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# Histopathologic study in jejunum portion of intestine by different doses of diclofenac sodium (NSAIDs) in mice models

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**ABSTRACT**

Diclofenac (NSAIDs) is an inhibitor of cyclooxygnase. Receiving Diclofenac died prior of completion of the study, exhibiting massive small intestinal ulceration and perforation. The only small intestinal abnormality observed was diffuse hypermia. So we have put our efforts to rule out the toxic menace of diclofenac in rodent's (Swiss albino) by administrating different does ranging from 0.1mg/kg body weight to 10mg/kg body weight the other doses are 0.3 mg/kg and 1mg/kg. The viable number of crypt cells in jejunal portion of intestine also reduced with increasing doses. Villi and crypt morphology and number were affected according to the dose concentration relatively higher doses induced higher damage and lower doses with lower damage.

**Key words:** Non-steroidal anti-inflammatory drug (NSAIDs), Diclofenac sodium, Swiss albino, intestinal cells, Crypt and Villi.

## INTRODUCTION

The use of nonsteroidal anti-inflammatory drug (NSAIDs) is associated with a wide array of alterations is gastrointestinal integrity and function. Various approaches have been taken to developing NSAIDs with reduced gastrointestinal toxicity, and few have been successfully reduced the incidence of adverse reactions[1]. Although NSAIDs are known to sometimes cause stomach problems, the prevalence and severity of small intestinal lesions[2]. Gastrointestinal Dyspepsia, heartburn, epigastric distress, and nausea, less frequently, vomiting, anorexia, abdominal pain, GI bleeding and mucosal lesions. Misoprostol (Cytotec), a synthetic prostaglandin that inhibits gastric acid secretion, may be given to prevent GI intolerance. It prevents gastric ulcers and their associated GI bleeding in patients receiving NSAIDs. Small intestine injury linked to traditional NSAIDs isn't as dramatic as the stomach bleeding seen in a small proportion of those who take the drug. Indeed, Graham notes that traditional NSAIDs cause problems in a small but significant percentage of people[3]. Receving Diclofenac died prior to completion of the study, exhibiting massive small intestinal ulceration and perforation. The only small intestinal abnormality observed was diffuse hyperemia. These studies demonstrate that nitrofenac has markedly reduced intestinal toxicity in healthy and colitis rats when compared to Diclofenac.

## MATERIAL AND METHODS

Swiss albino mice. Age/Weight/Size: 2-3 month's, 30 Grams to 35 Grams Gender-Male and Female both). Diclofenac sodium tablets dissolved is double distilled water in different concentrations for short and long term administration was divided into following groups: (High dose-10mg/Kg for One day only, Medium dose –1mg/Kg for 10 days only, Low –0.3mg/Kg for 30 days, Very low-0.1mg/Kg for

30 days, Control-Water without drug). Diclofenac sodium was administrated orally with different concentration of drug to separate groups from having 4-animals for each group in, low doses to high dose. The experimental animals were dissected immediately after cervical dislocation. The jejunum portion of small intestine was clean from all mesenteric fat. The jejunum lumen was flushed with normal saline, 2-3 times. It was kept moist with saline and fixed quickly to avoid degeneration of villi. The jejunum portion of the intestine was cut and fixed in Bouinis fixative for 18-12 hrs. The tissue was degraded in 30%, 50%, 70% and 100% ethanol and cleaned in paraffin wax and xylene. The tissue was embedded in parafilm wax. Five-micron thick section was cut using a rotatroy microtone. The section were spread in temperature regulated tissue float and fixed on clean slides. The section were stained with Harris Haematoxiline and counter stained with eosin. The slides were now mounted in DPX.

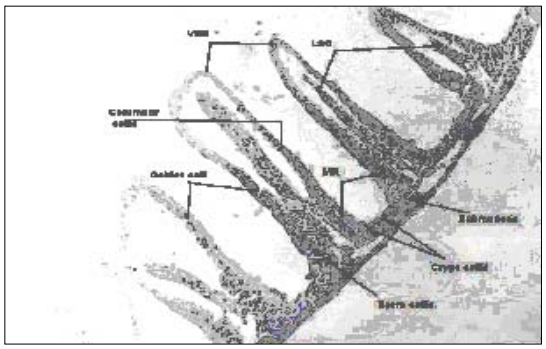


**Fig. 1: T.S jejunum portion controls, showing normal histology : Villi, Lamina propria, Sub mucous, Crypt cells. (Hematoxylin-eosin, x 60).**

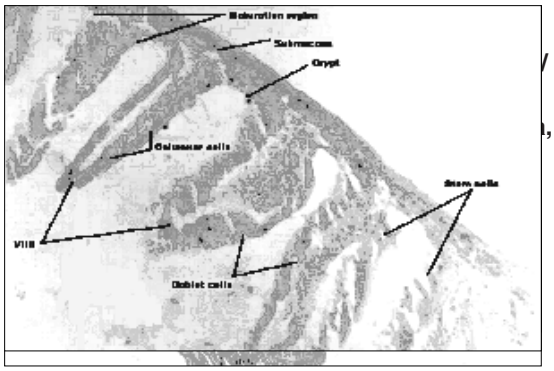



**Fig.3: Histologic T.S jejunum portion 0.3mg/kg diclofenac sodium administered group showing damage Villi, and Villi undergoing degeneration, eroted lamina propria, amage sub mucous & Crypt cells. (Hematoxylin-eosin,x 100).**

**Fig. 4: Histologic T.S jejunum portion 1mg/kg diclofenac sodium administered group showing damage Villi, eroted lamina propria, damage sub mucous & Crypt cells. (Hematoxylin-eosin,x 60).**

**Fig. 5: Magnified histologic T.S jejunum portion 10mg/kg diclofenac sodium administered group showing damage Villi, eroted lamina propria, damage sub mucous & Crypt cells. (Hematoxylin-eosin,x 100).**

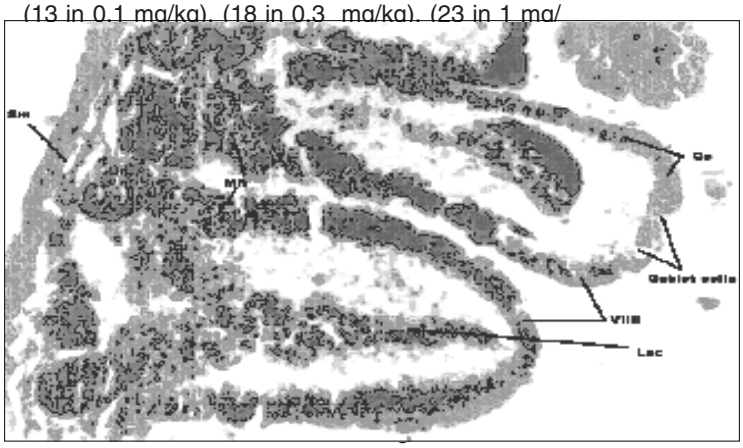
**Observation**

Changes in shape of crypt cells, villi cells and damaged villi cells were observed in test groups by using different concentration of diclofenac fed in test animal, comparing with control Fig.1. Showing normal histology: Villi. Lamina propria, Sub mucous, Crypt cells (Haematoxylin-eosin, x 60).

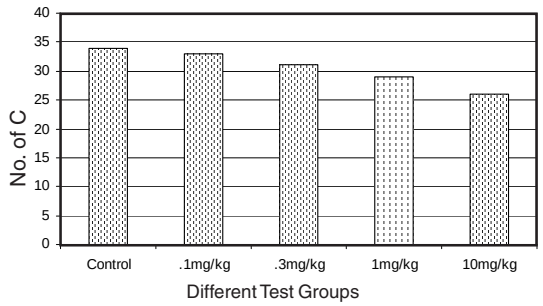
**RESULTS AND DISSCUSSION**

Reference to intestinal toxicity our data reveal's some significant changes with compare to test control there is speculate decrease in crypt cells with in increasing doses test control ranges (graph no. 1) (34 cells) in one T.S. of jejunum portion, as the doses increase cell cont decrease (0.1 mg/ kg body weight-33 cells), (0.3 mg/kg body weight-30 cell), (1mg/kg body weight 28 cells) (10 mg/kg body weight).

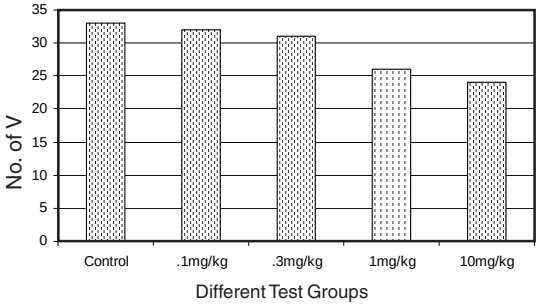
However the routine normal jejunum architectural study reveals per transect section 30-80 crypt cells and 30-100 villi cells. In a control sample the crypt and villi cells counted roughly around 30-35 this may be because of cell washed on during the slide preparation or by other etiology. Same results are counted in villi cells with test control these are control-33 villi cells, Graph –2), (0.1 mg/kg body weight-31 villi cells), (0.3 mg/kg-27),(1mg/kg- 27), (10mg/kg- 23 villi cells). Jejunum portion of intestine showing maximum cell damage with higher dose, damage villi cells increases wiht increasing dose, by comparing to test control (Graph-3) (11 villi cells are damage in control), (13 in 0.1 mg/kg), (18 in 0.3 mg/kg), (23 in 1 mg/



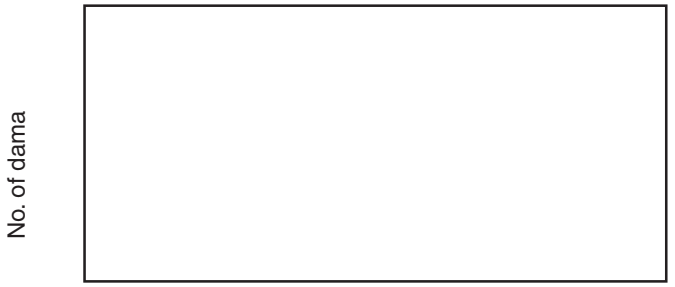

and the mean number of crypt cell is 30-45 in present study mice fed with higher concentration of diclofenac there was a high grade villi damage the maximum villi damage occurred in (10mg/kg body weight group-50% damage), (32% damage in mg/kg), (20.8% damage in 0.3 mg/kg), (10% damage in 0.1 mg/kg). The viable number of crypt cells also reduced with increasing doses. Villi and crypt morphology and number were affected according to the dose concentration relatively higher doses induced higher damage and lower doses with lower damage.



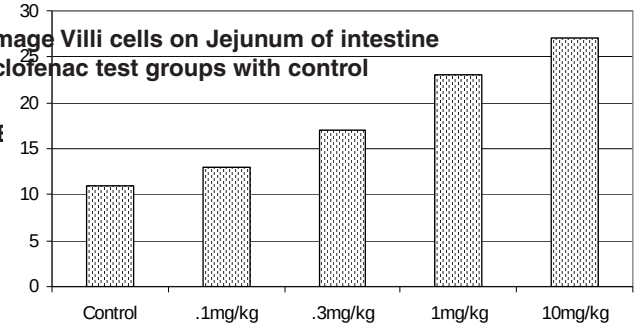

**Graph 1: Showing decrease no. of Crypt cells on Jejunum of intestine with increasing dose conc. of Diclofenac test groups with control**




**Graph 2: Showing decrease no. of Villi cells on Jejunum of intestine with increasing dose conc. of Diclofenac test groups with control**




**Graph 3: Showing increasing no. of damage Villi cells on Jejunum of intestine with increasing dose conc. of Diclofenac test groups with control**

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