with an Olympus BH-2 light microscope.

RESULTS

The mucosa of stomach and duodenum are composed of surface epithelium, lamina propria and muscularis mucosae. The lamina propria of stomach is occupied by closely packed gastric glands. In the control CMC,

Ibu+Alginate and Alginate groups, macroscopically neither ulcer nor hemorrhage was observed. Microscopically the structures of the gastric mucosa was normal. Surface epithelium of the stomach lined by columnar cells was intact and continuous. Neither erosion nor hemorrhage was observed in the gastric mucosa. Gastric glands in the lamina propria were also intact, they were neither dilated nor distorted (Fig 1). The duodenal mucosa was also normal like the gastric mucosa both macroscopically and microscopically. The structures of the villi extending towards the lumen, the Lieberkühn crypts (intestinal glands) and the other layers of the duodenal mucosa were all normal histologically (Fig 2).

In the macroscopical examination of the stomach of the Ibu+CMC group small erosive areas <1 mm in diameter were observed in some regions. Histologically there were a few eroded areas in the gastric mucosa. In these eroded areas only the surface epithelium was found to be exfoliated, whereas the gastric glands in these regions were not dilated and distorted. No hemorrhage was observed in these areas (Fig 3). In the same group the macroscopical examination of duodenum revealed no ulceration. The duodenal mucosa was found to be normal in histological examination like in the other groups(Fig 4).



Figure 1 Section from Ibu+Alginate group stomach. Gastric mucosa with continous and intact surface epithelium is seen. Gastric glands are structurally normal in appearance. Hematoxylene-eosineX200.



Figure 2: A section from Ibu+Alginate group duodenum. The mucosa of the duodenum and the other structures of the duodenal wall appear normal histologically. Hematoxylene-eosineX100.



Figure 3: In the Ibu+CMC group stomach one of the eroded areas is seen. The surface epithelium is exfoliated, whereas gastric glands are intact. Hematoxylene-eosineX200.



Figure 4: In the Ibu+CMC group structurally normal duodenal mucosa is seen, with intact surface epithelium and glands. Hematoxylene-eosineX200.

CONCLUSION:

In our study only in the Ibu+CMC group there were few eroded areas in the gastric mucosa, whereas no erosion was observed in duodenal mucosa. In the gastric mucosa only the epithelium was exfoliated, there were no congestion. Erosions were limited to the superficial mucosa and in the eroded areas necrotic tissue, and distorted areas were not seen. These observations reveal that there is no ulcer formation but superficial mild mucosal erosion in the gastric mucosa. Both the gastric mucosa and duodenal mucosa were structurally normal in other groups.

According to these findings we concluded that Ibu profen used in this dosage may lead to superficial mild mucosal erosion in the gastric mucosa, but in duodenal mucosa. Erosive effect of Ibuprofen dissappears when it was embedded into alginate, and alginate itself does not lead to any damage in gastric and duodenal mucosa.

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