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Research Paper

Efficacy of Capsicum Frutescens in Curing the Peptic Ulcer

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Abstract: *Chili peppers are often used around the world to make a wide variety of sauces, known as hot sauce, chili sauce, or pepper sauce. Red chilis contain high amounts of vitamin C and carotene (provitamin A). meanwhile Several studies found that capsaicin could have an anti-ulcer protective effect on stomachs infected with H. pylori by affecting the chemicals the stomach secretes in response to infection. The present study was designated to clear out the effect of aqueous extracts of red chilli pepper (RCP) and some spicy foods on healing acute gastric ulcer induced by aspirin in rats. Sixty six adult male albino rats (170±5g B.Wt.) of Sprague Dawley Strain were obtained from animal house of the faculty of medicine, Um Al Qura University were used and disported into 6 groups (n= 6 rats), one of them used as control -ve while other groups had given aspirin orally (200mg/kg B.Wt.), one of these groups left as control +ve and other groups administrated with aqueous extracts of RCP at doses of 300 and 600 mg/kg B.Wt. and 30% spicy nuggets and chicken for seven days. The length of gastric ulcer, volume of gastric juice, pH value, and histopathological changes were examined. Our results revealed that, oral administration of aspirin (200mg/kg B.Wt.) induced gastric ulcer in rats; the mean length of gastric ulcer in control +ve group was higher compared with in control -ve group. Also, Oral administration of RCP extract at a dose of 600mg/kg B.Wt., caused high decrease in the length of gastric ulcer. On the other hand, the lowest decrease of gastric ulcer length was happened in rats fed on 30% spicy nuggets. The results concluded that oral administration with all tested plants reduced the length of gastric ulcer, volume of gastric juice, and histopathological changes. On the other hand, RCP extracts*

increased pH value of gastric juice. According to the results, RCP could be used for healing acute gastric ulcer disease.

Keywords: Red chilli pepper (*Capsicum frutescens*), spicy nuggets, spicy chicken, aspirin ulcer, histopathological changes, pH value and gastric juice.

Introduction

Chili peppers have been a part of the human diet in the Americas since at least 7500 BC and perhaps earlier. There is archaeological evidence at sites located in southwestern Ecuador that chili peppers were already well domesticated more than 6000 years ago (Perry, 2007).

In the previous century peptic ulcer was an uncommon disorder. However, during the early part of the 1900s, the disease began to increase greatly. In the 1940s at least 10% to 15% of men were reported to have duodenal ulcers, with un-reported cases in women and children adding to those figures. This increasing seems to have peaked about the mid 1950s, and over the past 15 to 20 years, knowledge of the disease process and its medical management has progressed rapidly (Sue, 1995).

Increasing of acid output, *Helicobacter pylori* (*H. Pylori*), non steroidal anti-inflammatory drugs (NSAIDs) and stress are the basic risk factor in peptic ulcer disease (Bak-Romaniszyn *et al.*, 2004). Several studies found that capsaicin could have an anti-ulcer protective effect on stomachs infected with *H. pylori* by affecting the chemicals the stomach secretes in response to infection (Lee *et al.*, 2007 ; Satyanarayana, 2006 and O'Mahony *et al.*, 2005).

The pain is the predominant symptom of peptic ulcer, although it may be absent in 25% of gastric ulcer patients. And upper gastro-intestinal hemorrhage may be the presenting sign of peptic ulcer disease, anemia from chronic blood loss, repeated vomiting and weight loss possibly happen (Allen and Myers, 1986).

There are many plants used for treatment of peptic ulcer, such as vegetables, fruits and herbs. These substances had been experimented for treatment of peptic ulcer. But when we mention that spices use for healing ulcers, most people not only criticize us but also interpose with our speech. So a lot of studies had been done on behalf of spices specially red chilli pepper, some scientists didn't find any medicinal effect of these spices on healing ulcers, as that of Myers *et al.*, (1987) and Sue (1995).

On the other hand, other scientists found that some spices especially red chilli pepper has a good medicinal effect on healing ulcers. They found that red chilli pepper involves functional substances called capsaicin which has a gastro-protective effect against experimental gastric mucosal injury in animals (Kang *et al.*, 1992; Kang *et al.*, 1995; Yeoh *et al.*, 1995 and Cruz *et al.*, 1999).

Research in humans found that "after adding chili to the diet, the LDL, or bad cholesterol, actually resisted oxidation for a longer period of time, (delaying) the development of a major risk for cardiovascular disease" (Ahuja and Ball 2006).

On the contrary, Alasdair *et al.*, (1981) remarked that hot and spicy food as long use of aspirin is the main cause of chronic gastritis leading to ulcer disease. In this respect, red and black pepper incriminated in the increase of acid secretion (Vasudevan *et al.*, 2000 and Ononiwu *et al.*, 2002).

For as much as this clash, this study carried out to explain the cytoprotective activity against oxidative gastric damage induced by local effect of aspirin on gastric mucosa using aqueous extracts of red chilli pepper (RCP) and spicy foods as investigated on rats.

Materials and Methods

1-Materials and Rats:

a- Plants and spicy foods: Red chilli pepper (*Capsicum frutescens*), family solanaceae, this plant and spicy nuggets, spicy chicken were purchased from local market of KSA.

b- Aspirin: Aspegic (Mmiriya Pharmaceutical Industries, Cairo) injection was prepared by dissolving one vial in 25ml distilled water to obtain solution. A volume of 1ml of this solution was orally given (at the level 200mg/kg body weight) for one day to induce acute gastric ulcer in male albino rats.

c- Diet: The rats were fed on ration (a basal diet devoid from starch) composed of wheat bran, soya bean powder 44%, fish meal, molasses, fibers 3.3%, sodium chloride, calcium carbonate, calcium phosphate, methionine and ash (net protein 22% and fats 4.7%). The diet was fed and water was provided *ad libitum* for the experimental period.

d- Rats: sixty six adult male albino rats (170±5g B.Wt., each) of Sprague Dawley Strain were obtained from animal house of the faculty of medicine, Um Al Qura University.

2-Methods:

a- Preparation of aqueous extracts: The clean RCP (*Capsicum frutescens*), was ground using porcelain grinder to pass through sieve-mesh pores of 1mm diameter. The extract of red chilli was prepared by mixing 1gm powdered leaves with 100 ml distilled water. The mixture was boiled for 10 minutes and left to cool for 15 minutes. The aqueous extract was filtered using filter paper to remove the particulate matter (0.2mm) then the filtrate was freely dried (Lyophilized) and reconstituted in 1.5 ml of distilled water (100 mg/kg body weight).

b- Grouping design and feeding of rats: The experiment was performed in animal house of the faculty of medicine, Um Al Qura University. Rats were housed in wire cages in a room maintained at 25±2°C and kept under normal healthy conditions for two weeks. All rats were fed for one week on basal diet before starting the experiment for acclimatization. After one week period, rats were divided into two main groups. The first group (n= 6rats) was fed on the basal diet only as a control negative (healthy rats). All rats in the second main group (n= 30 rats) were given orally aspirin at a dose of 200mg/kg B.Wt., for induction of acute gastric ulcer according to Agrawal *et al.*, (2000). Rats with (aspirin-induced gastric ulcer) were disparted into five groups (n= 6rats for each group) as the following:

Group 1: Control negative -ve group was fed on basal diet (non treated rats).

Group 2: Control positive +ve group fed on basal diet basal diet+Aspirin (Asp) 200mg/kg B.Wt.

Group 3: positive rats fed on basal diet containing 30% spicy nuggets.

Group 4: positive rats fed on basal diet containing 30% spicy chicken.

Group 5: positive rats fed on basal diet+oral RCP extract at doses of 300 mg/kg B.Wt.

Group 6: positive rats fed on basal diet+oral RCP extract at doses of 600 mg/kg B.Wt.

The rats remained without food for one day prior to ether anesthesia (except for water)to avoid mixing of food with gastric secretions

c- Measurement the length of gastric ulcer: At the last day of experimental period, all rats were fasted for 12-14hrs and only allowed for drinking water. In the morning of the next day, all rats were sacrificed, and their stomachs were tied around both openings (cardiac & pyloric sphincters) and injected by distilled water (3ml). The gastric juice was then collected in sterilized tube. The stomachs were opened longitudinally, washed with saline and examined under dissecting microscope for ulcer. The length of gastric ulcer was measured and expressed as mean±SD for each group. The curative

ratio was then calculated for each treated group according to the method described by Akhtar and Ahmad (1995) using the following equation: Curative ratio (CR) = $(LC - LT / LC) \times 100$.

LC = length of ulcer in control positive group.

LT = length of ulcer in treated group

d- Measurement the volume of gastric juice: Gastric juice was collected according to the methods of Niida *et al.*, 1991 (abdomen was incised and both the stomach and duodenum was exposed and a fistula made by a poly ethane tube inserted into the stomach from a small incision made in the duodenum and held in place by a ligature around pylorus also esophagus was clamped to prevent reflux and loss of the gastric mucosa) in tubes and centrifuged at 500 R.P.M., for 5minutes. The volume of gastric juice was measured by graduated cylinder and expressed as ml.

e- Histopathological study: Specimens from stomachs were collected from rats of all experimental groups at the end of the experimental period, fixed in 10% neutral buffered formalin (pH=7.0), dehydrated in ethyl alcohol, then cleared in xylol and embedded in paraffin; 4-6 microns thickness sections prepared and stained with heamtoxylin and eosin for examining both for and glandular parts of the stomach (Carleton, 1976).

f- Statistical Analysis: Statistical analysis has been achieved by using statistical package for social science program (SPSS, 2008).

Results

The present study was designated to clear out the effect of aqueous extracts of RCP and some spicy foods on healing acute gastric ulcer induced by aspirin in rats. The parameters were length of gastric ulcer, volume of gastric juice, pH, and histopathological examination of fore and glandular parts of stomachs.

The effect of spicy nuggets, spicy chicken and aqueous extract of RCP (*Capsium frutescens*) at two doses on the length of gastric ulcer in rats were shown in table 1. The obtained results showed that, a single oral administration of aspirin (200mg/kg B.Wt.) induced gastric ulcer in rats; the mean length of gastric ulcer in control +ve group was higher compared with in control -ve group (normal rats) being 7.27 ± 0.093 and zero mm, respectively.

Oral administration of RCP extract at a dose of 600mg/kg B.Wt., for 7 days after aspirin (200mg/kg B.Wt.) caused high decrease in the length of gastric ulcer (1.71 ± 0.0584 mm). On the other hand, the lowest decrease of gastric ulcer length was happened in rats fed on 30% spicy nuggets, which was 4.35 ± 0.088 mm.

The curative ratios of ulcerated rats with oral administration of RCP extract at a dose of 600 and 300mg/kg B.Wt., 30% spicy chicken and 30% spicy nuggets were 76.48, 71.14, 43.19 and 40.17 respectively. The highest curative ratio obtained in a dose of 600 mg/kg B.Wt., of RCP.

As shown in table (2) the volume of gastric juice obtained from rats given aspirin-induced gastric ulcer (control +ve group) at a dose of 200mg/kg B.Wt., was 0.69 ± 0.008 ml ($P < 0.001$) compared with 0.23 ± 0.005 ml in normal rats (control - ve group). Oral administration with RCP extracts at a dose of 600mg/kg B.Wt. for 7 days after given aspirin (200mg/kg B.Wt.) caused the highest decrease in the volume of gastric juice in rats, but oral administration with 30% spicy nuggets for 7 days after given aspirin (200mg/kg B.Wt.) caused the lowest decrease in the volume of gastric juice in rats. The gradual ascending data were 0.31 ± 0.004 ml ($P < 0.001$), 0.34 ± 0.006 ml ($P < 0.001$), 0.39 ± 0.010 ml ($P < 0.001$) and 0.41 ± 0.008 ml ($P < 0.01$) for 600 and 300 mg/kg B.wt. of RCP and 30% spicy chicken and nuggets compared with +ve 0.69 ± 0.008 ml respectively.

Effect of spicy nuggets, spicy chicken and aqueous extract of RCP (*Capsium frutescens*) at two doses on the PH of gastric juice collected from stomachs of rats is listed in table(3). It is clear from data illustrated in table (3) that oral administration of aspirin at a dose of 200mg/kg B.Wt., (control +ve) decreased the pH of gastric juice (mean 3.47 ± 0.07) ($p < 0.001$) compared with (4.87 ± 0.049) of normal rats (control-ve). Data showed that oral administration of RCP extract at dose of 600 and 300mg/kg B.Wt., for 7 days after aspirin (200 mg/kg B.Wt.) reflected maximal value of pH level 4.82 ± 0.061 and 4.02 ± 0.060 resp. ($p < 0.001$) compared with control (+ve), however, oral feeding of 30% spicy nuggets for 7 days after aspirin (200mg/kg B.Wt.) caused no significant decrease value (3.48 ± 0.07).

Histopathological Results:

Microscopical examination of stomach from control untreated rats revealed the normal histological structure of the stomach which consists of four layers; mucosa, submucosa, muscularis and serosa (Fig.1). The surface epithelial cells which are mucus secreting cells formed a continuous epithelial sheet that covered the gastric surface and line pits of gastric glands. All the cells of the surface, gastric pits and gastric glands were intact and normal without evidence of erosion or hemorrhage in the gastric mucosa. (Fig.2&3). Conversely, stomach of rat from group 2 showing necrosis of the glandular mucosa associated with sloughing of laminal epithelium these superficial erosions were multiple, small in size and not reaching the muscularis mucosa (Fig.4). The sub epithelial tissues showed hemorrhage and edema with increased number of the blood vessels. There is mononuclear cells infiltrating lamina propria. Also the stomach of this group showed destruction of gastric glands, edema in lamina propria as well as mononuclear cells infiltration (Fig.5). Gastric glands are reduced in number which are abnormal in morphology and distribution (Fig.6). Some areas showed hyperplastic gastric glands other areas showed gastric ulceration. Covering a bier like network of hyperplastic gastric pits with destruction of upper part of gastric glands (Fig.4&6). Stomach of rat from group 3((Asp.) + 30% spicy nuggets) showing destruction of gastric glands, edema in lamina propria as well as mononuclear cells infiltration. (Fig.7&8). Stomach of rat from group 4 ((Asp.) + 30% spicy chicken) showing destruction of gastric glands, edema in lamina propria as well as mononuclear cells infiltration. (Fig.9&10). In Stomach of rat form group 5(Asp.)+RCP 300 showing the normal histological structure and edema in lamina propria. (Fig.11&12). There was a renewal of epithelium to line the surface of the stomach and gastric pits again which accompanied with significant increase in the number of gastric glands(Fig.13). Other areas showed return of these gastric glands to the normal pattern. (Fig.14).

Table (1): Effect of spicy nuggets, spicy chicken and aqueous extract of RCP (*Capsium frutescens*) at two doses on the length of gastric ulcer in rats

Groups		Aspirin, diet and extracts	Doses (mg/kg B.Wt.)	Gastric ulcer length (mm.)	CR (%)
				Mean±SE	
Control -ve	1	-	-	0.00 ^{***}	-
Control +ve	2	Aspirin (Asp.)	200	7.27±0.093	-
Treated Groups	3	(Asp.) + 30% spicy nuggets		4.35±0.088 ^{**}	40.17
	4	(Asp.) + 30% spicy chicken		4.13±0.042 ^{***}	43.19
	5	(Asp.) + RCP	300	2.10±0.077 ^{***}	71.14
	6	(Asp.) + RCP	600	1.71±0.0584 ^{***}	76.48

CR: Curative Ratio

*Differences are significant at 5% compared with +ve.

**Differences are significant at 1% compared with +ve.

***Differences are significant at 0.1% compared with +ve.

Table (2): Effect of spicy nuggets, spicy chicken and aqueous extract of RCP (*Capsium frutescens*) at two doses on the volume of gastric juice collected from stomachs of rats

Groups		Aspirin, diet and extracts	Doses (mg/kg B.Wt.)	Volume of gastric juice (mL.)	DR (%)
				Mean±SE	
Control -ve	1	-	-	0.23±0.005 ^{***}	-
Control +ve	2	Aspirin (Asp.)	200	0.69±0.008	-
Treated Groups	3	(Asp.) + 30% spicy nuggets		0.41±0.008 ^{**}	40.58
	4	(Asp.) + 30% spicy chicken		0.39±0.010 ^{***}	43.48
	5	(Asp.) + RCP	300	0.34±0.006 ^{***}	50.72
	6	(Asp.) + RCP	600	0.31±0.004 ^{***}	55.07

DR: Decrease Ratio

*Differences are significant at 5% compared with +ve.

**Differences are significant at 1% compared with +ve.

***Differences are significant at 0.1% compared with +ve.

Table (3): Effect of spicy nuggets, spicy chicken and aqueous extract of RCP (*Capsium frutescens*) at two doses on the PH of gastric juice collected from stomachs of rats

Groups		Aspirin, diet and extracts	Doses (mg/kg B.Wt.)	PH of gastric juice	IR (%)
				Mean±SE	
Control -ve	1	-	-	4.87±0.049 ^{***}	-
Control +ve	2	Aspirin (Asp.)	200	3.30±0.036	-
Treated Groups	3	(Asp.) + 30% spicy nuggets		3.48±0.07 ^{NS}	5.45
	4	(Asp.) + 30% spicy chicken		3.78±0.119 [*]	14.54
	5	(Asp.) + RCP	300	4.02±0.060 ^{***}	21.82
	6	(Asp.) + RCP	600	4.82±0.061 ^{***}	46.1

IR: Increase Ratio

*Differences are significant at 5% compared with +ve.

**Differences are significant at 1% compared with +ve.

***Differences are significant at 0.1% compared with +ve.

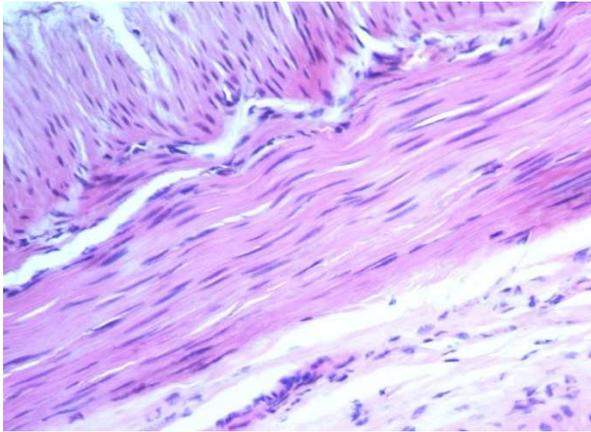


Fig. 1: Stomach of rat form group 1 (control-ve) showing the normal histological structure. (H & E x200).

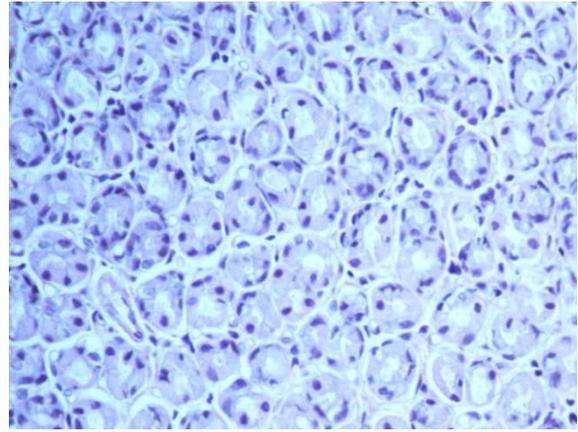


Fig. 2: Stomach of rat form group 1 (control -ve) showing the normal histological structure. (H & E x200)

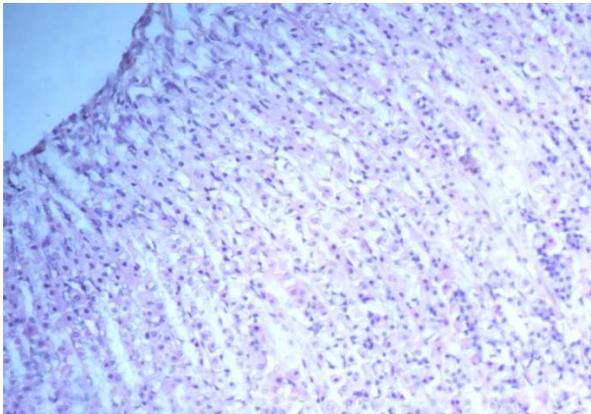


Fig. 3: Stomach of rat form group 1 (control -ve) showing the normal histological structure. (H & E x200)

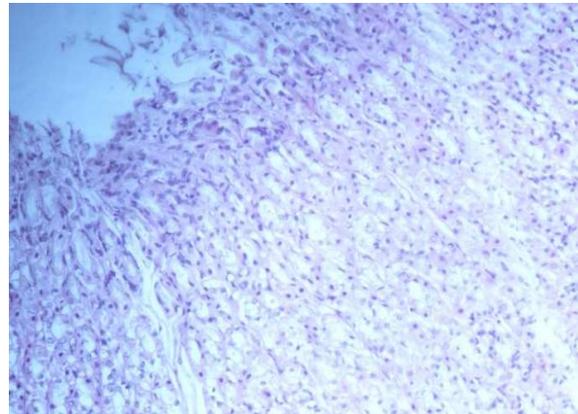


Fig. 4: Stomach of rat from group 2 (control +ve) showing destruction of gastric glands, edema in lamina propria as well as mononuclear cells infiltration. (H & E x 200).

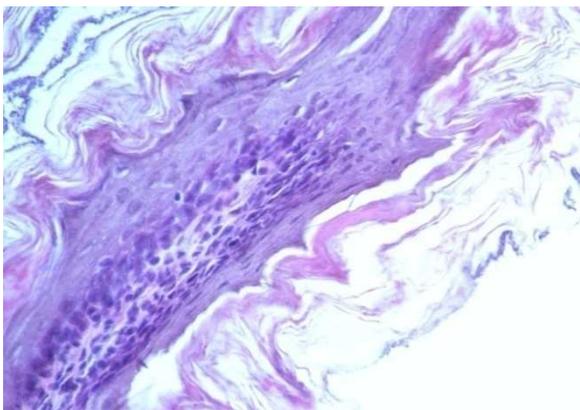


Fig. 5: Stomach of rat from group 2 (control +ve) showing mononuclear cells infiltration. (H and E x 200).

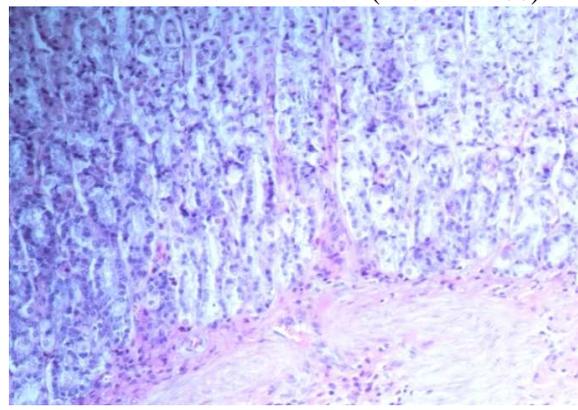


Fig. 6: Stomach of rat from group 2 (control +ve) showing destruction of gastric glands and edema in lamina propria. (H and E x 200).

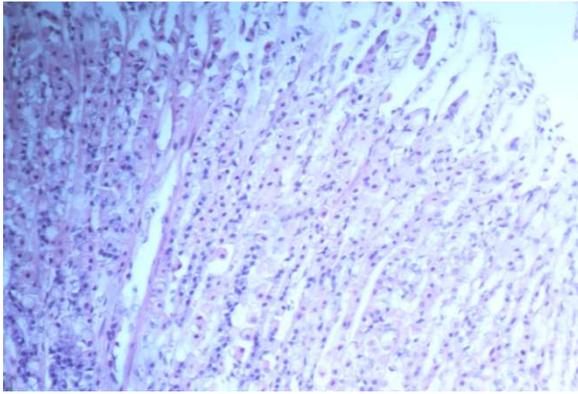


Fig. 7: Stomach of rat from group 3 (Asp.) + 30% spicy nuggets showing destruction of gastric glands and edema in lamina propria. (H and E x 200).

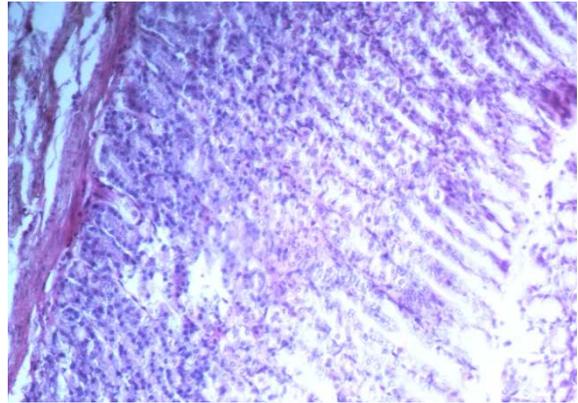


Fig. 8: Stomach of rat from group 3 (Asp.) + 30% spicy nuggets showing destruction of gastric glands, edema in lamina propria as well as mononuclear cells infiltration. (H and E x 200).

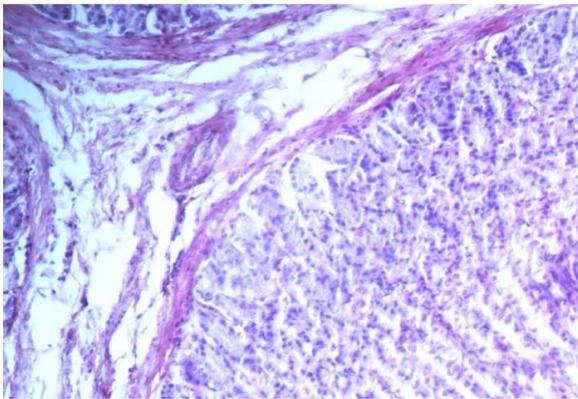


Fig. 9: Stomach of rat from group 4 (Asp.) + 30% spicy chicken showing destruction of gastric glands, edema in lamina propria as well as mononuclear cells infiltration. (H and E x 200).

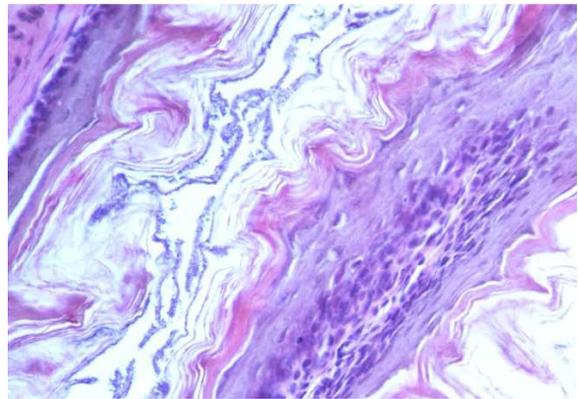


Fig. 10: Stomach of rat from group 4 (Asp.) + 30% spicy chicken showing mononuclear cells infiltration. (H and E x 200).

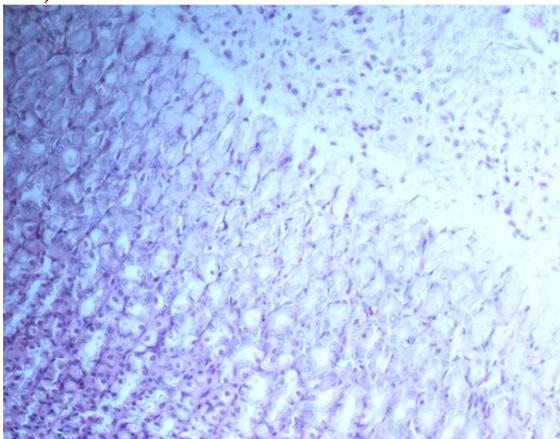


Fig. 11: Stomach of rat form group 5 (Asp.) + RCP 300 showing the normal histological structure in gastric glands.(H and E x200)

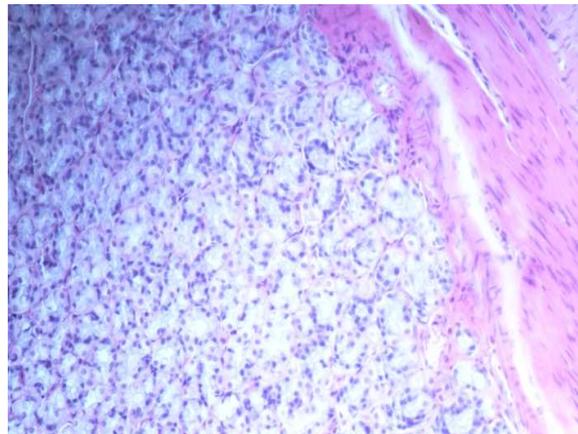


Fig.12:Stomach of rat form group 5(Asp.) + RCP 300 showing the normal histological structure and edema in lamina propria.(H& E x200)

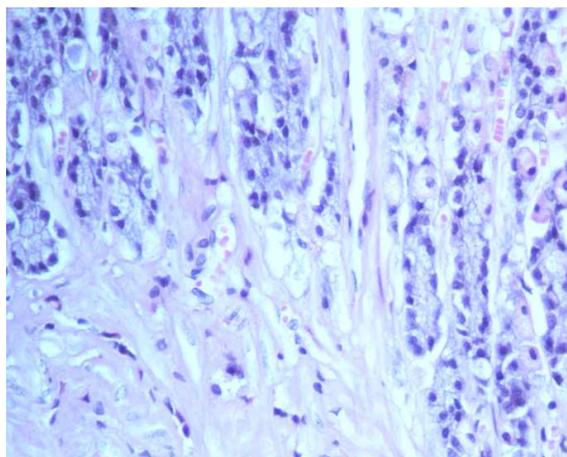


Fig. 13: Stomach of rat form group 6 (Asp.) + RCP 600 showing the normal histological structure in gastric glands.(H & E x200)

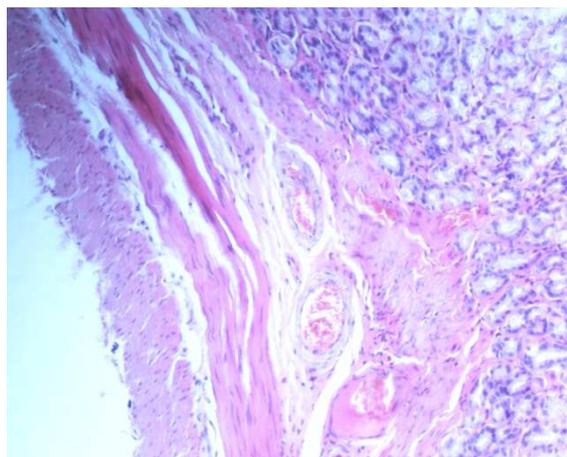


Fig.14: Stomach of rat form group 6(Asp.) + RCP 600 showing the normal histological structure.(H &E x200)

Discussion

Our results revealed that, oral administration of aspirin (200mg/kg B.Wt.) induced gastric ulcer in rats; the mean length of gastric ulcer in control +ve group was higher compared with in control -ve group. Also, Oral administration of RCP extract at a dose of 600mg/kg B.Wt., caused high decrease in the length of gastric ulcer. These results were in agreement Kang *et al.*, (1992) reported that chilli (*Capsicum frutescens*) may be expected to accelerate gastro-intestinal transit and hence to inhibit colonic carcinogenesis, while its active ingredient capsaicin protects against experimental gastric mucosal injury. Also, Yeoh *et al.*, (1995) found that capsaicin, the pungent ingredient of chilli, has a gastro-protective effect against experimental gastric mucosal injury in animals. Such an effect has not, however, been documented in humans to date, demonstrating a gastro-protective effect of chilli in humans subjects. In this respect, Shobana and Naidu (2000) reported that pepper has anti-oxidative activity, this can be applied for stomach preservation against ulcer and spices when included pepper in addition to impart flavor to the food, they possessed potential health benefits. Credence for this speech, Bombik *et al.*, (2002) concluded that the extracts of some herbs including chamomile increased the concentration of zinc, copper and iron in blood serum which was helpful for the flowing of blood to the stomach mucosa causing treatment of the pain; according to this action, these herbs were useful for healing of gastric ulcer.

Regrettably, Alasdair *et al.*, (1981) remarked that hot and spicy food or long continued use of aspirin are the main causes of mild chronic gastritis breeding ulcer disease. however, our results revealed that, the lowest decrease of gastric ulcer length was happened in rats fed on 30% spicy nuggets. Our results exposed that oral administration with RCP extracts at a dose of 600mg/kg B.Wt. caused the highest decrease in the volume of gastric juice in rats, but oral administration with 30% spicy nuggets for 7 days after given aspirin (200mg/kg B.Wt.) caused the lowest decrease in the volume of gastric juice in rats. These results were in line with that of Ress *et al.*, (1979) who reported that aspirin (acetyl salicylic acid) at a dose of 60mg/kg B.Wt. was the main cause of increasing in gastric juice inducing stomach ulcer in rats. Also Aguwa and Mittal (1981) concluded that aspirin at a dose of 200mg/kg B.Wt., increased acid secretion inducing ulcers. There were a lot of scientists sustained this utterance such as (Mitra *et al.*, 1996; Sen and Chaudhuri 1996; Maiti *et al.*, 1997; Akah *et al.*, 1998; Agrawal *et al.*, 2000; Rao *et al.*, 2000 and Sairam *et al.*, 2001).

Abdel-Salam *et al.*, (1997) reported that capsaicin given into the stomach of rats or cats inhibited gastric acid secretion. Moreover, Chen-Road and Su-Lin (1997) indicated that the increasing of acid secretion induced gastric damage and associated with greater acid back-diffusion and oxygen radical

generation, and lower mucosal glutathione and mucus production. Khayyal *et al.*, (2001) revealed that the extracts of some plants including (*Matricaria recutita*) reduce acid output and increase mucin secretion and prostaglandin E2, but released and decreased leukotrienes. They found that these extracts were anti-ulcerogenic agents which was confirmed histologically.

On the other hand, Limlomwongse *et al.*, (1979) suggested that the effect of capsaicin on the acid secretion and mucosal blood flow is by the release of endogenous gastric secretagogues which increase both tissue perfusion and the secretory activity. Also, Vasudevan *et al.*, (2000) studied the effect of spices on gastric acid secretion in anesthetized albino rats. They found that spices including red and black pepper increased gastric acid secretion, but red pepper produced maximum increasing in acid secretion.

Our data showed that oral administration of RCP extract at dose of 600 and 300mg/kg B.Wt., for 7 days after aspirin (200 mg/kg B.Wt.) reflected maximal value of pH level ($p < 0.001$) compared with control (+ve). These results agreed with Kang *et al.*, (1995) who revealed that chilli has a gastro-protective effect for healing ulcers in rats, supporting that chilli has a protective effect against gastric ulcer.

Conclusion

The results concluded that oral administration with all tested plants reduced the length of gastric ulcer, volume of gastric juice, and histopathological changes. On the other hand, RCP extracts increased pH value of gastric juice. According to the results, RCP could be used for healing acute gastric ulcer disease.

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