Anti-Ulcerogenic Impact pf *Passiflora edulis* Powder and Extract on Gastric Ulcer in Rats

Ali Monahi Nazal Alshammari

Faculty of Home Economic at The public Authority For Applied Education and Training in Kuwait
anaba71@hotmail.com

Abstract: This study has therefore been designed to evaluate the anti-inflammatory and anti-ulcerogenic potential of *Passiflora edulis* powder and extract to evaluate their beneficial effects on the anti-inflammatory profiles of indomethacin in male rats. Thirty six rats weight 125±5g were divided into 6 groups, (n=6) for six weeks. The first group (negative control). Other groups had given indomethacin orally (30 mg/kg/btw.rats). One was left as positive control and other treated with either ranitidine drug (10g/kg/diet), *Passiflora* powder, 5 ml/kg/rats *Passiflora* extract and mixtur *Passiflora* powder and extract. Administration of *Passiflora* powder, extract, and mixture achived increase in weight gain, feed intake and feed efficiency ratio, pH gastric and prostaglandin E2, gastric cytochrome P450 reductase,, glutathione peroxidase (GPX) and superoxid dismutase (SOD), compared with their corresponding +ve control compared with their corresponding +ve control group. On the other side of gastric ulcer length and volume of gastric juice, nitric oxide, cyclooxygenase, and malondialdehyde (MDA) decreased significantly compared with (+ve) control. The overall finding of this study demonstrates (anti-ulcerogenic and antioxidant effects) of *Passiflora* suggesting that *Passiflora* powder and extract can be promising for treatment of gastric ulcers as rich source of natural antioxidants such as phenolics compounds.
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1. Introduction

The interest in *Passiflora edulis* has been increased because of its antioxidant compounds (**Cola et al., 2006).** In addition *Passiflora edulis* (*Passion Fruit*) known for its amazing nutritional and medicinal place. Plants have been widely used throughout the world for their beneficial medicinal benefits. Plants are the richest generator of phyto-element **(Phamiwon and Sheila 2016).** *Passiflora edulis* are well famous for hypercholesterolemia and hyperglycemia, also as a nutritional supplement (**Babu and Chaudhuri, 2005 and Asare, et al., 2018).**

The fruit, flowers and immature pods of this tree are used as a highly nutritive fruit (**Anwar et al., 2005**). *Passiflora edulis* fruit are a rich in (β-carotene, protein, essential amino acids, vitamins A, B, C and E, calcium, phosphorus, copper and potassium) a good source of natural antioxidants; contained (ascorbic acid, flavonoids, phenolics and carotenoids) (**Sengev and Gernah, 2012** and **Siddhuraju and Becker, 2013).**

Ranitidine is from histamine group. It reduce the amount of acid in stomach, treat and prevent stomach and intestines ulcers. It also treatment gastroesophageal (acid backs up from the stomach into the esophagus), causing heartburn (**Lightdale, et al., 2013).**

Indomethacin is a drug reduces (fever, pain and inflammation). Indomethacin reducing the production of prostaglandins which body produces and cause fever and pain that are associated with inflammation (**Takeuchi et al., 1991)**. Indomethacin blocks the enzymes that make prostaglandins (COX1 and COX 2) and thereby reduces the levels of prostaglandins. (**Dela Lastra et al., 2002)**. The current study was the effect of *Passiflora* fruits reduction of stress-induced gastric ulcers by indomethacin in rats.

2. Materials and Methods

A – Materials:

Chemicals:

Indomethacin:

Drug tablets were obtained from SEDICO Pharmaceutical Company, Giza, Egypt.

Ranitidine hydrochloride (Ranitak©):

150 mg tablets-SEDICO Pharmaceutical Company, Giza, Egypt.

Experimental plants:

*Passiflora edulis***:** fruits were obtained from local markets, Cairo, Egypt.

Experimental animals

Thirty six rats weighted 125±5g. Rats kept addiption for five days before experiment fed on. standard diet which comprised of casein (200g/kg), cellulose (30 g/kg), corn starch (497g/kg), corn oil (50g/kg), sucrose (100g/kg), vitamin mixture (20g/kg) mineral mixture (100g/kg), and DL-methionine (3g/kg), according to **Reeves et al. (1993).**

B- Methods:

Indomethacin-induced gastric ulcer:

Single oral dose of indomethacin (30 mg/kg body weight) to induce gastric damage **(Sayanti et al., 2007)**

Experimental procedures:

The first group (n= 6 rats) was kept as (C –ve) normal rats. The rats of second main group (30 rats) indomethacin, (30 mg/kg/diet) was administered to all animals orally to induce gastric damage according to (**Sayanti et al. 2007**), after the administration division into 5 sub-groups as follows:

Sub-group (2): Orally rats by indomethacin as a positive control (C +ve).

Sub-group (3): Sub-group (2). and treated with dose 30 mg/kg ranitidine drug.

Sub-group (4): Sub-group (2). and fed on 10g/kg/diet *Passiflora edulis* powder.

Sub-group (5): Sub-group (2). and fed on 5 ml/kg/ rats *Passiflora edulis* extract**.**

Sub-group (6): Sub-group (2). and 10g/kg/diet and 5 ml/kg/ rats mixture of *Passiflora edulis* powder and extract**.**

Daily feed intake and weekly body weight gain were calculated, Food efficiency ratio (FER) was determined according to the method of **Chapman et al. (1959**). Experiment ended after (6 weeks).

Pylorus ligation-induced gastric ulcer:

Were determined according to **Bhave *et* al. (2006)**. Animals were deprived of both food and water during the postoperative period **(Parmar and Desai, 1993).**

Gastric mucosal injury was assessed:

Ulcer index was calculated by following formula (**Parmar and Desai, 1993).**

UI = 1 × (number of lesions of grade 1) + 2 × (number of lesions of grade 2) + 3 × (number of lesions of grade 3).

The gastric secretion fluid was collected, volume and pH was measured (**Kilic, et al., 2006).**

Curative ratio=(length of gastric ulcer in control positive group - length of gastric ulcer in treated group / length of gastric ulcer in control positive group) ×100.

Biochemical analysis:

Determination of gastric mucosa:

Gastric mucosal of cyclooxygenase ($Cox\text{-}_2$), prostaglandin E_2 (PGE_2), cytochrome P_{450} reductase (Cyto P_{450}) were determined according to **Hemler and Lands (1976); Hamberg and Samuelsson (1973); Mc-Lean and Day, (1974),** respectively.

Statistical analysis:

The obtained data were statistically analyzed using computerized SPSS. Effects of different treatments were analyzed by one way ANOVA **(Snedecor and Cochran, 1967).**

3. Results and Discussion

Data recorded in Table 1 illustrated that the positive control rats showed a significant decrease in weight gain, feed intake and FER compared to their corresponding normal control group. These results may be attributed to loss of appetite, caused by gastric ulcer disturbance in the gastric enzymes secretions, changes in the pH of gastric secretion and alteration in the level of hormone s in the body. These data are similar to that of **Hunt et al. (2006).** Weight gain feed intake and FER of all treated groups (10 g/kg, 5ml & mixture) *Passiflora edulis* powder and extract and drug group significantly increased as compared to the positive control group, this is in agreement with the previous studies done some by **Omotesho et al. (2013)** who reported that *Passiflora edulis* fruits contain important polyphenolic compounds such as high level of salicylic, querctin and ellagic acid. These results are in parallel with those reported by **Mona et al. (2013) and Masni et al, (2017).**

The results of the anti-ulcer studies Table 2 showed that pH, volume of gastric secretion were significantly reduced by of all treated groups (10 g/kg, 5ml & mixture *Passiflora edulis* powder and extract and drug group as compared to the control (+ve) group The volume of gastric juice was significantly reduced in all treated groups as compared to control (+ve) while being significantly higher than the normal group. Moreover, the reduction was found to be significant between all treated groups as compared to each other except for (10 g/kg, 5ml mixture) *Passiflora edulis* powder and extract treated groups (insignificant difference). The highest reduction of the ulcer index was obtained by drug group followed by mixture of powder and extract (58.51), and 5 ml/kg *Passiflora edulis* extract (52.18). The Curative ratio showed significant decrease in treated groups (10 g/kg, 5ml & mixture *Passiflora edulis*. The results are in agreement with those obtained by **Debnath et al. (2007)** which conclude that the *Passiflora edulis* improve the state of ulceration experimental animals, it considered as antiulcer against indomethacin. Significant inhibition was also observed in gastric secretion and indomethacin induced gastric ulceration in pylorus legated rats. *Passiflora edulis* may be used to be a drug of natural materials which has both anti-inflammatory and antiulcer activity **Farooq et al. (2007)**.

The biomarkers analysis in Table 3 revealed that significantly decrease in the level of cyclooxygenase activity compared with control (+ve) group, and increase in the level of prostaglandin (PGE2) concentration and cytochrome (P450) reductase

activity in all treated rat groups compared with control (+ve) group. The groups treated with (10 g/kg, 5ml & mixture) *Passiflora edulis* powder and extract and drug group showed non insignificant difference compared to control (-ve) group. The effect of mixture on the biomarkers cytochrome (P450) was found to be the highest among the other treated groups followed by extract group, drug group and *Passiflora* powder group**.** Another study by **Anjorin et al. (2010) and Mangale et al. (2012)** who reported that the *Passiflora edulis* has an inflammatory action that enhance healthy metabolism and activity of arachadonic acid, prostaglandins, leukotrienes and platelets. *Passiflora edulis* is a natural COX-2 enzyme modulator, by stopping effect caused by COX-2 enzyme and an antioxidant that helps to scavenging free radicals.

In Table 6 showed that the positive control group showed a significant decrease in glutathione peroxidase (GPX) and superoxid dismutase (SOD), while a significant increase in malondialdehyde (MDA) compared to (-ve) control group. It is potential that increased reactive oxygen species (ROS) production in the serum may be responsible for this damage of the organ as reflected by the change in the levels of MDA and activities of SOD in the study. Treatment with drug and *Passiflora edulis* showed also significant increase glutathione peroxidase (GPX), superoxid dismutase (SOD) all treated groups (10 g/kg, 5ml & mixture) *Passiflora edulis* powder, extract and drug group. The results Table 4 the antioxidant active effect is mainly due to enhancement of phenolics and peroxidase production in suspension cultures of *Passiflora edulis* was investigated **Farooq et al. (2007) and Aja et al. (2014).**

Table (1): Effect of *Passiflora edulis* administration on body weight gain, feed intake (FI) and food efficiency ratio (FER) of rats

Parameters / Groups	Weight gain (g)	FI (g/d)	FER
Normal (-ve)	113.76± 8.11 a	15.94± 2.20 a	0. 255± 0.03a
Control (+ve)	66.59± 6.11 b	13.58± 2.03 b	0.175± 0.02 b
Drug RHL	105.13± 9.13 a	15.25± 2.32 a	0.246± 0.04 a
Passiflora powder	101.77± 9.17 a	15.46± 2.21 a	0.217± 0.03 a
Passiflora extract	106.86± 9.17 a	15.68± 2.92 a	0.230± 0.04 a
Mixture powder & extract	109.86± 9.17 a	15.68± 2.92 a	0.250± 0.04 a

Values with the same letters indicated insignificant difference and vice versa

Table (2): Effect of *Passiflora edulis* administration on the length of gastric ulcer, volume of gastric juice and PH of rats

Parameters / Groups	Gastric ulcer length (mm.)	Curative ratio (%)	Volume of gastric juice (1ml)	Decrease ratio (%)	PH (mEq/L)
Normal group (-ve)	0.00± 0.00	-	2.84± 0.08 e	-	6.62± 0.53 a
Control (+ve)	8.21± 1.98 a	-	8.05± 0.16 a	-	2.01± 0.41 c
Drug RHL	3.89± 0.18 d	52.62± 5.16 a	3.08± 0.16 d	61.74± 1.09 a	3.11± 0.17 b
Passiflora powder	5.77± 0.83 b	29.84± 6.89 c	5.39± 0.25 b	33.05± 2.38 d	3.76± 0.39 b
Passiflora extract	4.28± 0.46 c	47.86± 5.47 b	3.85± 0.14 c	52.18± 1.92 c	3.50± 0.24 b
Mixture powder & extract	4.05± 1.50 cd	50.69± 6.64 ab	3.34± 0.10 c	58.51 ± 1.88 b	3.25± 0.42 b

Values with the same letters indicated insignificant difference and vice versa

Table (3): Effect of *Passiflora edulis* administration of gastric tissues cyclooxygenase activity (Cox-2), Prostaglandin (PGE2), and P_{450} reductase (P450) activity of rats

Parameters / Groups	Cox-2 (ng/mg)	PGE2 (pg/mg)	P450 Cyto (ng/mg)
Normal (-ve)	6.33± 0.55e	513.55± 45.19 a	4.26± 0.32 a
Control (+ve)	19.72± 3.82 a	367.56± 25.27 c	0.76± 0.07 e
Drug RHL	7.84± 1.35 d	492.39± 31.92 ab	3.77± 0.24 ab
Passiflora powder	10.67± 1.79 b	474.76± 33.12 b	2.98± 0.47 c
Passiflora extract	8.78± 1.51 bc	485.90± 34.62 b	3.14± 0.04 b
Mixture powder & extract	7.60± 1. 92 d	482.64± 42.68 b	3.49± 0.58 b

Values with the same letters indicated insignificant difference and vice versa

Table (4): Effect of *Passiflora edulis* administration of glutathione-peroxidase (GSP), superoxide dismutase (SOD) and malondialdehyde (MDA) of rats

Parameters / Groups	GSP (mmol/l)	SOD (mmol/l)	MDA (mmol/l)
Normal (-ve)	8.35± 1.37a	20.71± 9.21a	5.22± 0.25b
Control (+ve)	4.34± 0.44d	13.41± 3.21c	9.71± 1.41a
Drug RHL	6.91± 1.46b	19.71± 3.21b	5.71± 0.68b
Passiflora powder	5.31± 1.32c	17.00± 4.11b	4.41± 0.61b
Passiflora extract	5.33± 1.16c	17.71± 4.61b	4.36± 0.77b
Mixture powder & extract	6.91± 0.53b	18.38± 4.61ab	4.21± 1.10b

Values with the same letters indicated insignificant difference and vice versa

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