

## Healing role of *Ipomoea batatas* (sweet potato) extract in aspirin induced duodenal ulcer in male albino rats; A histological and Immunohistochemical study

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### Abstract

The study was conducted in the animal house of the faculty of veterinary medicine / university of al- Qadisiyah in order to identify the role of the alcoholic extract of sweet potato roots *Ipomoea batatas portrico* in the treatment of aspirin induced gastric ulcer by using 70 male rats of *Rattus norvegicus*. The animals was divided into two main groups as follows: the negative control group (C) was given the standard diet and distilled water only and the treatment groups (T), which developed peptic ulcer through oral dosage of (100 mg / kg body weight aspirin) for one week and then sacrificed 5 animals to confirm the presence of gastric ulcer and conducting the gross examination of the test. The treatment groups were divided into three groups, the first treatment group was considered as a positive control group (T1) or aspirin group only. The second group (T2) treated with (800 mg / kg body weight) extract of the sweet potato root by oral dose once daily for three consecutive weeks. The third treatment group (T3) was treated omeprazole orally (20 mg/kg bw) once daily for three consecutive weeks. The stomach was removed from each animal for the purpose of examining histological changes using three different stains: haematoxylin and eosin, Masson's trichrome and periodic acid-schiff stain (PAS). The immunohistochemical technique was used to identify the epidermal growth factor receptors. The results of the histological examination using hematoxylin and eosin showed histopathological changes in the treatment group with aspirin in the duodenal tissue. The presence of ulcers, congestion and infiltration of inflammatory cells and bleeding and a clear reproduction of eucalyptus cells, as noted for the mucous layer of muscle mucosa in the tissues of the duodenum, while the disappearance of ulcers, bleeding and signs of congestion and gradual healing progress of the extension of experience in animals treated with both the extract of sweet roots of sweet potatoes (T2) The standard treatment (Omeprazole) (T3). The results showed that there was a small or no amount of mucus and collagen fibers in the treatment group with aspirin (T1). However, there was a gradual increase and a gradual increase in the amount of mucus and collagen fibers in the stomach tissue. Three in the second and third treatment groups (T3, T2).

The results of immunohistochemistry of the duodenum showed no immune response to epidermal growth factor receptors in the T1-treated animals group. Immunogenesis was either very poor or nonexistent, while a gradual increase in immune reaction and pigment strength was observed in the two groups of sweet potato extract (T2) and Omeprazole (T1) group with the duration of treatment was more pronounced in the animals of the second group (T2).

Aim of the study: to strengthen and confirm the role of sweet potatoes as a means of promoting health and alternative treatment of duodenal ulcer.

### Introduction

Duodenal ulcer is erosion and rupture of the mucosa due to a number of factors, most notably the imbalance in the secretion of gastric acid and Pepsin, which affect the proportions of Bicarbonate and Prostaglandin, which are important defensive factors (21) The digestion of the mucosa with acid and Pepsin is based on the fact that the duodenal ulcer is mostly due to gastric dysfunction.

An important cause of the ulcer is the infection of *Helicobacter pylori* and the use of non-steroidal anti-inflammatory drugs (NSAIDs), such as Aspirin, which are used as anti-inflammatory or to prevent the occurrence of blood clots, and the excessive use of these drugs led to increased secretion of gastric acid. Low blood flow and gastrointestinal mucosa damage (19). Although there are several types of medicines in the treatment of ulcers such as antacids and the group of Proton pump inhibitors such as Omeprazole and the group of anti-

histamine H<sub>2</sub>-Receptors antagonists such as Rantidine and the success of these drugs in the healing of many cases of ulcers, but these drugs side effects such as disturbance strikes Heart, dry mouth, difficulty breathing, headache (30). This is why nature has been approached to find safe plant or animal alternatives free from side effects or that their effects are limited. (7) have referred to the use of many plants in the treatment of ulcers.

*Ipomoea batatas* (L) is a medically important herb for its rich and effective contents. It is an important and natural source of antioxidants and anti-inflammatory drugs. It also contains many vitamins, minerals, fiber and sugars that have a role in reducing the risk of chronic diseases. They also contain important phytochemicals for human health, a plant that is multi-use and underutilized (24).

It is also an important food source in many countries, especially South Africa, for its high content of carbohydrates and saturated fats (4). Several studies have indicated their role in the treatment of tumors and ulcers. They are also used in the treatment of hypertension and diabetes treatment. It is antibacterial and fungal as well as anti-cancer as well as its role in improving the mood and psychological state of its containment of minerals (12) The sweet potato has a major role in the treatment of gastrointestinal disorders including gastrointestinal ulcers and the treatment of tumors and mouth ulcers (14) and to strengthen and confirm the role of sweet potatoes as a means of promoting health and alternative treatment of ulcer.

## Materials and methods

### Collection and preparation of plant samples:

The sweet potato plant was obtained *Ipomoea*. Department of Horticulture - Faculty of Agriculture - University of Baghdad. And then brought to the laboratory isolated the roots of the plant and washed with distilled water to remove the dust and dirt, then cut the knife into small pieces and dried in the shade to get rid of water and then use the electric oven at a temperature of 40 m for the disposal of the rest of the water. The dry roots were grinded using an electric mill and the crushed material was kept in glass containers until extraction. Has been classified at the College of Agriculture \ University of Baghdad as the local type *Ipomoea* potato. 20gm of Sweet

Potato powdered leaves were taken and extracted with soxhlet apparatus ethanol 70% Within 24 hours, and then taking the extract and place it in a ptry dish and put in the oven at a temperature of 40°C within 48 hours, The result of extract was stored at 4°C until use (13).

## Experimental animals

*Rattus norvegicus* was obtained from the Animal House at the Faculty of Veterinary Medicine, University of Qadisiyah. It was placed in plastic cages 50 x 35 x 15 centimeters in size and weighing between 200-250 grams. The floor of the cages was sprayed with sawdust and the cages were cleaned and sterilized with disinfectants. The animals were subjected to the same laboratory conditions in terms of ventilation, temperature (23-25 ° C) and humidity (45-50%). Lighting was organized at 14 hours lighting and 10 hours darkness length of study. Animals were given a standard laboratory food feed (19% protein and 3000 calories energy).

## Experimental design

In this study, 70 male rats with a weight of 200-250 mg were used. After one week of acclimatization, they were divided into four equal groups..

1- Negative control group (non-treatment) (C): This group was given distilled water only for the duration of the experiment. 2 - positive control group (T1): which developed ulcer by giving the drug aspirin (100 mg / kg body weight) for a period of (7) consecutive days.

3- Treatment group II (T2): The ulcer was developed by giving aspirin (100 mg / kg body weight) for 7 consecutive days. The sweet extract of sweet potato roots was given 800 ml / kg body weight daily for 21 consecutive days. 4 - treatment group III (T3): also was developed ulcer by giving the drug aspirin (100 mg / kg body weight) for a period of (7) consecutive days. The drug was then given Omeprazole (20 mg / kg) of body weight for 21 consecutive years.

**Preparation of aspirin and omeprazole:**In order to obtain the required dose aspirin and omeprazole a solution was prepared depending on ( 27,28 ).

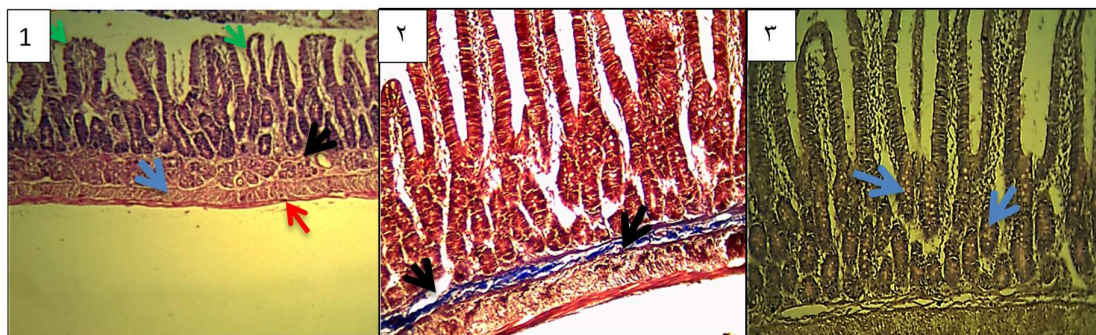
**Development of duodenal ulcer:** Intestinal ulcer was introduced in all experimental groups except the negative control group by giving aspirin (100 mg / kg) of body weight by a single dose daily after starving the animals for 14 hours before giving aspirin for 7 consecutive days. Five animals were killed each A group to confirm the infection of the ulcer by anesthetizing the animals then sacrificed five animals from each group at the end of the first week and the second and third after 7 and (14) and (21) days to detect the healing of the ulcer.

**Histological Sections:** The method (5) was followed for the purpose of preparing textile sections. The special stains The method (9,20) were followed for the purpose of preparing textile sections.

**Study of immunohistochemical:** Textile sections were prepared according to manufacturer's instructions (DAKO EnVision FLEX, Denmark) .

## Results

The histological examination of sections of the duodenum and stained with haematoxylin-eosin for animals a negative control group (C) showed that the wall consisted of four main layers, respectively, from the inside out: the mucosa layer, in the form of paper structures, representing villi and extending at the bases of these glands Intestinal glands or so-called crypts of lieberkuhn within the connective tissue component of the original plate and included the mucus layer muscle formed from strips of muscle fibers smooth and represent the muscle layer mucus Muscularis mucosae The mucous layer was based on another layer of connective tissue representing the submucosa and outside of it, the external muscle layer Muscularis externa, and two secondary layers, one of which is the circular arrangement to the inside and the other the longitudinal arrangement outward and the serosa layer outside (image1) On the other hand, the tissue test using the Masson's trichrome stain showed a dense presence of collagen fibers in the (C) control group (image2). When using a PAS stain, positive reaction was observed with the stain (image3).

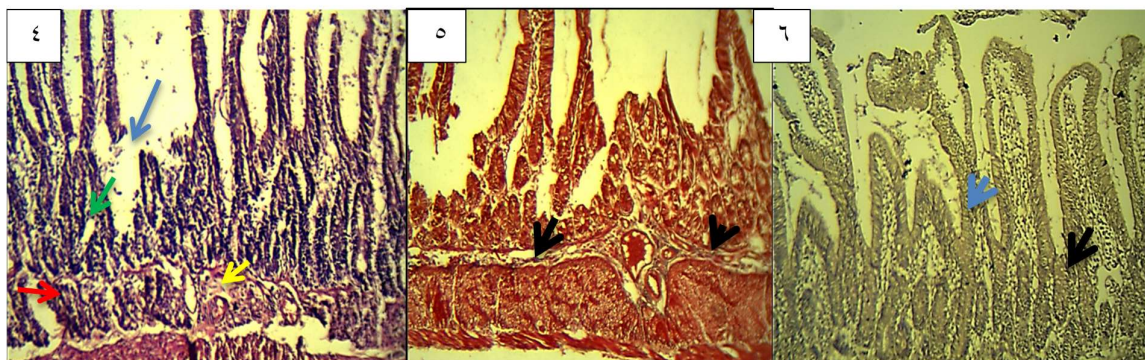


**Image(1)**A section in the duodenum of the rat from the control group (C) shows the normal structure of the four main layers: the mucous layer (the green arrow), the subatomic layer (the black arrow), the muscle layer (blue arrow), Serosa layer (red arrow) (H & E, 20X). image(2) A section in the duodenum of the rat from the control group (C) shows the blue collagen fibers present naturally and intensely (black arrow) (Masson, 50X).image(3) A section in the duodenum of the rat from the control group (C) shows Positive reaction (+) with stain (blue arrow) (PAS, 50X).

glands) in the subcutaneous layer (image4). In the sections stained with the (Masson), it was observed that there is a slight presence of collagen fibers, which appeared in pale blue (image 5) and when dye pigmented periodical detector (PAS) observed lack of existence of cells Goblet cells and the intensity of the interaction is very weak Compare with control group (C) (image 6).

Tissue histopathological changes in the duodenum T1 sections, in which only aspirin ulcers, haematoxylin and eosin dyes were injected with some parts of the mucosa with severe degeneration of the glands, damage to the intestinal glands (lieberkuhn), muscular mucosal layer, Inflammatory cells as well as bleeding and decomposition of the duodenal glands (Bruner

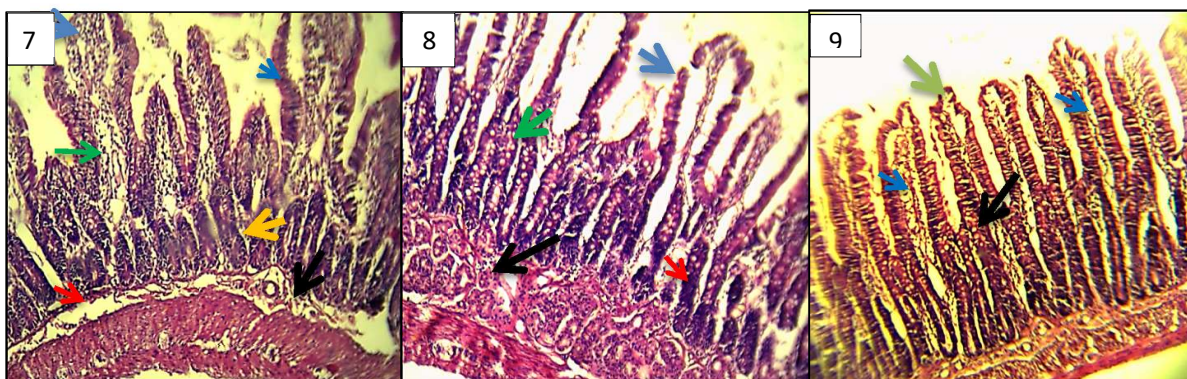




**image(4)** A section of the duodenum of the rat of the first treatment group (T1) Showing mucous membrane dissociation with severe degeneration of the villi (blue arrow), damage to the intestinal glands (green arrow), inflammation of the inflammatory cells (yellow arrow) (H & E, 50X). **image(5)** A section of the duodenum of the rat of the first treatment group (T1) Showing a slight presence of collagen fibers (black arrow) (Masson, 200X). **image(6)** A section of the duodenum of the rat of the first treatment group (T1) Showing The lack of goblet cell (blue arrow) and weak interaction (black arrow) (PAS, 50X).

was a proliferation of goblet cells and it was observed that the striated border of the villi was recombined with infiltration of defensive cells, increased elongation of the cysts and increased thickness of the mucosal layer with degeneration of some of the Brunner glands in the subcutaneous layer (image8. ) At the end of the third week, the planned edge of the absorptive cells and the exponential increase in the number of goblet cells were observed with the presence of ribbons of muscle fiber belonging to the mucosal layer of the villi core (image 9).

On the other hand, when the animals were treated with the sweet extract of sweet potato roots in the second treatment group (T2) and at the end of the first week The histological examination of the duodenum haematoxylin and eosin showed that there was Hyperplasia in the goblet cells and a clear elongation of the intestinal glands And the beginning of thickening of the musculoskeletal layer with a slight hemorrhage in the subcutaneous layer (image7) At the end of the second week there



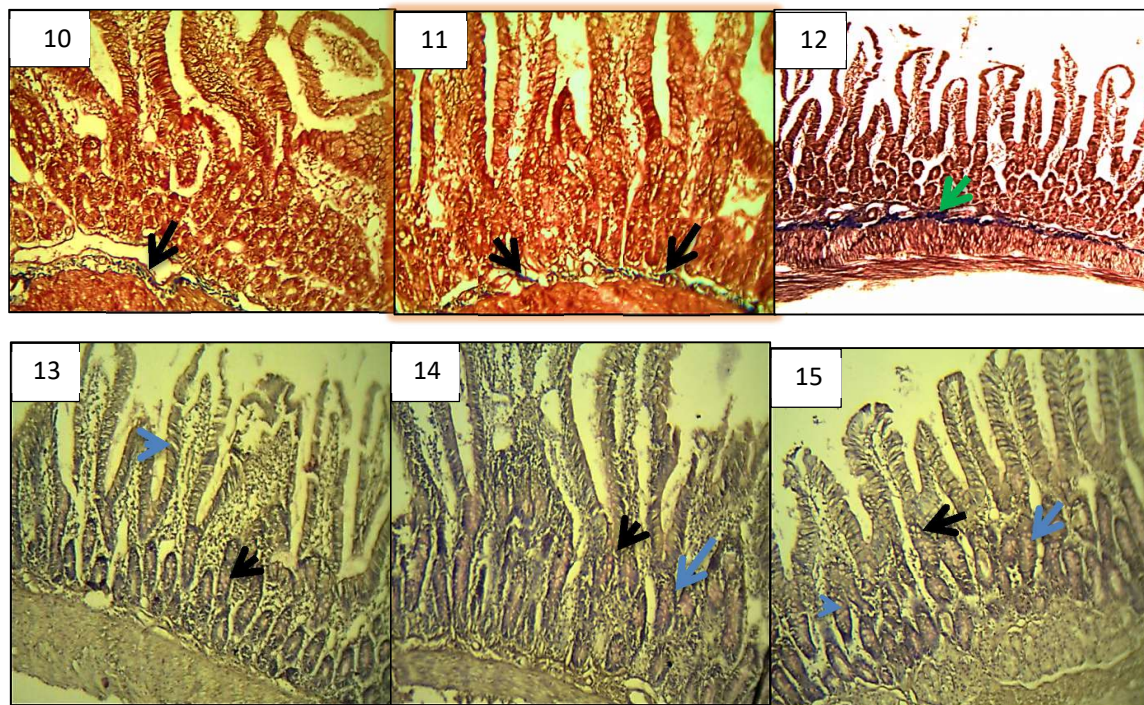
**image(7)** A section of the duodenum of the rat of the second treatment group (T2)in the first week Showing Hyperplasia in the goblet cells (blue arrow) elongation in the intestinal glands (yellow arrow) with minor hemorrhage in the subcutaneous layer (black arrow) and thickening of the mucosal muscle layer (red arrow) and inflammation of inflammatory cells (green arrow) (H & E, 50X). **image(8)** A section of the duodenum of the rat of the second treatment group (T2)in the second week showing The striated border of the villi (blue arrow) is a clear reproduction of the goblet cells(green arrow), the degeneration of some of the Brunner glands(black arrow) and the elongation of the intestinal glands (red arrow) (H & E, 50X). **image(9)** A section of the duodenum of the rat of the second treatment group (T2)in the third week showing The striated border of the villi



(green arrow) and an increase in the number of goblet cell (black arrow) are completed with the presence of ribbons of the muscle fibers within the pulp of the villi (H & E, 50X).

histological sections of a periodic liposuction pigment (PAS) was observed, there was an increase in both the goblet cells and the intensity of the reaction with the dye gradually increased over a period of time the experiment was more pronounced at the end of the third week (images13,14,15)

The deposition of collagen fibers in the animals of the second group (T2) using the stain of the (Masson) showed a gradual increase in the amount of collagen fibers within the subcutaneous layer and the highest density of these fibers at the end of the third week (images10,11,12). When staining the



**image(10)** A section of the duodenum of the rat of the second treatment group (T2) in the first week showing the collagen fibers in a light (black arrow) (Masson, 50X). **image(11)** A section of the duodenum of the rat of the second treatment group (T2) in the second week showing medium collagen fibers (black arrow) (Masson, 50X). **image(12)** A section of the duodenum of the rat of the second treatment group (T2) in the third week showing collagen fibers that are thicker than the previous two weeks (green arrow) (Masson, 50X). **image(13)** A section of the duodenum of the rat of the second treatment group (T2) in the first week showing the beginning of the increase in the number of goblet cells (blue arrow) and the beginning of interaction with the dye (+) (black arrow) (PAS, 50X). **image(14)** A section of the duodenum of the rat of the second treatment group (T2) in the second week showing an increase in the number of goblet cells (black arrow) and clear interaction with the dye in the region of the glands (blue arrow) positive interaction (++) (PAS, 50X). **image(15)** A section of the duodenum of the rat of the second treatment group (T2) in the third week showing clear propagation of the goblet cells (black arrow) and positive interaction (+++) in the glands region (blue arrow) (PAS, 50X).

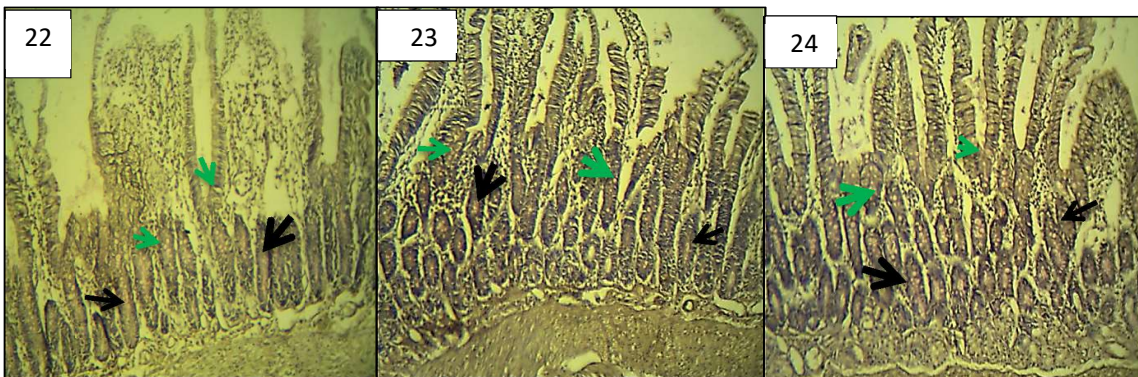
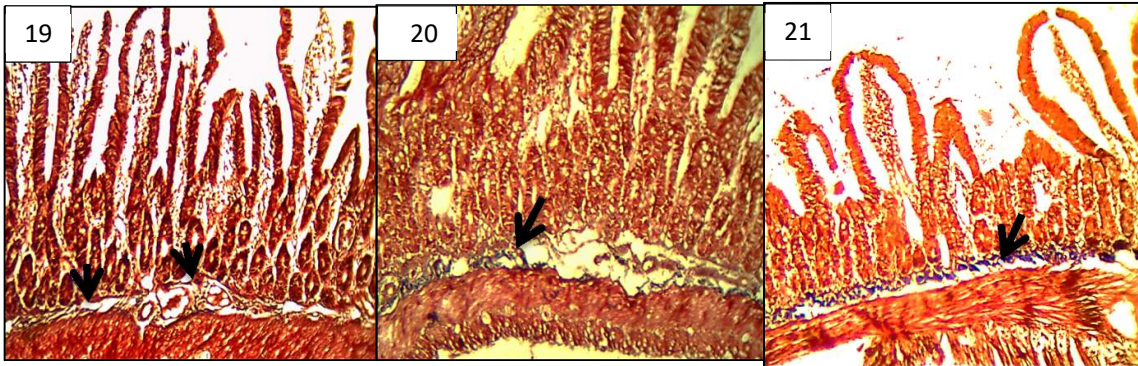
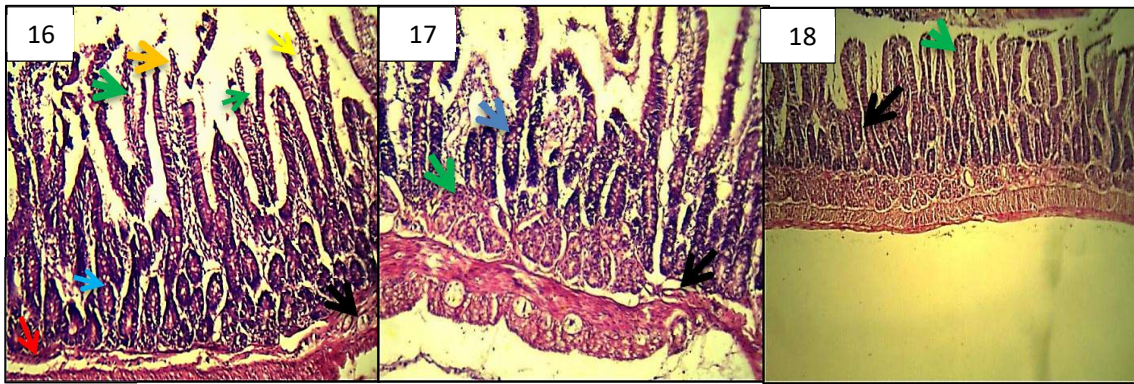
and a clear elongation of the intestinal glands (Lieberkuhn glands). Inflammation of inflammatory cells and clear thickness of the mucosal layer and expansion of blood vessels in the subcutaneous layer (image16). Partial healing of the surface of the villus and an increase in the

The cross-sectional passages from the duodenum group omeprazole (T3), which were dyed with haematoxylin and eosin, showed a partial degradation of the surface of the villus accompanied by high segmental activity of the epithelial cells surrounding the rest of the villi



collagen fibers in the subcutaneous stratum. The duration of treatment ranged from low deposition at the end of the first week and the average at the end of the second week and then deposition of high density at the end of the third week (images 19,20,21) When dyeing the (PAS) was also observed a gradient in the intensity of the reaction was gradually increased during the three weeks as well as a gradual increase in the abundance of epithelial cells over the three weeks (images 22,23,24)..(

number of goblet cells were observed with inflammatory cell infiltration and congestion in the vessels at the end of the second week (image17). At the end of the third week, the growth of the villus surface was observed with an abundance of goblet cells and thus healing the ulcer (image18). The histological sections of this group (T3) using special stains showed results similar to those observed in the T2 group when stained with the Masson It was noted that there was also a gradual increase in the deposition of





**image(16)** A section of the duodenum of the rat of the third treatment group (T3) in the first week Showing Partial dissolution of the surface of the villus (yellow arrow) with congestion of blood vessels (black arrow) and inflammation of inflammatory cells (green arrow) and thickness of the muscle layer (red arrow) with elongation of the intestinal glands (blue arrow) (E & H, 50X).

**image(17)** A section of the duodenum of the rat of the third treatment group (T3) in the second week Showing An increase in the goblet cells (blue arrow) with inflammatory cells (green arrow) and blood vessel congestion (black arrow) (E & H, 50X).

**image(18)** A section of the duodenum of the rat of the third treatment group (T3) in the third week Showing the healing of the planed edge of the villi (green arrow) and abundance in the preparation of goblet cells (black arrow) (E & H, 20X).

**image(19)** A section of the duodenum of the rat of the third treatment group (T3) in the first week Showing the collagen fibers in a light (black arrow) (Masson, 50X).

**image(20)** A section of the duodenum of the rat of the third treatment group (T3) in the second week showing Medium collagen fibers (black arrow) (Masson, 50X).

**image(21)** A section of the duodenum of the rat of the third treatment group (T3) in the third week showing Collagen fibers are thicker than the previous two weeks (black Arrow) (Masson, 50X).

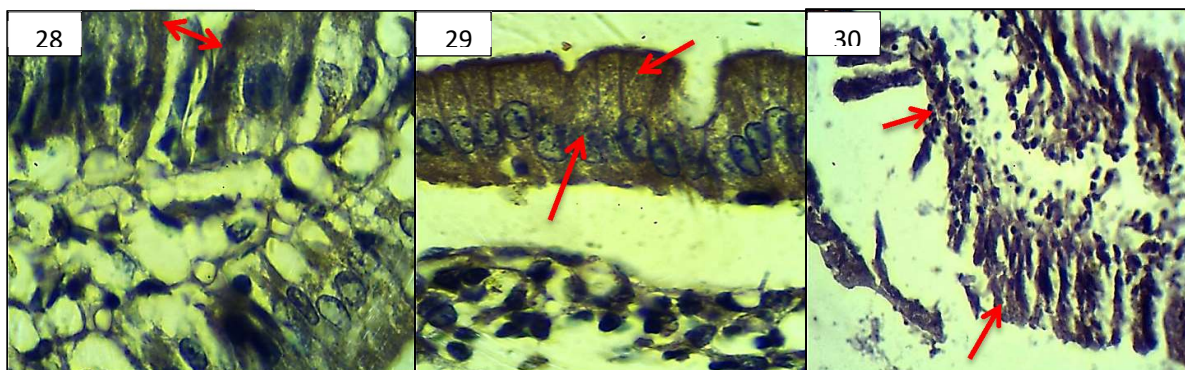
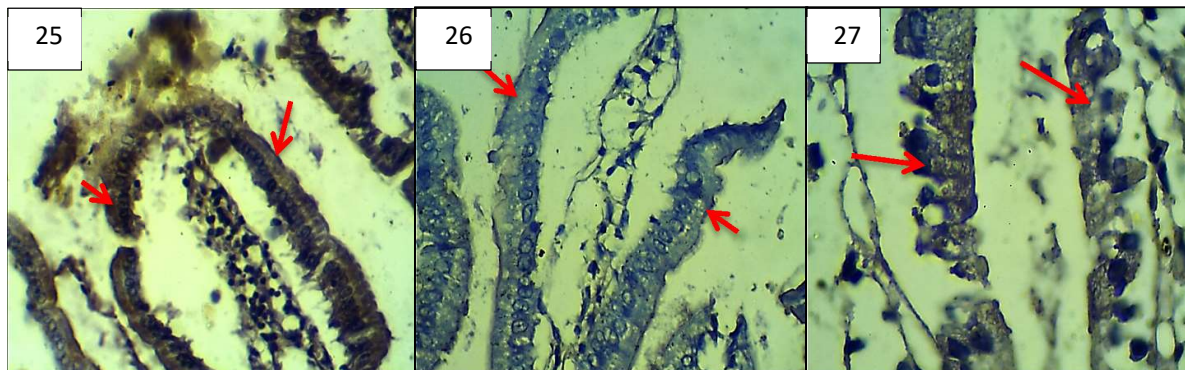
**image(22)** A section of the duodenum of the rat of the third treatment group (T3) in the first week Showing The beginning of the increase in the number of goblet cells (green arrow) and the beginning of interaction with the dye (+) (black arrow) (PAS, 50X).

**image(23)** A section of the duodenum of the rat of the third treatment group (T3) in the second week showing The increase in the number of goblet cells (green arrow) and clear interaction with the dye in the region of the glands (black arrow) positive interaction (++) (PAS, 50X).

**image(24)** A section of the duodenum of the rat of the third treatment group (T3) in the third week Showing Clear propagation of the goblet cells (green arrow) and positive interaction (+++) in the glands region (black arrow) (PAS, 50X).

(T2) There was a gradual increase in the number of positive cells that reacted clearly with the dye as the intensity of the immune response increased as the treatment progressed. The intensity of immunoglobulin was very high in the third week of treatment with the extract as indicated by the immunological tissue sections of the duodenum (images 27,28,29) treatment with standard treatment (omeprazole) in animals of the third treatment group (T3) in duodenum there was also a gradual increase in the intensity of the immune reaction gradually escalated as treatment progressed. As the images suggest (30,31,32).

The results of the study of immunohistochemical to detect the epidermal growth factor receptors in the mucosa of the duodenal wall in the animals of the negative control group (C) A positive reaction was found by the presence of large numbers of positive dye cells (image25) However, this interaction is almost non-existent or weak and the pigment strength is weak in the animals of the positive control group representing the first treatment group (T1). This is illustrated by the image (26) On the other hand, the results of immunoglobulin of the duodenal sections of the group animals treated with sweet potato extract



**Image(25)**A section in the duodenum of the rat from the control group (C) shows the intensity of the EGFR immune response with immunoglobulin intensity (positive reaction) (red arrow) (IHC, 500X). **image(26)** A section of the duodenum of the rat of the first treatment group (T1) Showing The immune response is very weak (negative reaction) and the immune pigment is not (red arrow) (IHC, 500X). **image(27)** A section of the duodenum of the rat of the second treatment group (T2)in the first week Showing The immune response is very weak (negative reaction) and the immune pigment is not (red arrow) (IHC, 500X). **image(28)** A section of the duodenum of the rat of the second treatment group (T2)in the second week Showing Immunohistochemical reaction with medium intensity pigmentation ++ (red arrow) (IHC, 500X). **image(29)** A section of the duodenum of the rat of the second treatment group (T2)in the third week Showing Intensity and intensity of immune response +++ with strength and intensity of immunoglobulin (red arrow) (IHC, 500X). **image(30)** A section of the duodenum of the rat of the third treatment group (T3)in the first week Showing the immune response is weak (red arrow) (IHC, 500X). **image(31)** A section of the duodenum of the rat of the third treatment group (T3)in the second week Showing Intermediate immunoglobulin reaction+ + (red arrow) (IHC, 500X). **image(32)** A section of the duodenum of the rat of the third treatment group (T3)in the third week Showing Intensity and intensity of immune response +++ with pigmentation strength (red arrow) (IHC, 500X).

## Discussion

The results of tissue sections of the duodenum, stained with hematoxylin, and eosin showed clear signs of malformation, erosion, mucus degeneration, With signs of congestion of blood vessels and bleeding in the first treatment group (T1). For the sweet potato extract group (T2), the current results showed mucosal integrity for duodenum With no signs of change or signs of congestion and bleeding, which shows the re-formation of damaged tissue and the disappearance of signs of disintegration and congestion and bleeding and recovery and is observed is the absence of differences between the group mentioned and the treatment group omeprazole( T3). These changes are due to the therapeutic role of sweet potato extract in the

reduction of pathological changes significantly due to having clear therapeutic properties such as containing structural proteins such as amino acids Which has protective and immunological functions and contains many vitamins such as vitamin C, E and A and important minerals such as Mg and Fe, Cu and Zn, which are anti-oxidants and works to curb the effects of free radicals and reduce tissue damage( 1). (15), which found hemorrhagic ulcers in the stomach of indomethacin-treated rats and the disappearance of these ulcers when treated with vitamin E. and with (3) found that the use of the extracts of basil (*Ocimum Gratissimum*) in the treatment of gastric ulcer and duodenal ulcers contributed to the healing of ulcers and the disappearance of signs of congestion and bleeding. The results of the present study



showed a gradual increase in the density of collagen fibers in the subcutaneous layer of the duodenum. This indicates the effectiveness of the treatment used in the healing of the ulcer, whether sweet potato (T2) or omeprazole (T3). However, it was observed that the increase in collagen fiber was more likely to be treated with sweet potato extract, possibly because it is rich in vitamin A, which is an effective ingredient in collagen synthesis (17). Such as the study carried out by Devaraj et al. (2007), which demonstrated the effect of leaves and fruits of *Moringa oleifera* in the healing of gastric and duodenal ulcers and indicated a clear increase in the number of cells producing fiber and collagen fibers and their effective contribution to healing (10) also reported that there was a clear increase in collagen fiber in patients with gastric ulcers after treatment and also (29)., In which the stomach ulcer was treated using omeprazole and observed a dense and clear collagen fiber during the treatment period. This corresponds to the results of the current study which indicated a gradual increase in the collagen fiber deposition rates as the treatment progressed up to healing Full ulcer. Periodic Acid - Schiff is used to detect and investigate molecules with a high percentage of carbohydrate content such as glycogen and mucin. These substances are important in their protective role by protecting the epithelial cells from the strong influence of acid and digestive enzymes (18) The clear positive interaction of pigment in the histological sections of the duodenum regions of the intestinal glands and the area of goblet cells in the villus. Is based on the fact that most of the duodenal ulcer is caused by gastric dysfunction and that the positive interaction with the dye indicates an increased secretion of alkaline mucus, which resists acidity of the stomach and contributes to the protection of mucous membranes (22) On this basis, the current results indicated that the treatment with sweet potato extract in the second group (T2) led to greater clarity in the interaction of the third treatment group (omeprazole group) due to the ability of the extract to stimulate the production of prostaglandin, which stimulates the secretion of mucus. (25) have already pointed to the role of goblet cells by their proliferation and increased mucus secretion in the healing of the duodenal ulcer. (23) found similar results when conducting a comparative study of the amount of mucus removed from The glandular glands and

Brunner glands when the ulcer and the role of mucus in promoting healing..

In the present study, Epidermal Growth Factor Receptors (EGFR) Whose presence is evidence of the proliferation of epithelial cells and their migration to the ulcer base and evidence of EGF being the major contributor to healing The process of healing and healing of the ulcer includes the proliferation of epithelial cells and the re-formation of the granular tissue and the formation of blood vessels and reconstruction of the glands and mucosal muscle layer and these events are under the control of growth factors that exist in the area of ulceration and the epidermal growth factor (EGF) Is present in wound healing as it has a role in regeneration of the lining of the gastrointestinal tract by stimulating the secretion of bicarbonate (Perez et). The results showed positive EGFR during the treatment weeks of the second treatment group (T2) and the third (T3) in the duodenal tissues. The results showed that the (T2) group had a stronger immune response than (T3). This indicates the therapeutic efficacy of the sweet potato plant and its ability to induce healing because it contains high levels of antioxidants, vitamins and minerals Which have the potential to stimulate and grow epithelial cells and their reproduction as well as contain sweet potatoes on the elements of iron and copper are very important in the formation of blood vessels Angiogenesis (8) such as the study of (5), in which the water extract of sweet potato plant have been used in the treatment of high cholesterol in the rabbit. The immune expression of Nrf2 showed an increase in epithelial cells (2) comparing the *Jasminum Sambac* and omeprazole extract in the healing of the peptic ulcer using IHC technique, where the plant cause increased immune expression of the Hsp70 protein which has a role in healing. In the same vein (6) noted the importance of protein (EGFR) in the development of treatment for liver cancer patients For its role in stimulating biochemical processes such as oxidative phosphorylation and activation of the signal between proteins to synthesize DNA and form healthy cells.

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