Section A-Research paper



Antioxidant activity and Gastroprotective activity: *Cucurbita pepo* and *Benincasa hispida*

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Abstract

Ethanol extracts of selected plants have exhibited significant gastroprotective activity. The ethanol extract of cucurbita pepo at a dose of 200 and 300 mg/kg b.w has showed significant gastroprotective activity than ethanol extract of benincasa hispida at a dose of 200, 300mg/kg b.w. Gastroprotective action of certain phytoconstituents like flavonoids, alkaloids, Tannins Have been well documented in the literature. The above mentioned phytoconstituents alone or in combination may be resposible for the gastroprotective activity of the selected plants.

The result obtained when animals were subjected with HCl–ethanol induced ulcer and pretreated with Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) at doses of 100, 200 and 300 mg/kg. The 200 mg/kg and 300 mg/kg were showed inhibitory effect in ulcer index while 100 mg/kg did not show any significant effect in ulcer index.

INTRODUCTION

Peptic ulcers are sores or lesions in the gastrointestinal mucosa extending throughout the muscularis mucosae, typically characterized by different stages of necrosis, neutrophil infiltration, blood flow reduction, increased oxidative stress and inflammation. PU manifest

as a non-fatal disease, majorly represented by periodic symptoms of epigastric pain, which are often relieved by food or alkali, besides to trigger much discomfort to patients, disrupting their daily routines and also causing mental agony. The disease is mostly categorized based on its anatomical origins, such as gastric (found along the lesser curvature of the stomach) and duodenal (occurring in the duodenal bulb—the most posed area to gastric acid) ulcers.

Studies have shown that peptic ulcer disease occurs because of an imbalance between aggressive injurious (e.g., pepsin, HCl) and defensive mucosa-protective factors (e.g., prostaglandins, mucus and bicarbonate barrier and adequate blood flow). All ulcers of the upper gastrointestinal tract were originally thought to be caused by the aggressive action of pepsin and gastric acid on mucosa[1].

However, the denomination "peptic ulcer" has lately pointed to Helicobacter pyloriinfection, where the chronic use of non-steroidal anti-inflammatory drugs (NSAIDs) and acetylsalicylic acid (ASA) are some of the disease-causing factors. Thus, based on the latest advances on this field and stress the fact that PUD is an important cause of morbidity and health care costs, the present report aims to provide a general overview on peptic ulcers, namely considering their epidemiology, main symptoms and clinical features, pathogenesis, where a particular emphasis will be given to H. pylori infection, pharmacological agents used in an effective management and also pointing out the latest challenges and opportunities of using plant phytochemicals as upcoming antiulcerogenic agents. Lastly, a special emphasis was given on plant products safety and security, in order to trigger the interest in deepening skills on this matter and to ensure an effective managing competence for health-related systems[2].

Gastro Protective Activity

Gastro Protective Activity of extract of Cucurbita pepo fruit and Benincasa hispida fruits were performed on various ulcer induce model including aspirin + Pylorus ligation induced, acetic acid induced chronic ulcer, HCl- ethanol induced ulcer. Ethanol extracts of Cucurbita pepo fruit and Benincasa hispida fruits were found more potent in antioxidant activity so ethanol extract were selected for further gastroprotective activity. Ethanol extracts of both plant at dose of 100 200 and 300 mg/kg were tested for gastroprotective activity using above ulcer model[3].

Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) and Benincasa hispida fruit (EOBH) on Aspirin + Pylorus ligation induced ulcer

Aspirin+pylorus ligation-induced gastric ulcer model is a useful model to induce severe ulceration in experimental animals. Aspirin causes mucosal damage by interfering with prostaglandin synthesis, increasing acid secretion and back diffusion of H+ ions. The inhibition of mucosal prostaglandin production occurs rapidly following oral administration of aspirin. This is correlated with the rapid absorption of these drugs through the mucos. In pylorus ligation, the digestive effect of accumulated gastric juice and interference of gastric blood circulation are responsible for the induction of ulceration

Aspirin causes mucosal damage by interfering with prostaglandin synthesis, increasing acid secretion and back diffusion of H+ ions. In pyloric ligation, the digestive effect of accumulated gastric juice and interference of gastric blood circulation are responsible for the induction of ulceration. Aspirin was administered to PL rats; thus, aspirin further aggravated the acidity and the resistance of the gastric mucosa was decreased thereby causing extensive damage to the glandular regions of the stomach.

Ethanol extracts of Cucurbita pepo fruit and Benincasa hispida fruits at a dose of 100 200 and 300 mg/kg b.w., were tested for gastroprotective activity using pyloric ligation rat model. Peptic ulcer is results from an imbalance between aggressive factors and the maintenance of mucosal integrity through the endogenous defense mechanisms. To regain the balance, different therapeutic agents are used to inhibit the gastric acid secretion or to boost the mucosal defense mechanisms by increasing mucosal production, stabilizing the surface epithelial cells or interfering with the prostaglandin synthesis. The causes of gastric ulcer pyloric ligation are believed to be due to stress induced increase in gastric hydrochloric acid secretion and/or stasis of acid and the volume of secretion is also an important factor in the formation of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid [3].

Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on aspirin + Pylorus ligation induced ulcer

Antiulcer study has been performed using 100, 200 and 300 mg/kg of ethanol extract of Cucurbita pepo fruit against aspirin + Pylorus ligation gastric ulcer models. The ethanol extract were administered to various groups, orally, twice a day as described earlier. The result indicated a dose-dependent antiulcerogenic activity of extract EOCP. The best effect observed was at dose of 300 mg/kg onwards with EOCP. So for further studies on other biochemical parameters of gastric secretion or mucosal studies, a dose of 300mg/kg was selected[4].

 Table 1: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on aspirin +

 Pylorus ligation induced ulcer

Group	Treatment Dose(mg/kg)	Ulcer index(mm²/rat)	% Protection
Ι	Control	15.1 ± 2.4	-
II	standard	2.7 ± 1.5	83.78
III	EOCP (100 mg/kg)	6.9 ± 2.2	53.29
IV	EOCP (200 mg/kg)	$4.4\pm2.2^*$	73.18
V	EOCP (300 mg/kg)	$3.1 \pm 1.7^{**}$	80.21

Values are mean \pm SEM for 6 rats

* P < 0.05, **P < 0.01, compared to control group

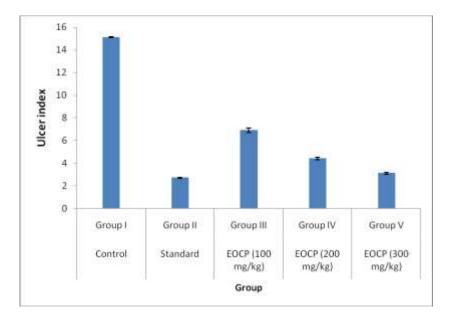


Figure 1: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on ulcer index in aspirin + Pylorus ligation induced ulcer

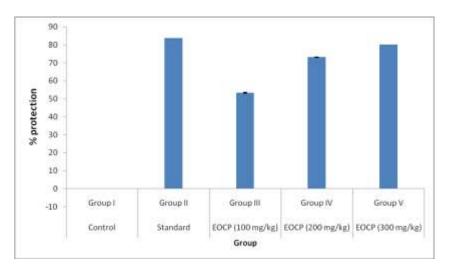


Figure 2: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on percent protection in aspirin + Pylorus ligation induced ulcer

Section A-Research paper

Effect of ethanolic extract of Benincasa hispida fruit on aspirin + Pylorus ligation induced ulcer

The ethanolic extract of Benincasa hispida fruit against aspirin + Pylorus ligation gastric ulcer models. The result indicated that extract of fruits decrease ulcer index in dose dependent manner. The maximum effect observed was at dose of 300 mg/kg. So for biochemical parameters of gastric secretion and mucosal studies, a dose of 300 mg/kg was selected[4].

Table 2: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on aspirin+ pylorus ligation induced ulcer

Group	Treatment Dose	Ulcer index	Percent
	(mg/kg)	(mm ² /rat)	protecti
			on
Ι	Control	15.1 ± 2.4	-
II	standard	2.7 ± 1.5	83.78
III	EOBH (100 mg/kg)	9.1 ± 1.0	41.12
IV	EOBH (200 mg/kg)	$7.1 \pm 1.1*$	64.21
V	EOBH (300 mg/kg)	$4.1 \pm 0.9^{**}$	74.35

Values are mean ± SEM for 6 rats

* P < 0.05,** P < 0.01 compared to control group

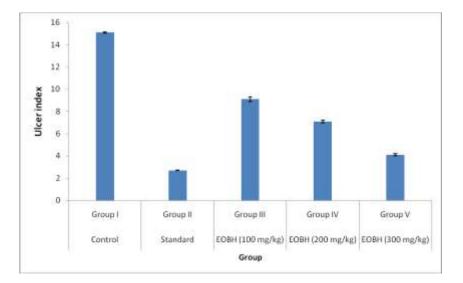


Figure 3: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on ulcer index on aspirin + pylorus ligation induced ulcer

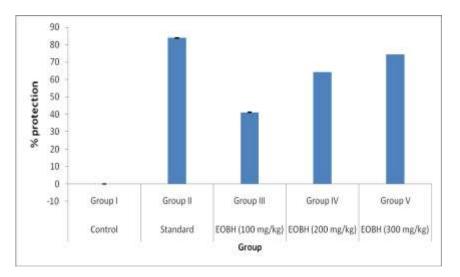


Figure 4: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on ulcer index on aspirin + pylorus ligation induced ulcer

Section A-Research paper

Effect of ethanol extract of Cucurbita pepo fruit (EOCP) on volume, acid and pepsin secretion, mucin secretion, mucosal glycoprotein

The effect of ethanol extract of *Cucurbita pepo* fruit (300 mg/kg) when administered orally, twice daily for 5 days was studied for their effect on volume, acid and pepsin secretion in aspirin + 4hrs pylorus ligation rats. The EOCP showed a trend to decrease in volume, acid-pepsin concentration and output. The result EOCP were caused significant decrease on volume, acid and pepsin concentration and acid output comparable to standard. The data are presented in table [5].

Mucoprotein was estimated in the 90% alcoholic precipitate of the gastric juice in aspirin + 4hrs pylorus ligation rats treated with ethanol extract of *Cucurbita pepo* fruit. Treated group with EOCP showed enhance the concentration of total carbohydrates and individual carbohydrates like total hexoses, hexosaamine, fucose and sialic acid with a tendency to decrease protein content leading to a significant incease in TC: P ratio, indicating an increasing in mucin secretion which was comparable with the effect of ranitidine. The data are presented in table.

Gastric mucosal glycoproteins were studied in the 90% alcoholic precipitate of the homogenates of gastric mucosal scraping of the rats. Treated group with EOCP showed enhance the concentration of individual carbohydrates or total carbohydrates with a little change in protein level leading to an increase in total carbohydrate: protein ratio and thus, mucosal glycoprotein in the treated groups. The data are presented in table.

Group I (Aspirin+PL) rats, there was significant increase in protein concentration, but decrease in individual as well as total carbohydrate levels. The drug treatment significantly decreased the protein level and increased the total carbohydrate (TC) level. The index of mucin activity TC:P was found to be decreased in the Aspirin+PL rats. The EOCP and EOBH at the tested dose levels significantly increased the TC:P ratio when compared with control group[5].

Table 3: Effect ethanolic extract o	f Cucurbita pepo fruit	(EOCP) on aspirin +
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		Aci	d	Peptic		
Treatment	Volume	Concentration	Outp	Concentration	Output	
Ireatment	(µml/100g)	(µEq/ml)	ut	(µmol/ml)	(µmol/4 h)	
			(µEq/			
			4 h)			
Control	2.51 ± 0.12	97.8 ± 10.2	282.1 ±	289.1 ± 21.7	715.4 ±	
Control	2.01 - 0.12	<i>y</i> 1 0 1 0 1	12.7	207.1 = 21.7	68.2	
Standard	1.99 ± 0.09	74.2 ± 5.6	179.6 ±	200.2 ± 19.3	$440.2 \pm$	
Standard	1.55 = 0.05	,	19.4		58.4	
EOCP (300	2.04 ± 0.08	78.5 ± 9.7	156.0 ±	229.1 ± 9.4	475.5 ± 23.7	
mg/kg)	0.00		12.9			

pylorus ligation induced ulcer on volume, acid and pepsin

Values are mean ± SEM of 6 rats in each group

Table 4: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on gastricsecretion in aspirin + pylorus ligation induced ulcer

	Мисори	Mucoprotein (µg/ml)								
Treatment	Total hexose (A)	Hexosamine (B)	Fucose (C)	Sialic acid (D)	T (A+B+C+D)	Protein (P)	TC : P			
Control	248.2 ± 19.2	161.6 ± 11.2	64.2 ± 2.4	25.3 ± 2.5	499.3 ± 35.3	530.4 ± 39.6	1.02 ± 0.12			
Standard	299.2 ± 14.2	171.9 ± 10.4	71.6 ± 3.8	35.2 ± 1.9	577.9 ± 30.3	385.2 ± 28.5	1.55 ± 0.09			
EOCP (300 mg/kg)	329.3 ± 14.2	179.7 ± 12.1	73.5 ± 3.9	33.4 ± 1.7	615.9 ± 31.9	424.1 ± 31.6	1.46 ± 0.10			

	Glycoprotein (µg/100 mg wet tissue)							
Treatment	Total	Hexosamine	Fucose	Sialic acid	ТС	Protein	TC : P	
	hexose (A)	(B)	(C)	(D)	(A+B+C+D)	(P)		
Control	2456 ± 156	1532 ± 99	298 ± 17	105 ± 9	4626 ± 319	6329 ± 245	0.75 ± 0.09	
Standard	3629 ± 164	2189 ±198**	369 ± 12	169 ± 8	$6550 \pm 399^{**}$	6298 ± 316	1.09 ± 0.12	
EOCP (300 mg/kg)	3321 ± 201	1889 ± 121*	364 ± 16	237 ± 21	$6010 \pm 343^*$	5717 ± 187	1.06 ± 0.08	

Table 5: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on gastricmucosal glycoprotein in aspirin + pylorus ligation induced ulcer

Values are mean \pm SEM of 6 rats in each group

*P <0.05, **P <0.01 compared to respective control group

Effect of ethanol extract of Benincasa hispida fruit (EOBH) on volume, acid and pepsin secretion, mucin secretion, mucosal glycoprotein

The effect of ethanolic extract of Benincasa hispida fruit (EOBH) at a dose of 300 mg/kg on volume, acid and pepsin secretion showed a tendency to decrease in said parameter, while standard drug ranitidine (50mg/kg) also showed significant decrease on volume, acid and pepsin concentration and acid output. The data are presented in Table.

Mucoprotein was estimated in gastric juice of aspirin + 4 hrs pylorus ligation rats treated with EOBH. It was showed a tendency to increase the concentration of total carbohydrates and individual carbohydrates like total hexoses, hexosamine, fucose and sialic acid with a tendency to decrease protein content indicated that secretion of mucin increased. Results are given in table.

The Gastric mucosal study of glycoproteins result indicated a tendency to increase in the concentration of individual carbohydrates and total carbohydrates with a change in protein level increase in glycoprotein content[6]. The data are given in table.

		Acid		Peptic		
Treatment	Volume (ml/100g)	Concentrati on (µEq/ml)	Output (µEq/4 h)	Concentration (µmol/ml)	Output (µmol/4 h)	
Control	2.51 ± 0.12	97.8 ± 10.2	282.1 ± 12.7	289.1 ± 21.7	715.4 ± 68.2	
Standard	1.99 ± 0.09	74.2 ± 5.6	179.6 ± 19.4	200.2 ± 19.3	440.2 ± 58.4	
EOBH (300 mg/kg)	2.13 ± 0.11	82.6 ± 6.3	165.0 ± 9.8	275.1 ± 10.2	498.5 ± 68.3	

Table 6: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on aspirin

Treatment	Volume (ml/100g)	Concentrati on (µEq/ml)	Output (µEq/4 h)	Concentration (µmol/ml)	Output (µmol/4 h)
Control	2.51 ± 0.12	97.8 ± 10.2	282.1 ± 12.7	289.1 ± 21.7	715.4 ± 68.2
Standard	1.99 ± 0.09	74.2 ± 5.6	179.6 ± 19.4	200.2 ± 19.3	440.2 ± 58.4
EOBH (300 mg/kg)	2.13 ± 0.11	82.6 ± 6.3	165.0 ± 9.8	275.1 ± 10.2	498.5 ± 68.3

+ pylorus ligation induced ulcer on volume, acid and pepsin

Table 7: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on gastric secretion in aspirin + pylorus ligation induced ulcer

Mucoprotein (µg/ml)							
Treatment	Total hexose (A)	Hexosamine (B)	Fucose (C)	Sialic acid (D)	T (A+B+C+D)	Protein (P)	TC : P
Control	248.2 ± 19.2	161.6 ± 11.2	64.2 ± 2.4	25.3 ± 2.5	499.3 ± 35.3	530.4 ± 39.6	1.02 ± 0.12
Standard	299.2 ± 14.2	171.9 ± 10.4	71.6 ± 3.8	35.2 ± 1.9	577.9 ± 30.3	385.2 ± 28.5	1.55 ± 0.09
EOBH (300 mg/kg)	302.3 ± 11.6	175.3 ± 9.2	72.7 ± 1.98	31.6 ± 1.2	598.7 ± 1.2	403.1 ± 12.2	1.44 ± 0.12

	Glycoprotein (µg/100 mg wet tissue)							
Treatment	Total	Hexosamine	Fucose	Sialic acid	ТС	Protein	TC : P	
	hexose (A)	(B)	(C)	(D)	(A+B+C+D)	(P)		
Control	2456 ± 156	1532 ± 99	298 ± 17	105 ± 9	4626 ± 319	6329 ± 245	0.75 ± 0.09	
Standard	3629 ± 164	2189 ±198**	369 ± 12	169 ± 8	6550 ± 399 ^{**}	6298 ± 316	1.09 ± 0.12	
EOBH (300 mg/kg)	3256 ± 18	1756 ± 103*	35 ± 10	225 ± 14	$5981 \pm 203^{*}$	5654 ± 132	1.04±0.11	

Table 8: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on gastricmucosal glycoprotein in aspirin + pylorus ligation induced ulcer

Values are mean \pm SEM of 6 rats in each group

*P <0.05, **P <0.01 compared to respective control group

Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) and Benincasa hispida fruit (EOBH) on on 6thday acetic acid- induced chronic ulcer

Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on 6thday acetic acidinduced chronic ulcer

The study of healing property of ethanolic extract of Cucurbita pepo fruit (EOCP) on acetic acid induced ulceration has been done using dose of 100, 200 and 300 mg/kg and the healing effect was indicated a dose-dependent antiulcerogenic activity of ethanolic extract. The ulcer area was reduced after 5 day treatment respectively at a dose of 200 and 300 mg/kg while 100 mg/kg did not show significant reduction of ulcer[7].

Table 9: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on 6 th day acetic
acid- induced chronic ulcer

Group	Treatment	Ulcer area (mm ² /rat)	Healing Percentage
Ι	Control	19.8 ± 2.9	-
II	standard	$3.1 \pm 0.9^{**}$	84.21

III	EOCP (100 mg/kg)	14.1 ± 1.9	37.08
IV	EOCP (200 mg/kg)	$9.1 \pm 1.4^{*}$	58.33
V	EOCP (300 mg/kg)	$4.3 \pm 1.2^{**}$	77.21

Values are mean \pm SEM for 6 rats ^{*} P < 0.05, ^{**} P < 0.01 compared to respective control

group

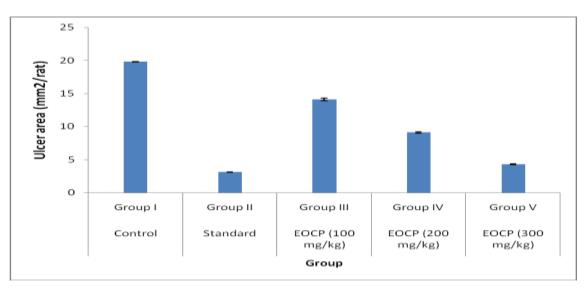


Figure 5: Effect of ethanolic extract of *Cucurbita pepo fruit* (EOCP) on ulcer index 6th day acetic acid- induced chronic ulcer

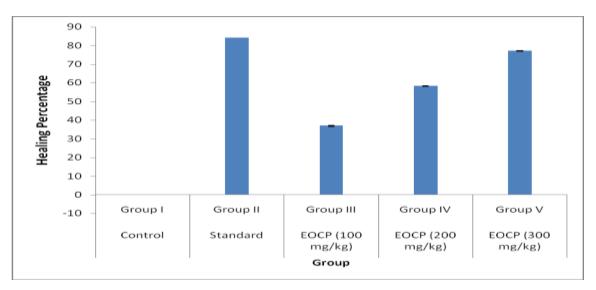


Figure 6: Effect of ethanolic extract of *Cucurbita pepo fruit* (EOCP) on healing percentage 6th day acetic acid- induced chronic ulcer

Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on 6thday acetic acidinduced chronic ulcer

The effect of Benincasa hispida fruit (EOBH) on 6th day acetic acid-induced chronic ulcers indicated that the ulcer area was reduced. 200 mg/kg and 300 mg/kg dose levels showed a highly significant when compare with control (p<0.01) decrease in ulcer area[8-12]. The graphical representation and Gastric appearance of ulcers in control and treated groups are shown in figure.

 Table 10: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on 6thday

 acetic acid- induced chronic ulcer

Group	Treatment	Ulcer area (mm²/rat)	Healing Percentage
Ι	Control	19.8 ± 2.9	-
II	standard	$3.1 \pm 0.9^{**}$	84.21
III	EOBH (100 mg/kg)	15.2 ± 1.3	35.02
IV	EOBH (200 mg/kg)	$9.8 \pm 1.1^{*}$	52.67
V	EOBH (300 mg/kg)	$4.9 \pm 0.8^{**}$	71.09

Values are mean \pm SEM * P < 0.05, ** P < 0.01 compared to respective control group

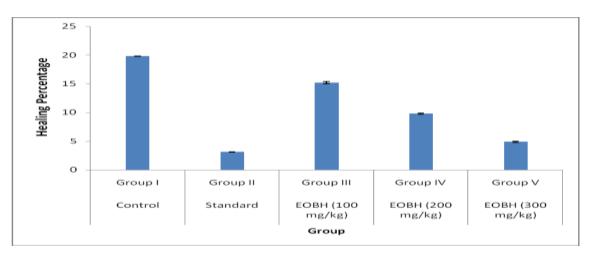


Figure 7: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on ulcer index 6thday acetic acid- induced chronic ulcer

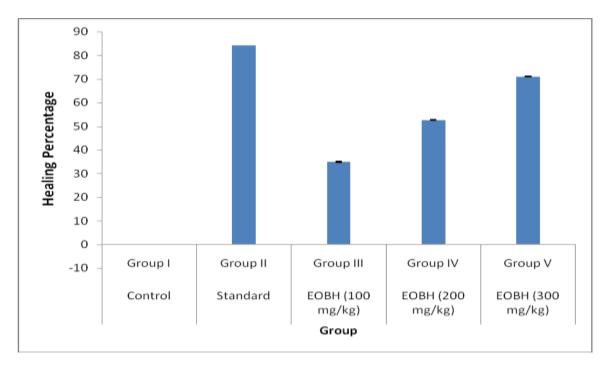


Figure 8: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on healing percentage 6th day acetic acid- induced chronic ulcer

Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on 6th day acetic acidinduced chronic ulcer on lipid peroxidation (LPO), Catalase (CAT) and Superoxide dismutase (SOD) activities

The results of the present study on free radical-mediated Lipid peroxidation and alteration in circulating enzymatic antioxidants, CAT and SOD, indicate the involvement of these enzymes in ulcer[13-16].

Table 11: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on lipid peroxidation (LPO), superoxide dismutase (SOD), and catalase (CAT) in acetic acid-induced chronic ulcer.

Group	Treatment	lipid peroxidation (LPO)	superoxide dismutase(SOD)	catalase (CAT)
Ι	Control	0.70 ± 0.03	220.3 ± 9.3	19.3 ± 1.7
I I	standard	0.51 ± 0.03**	96.5 ± 7.3**	35.3 ±1.8**
I I	EOCP (100 mg/kg)	0.65 ± 0.06	183.2 ± 2.2	23.8 ± 1.1

Ι				
T	EOCP (200	$0.58 \pm 0.01^{**}$	$142.0 \pm 2.4^{**}$	$30.2 \pm 1.9^{**}$
V	mg/kg)	0.58 ± 0.01	142.0 ± 2.4	50.2 ± 1.9
V	EOCP (300	$0.52 \pm 0.02 **$	109.2 ± 2.9**	37.0 ± 2.1**
v	mg/kg)	0.32 ± 0.02	$109.2 \pm 2.9^{+1}$	37.0 ± 2.1 · ·

Values are mean \pm SEM ^{*} P < 0.05, ^{**} P < 0.01 compared to respective control group

Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on acetic acidinduced chronic ulcers on lipid peroxidation (LPO), Catalase (CAT) and Superoxide dismutase (SOD) activities

Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on in vivo antioxidant parameters like LPO and SOD level decreases respectively when compare with control (P < 0.001) at a dose level 100, 200, 300 mg/kg while increased CAT Level (P < 0.01). The level of these enzymes indicates the involvement in ulcer[17-19].

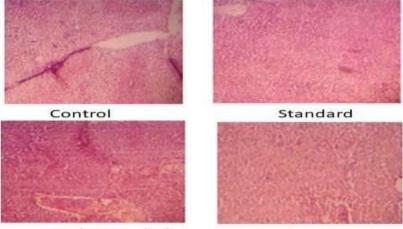
Table 12: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on acetic acid-induced chronic ulcers on lipid peroxidation (LPO), Catalase (CAT) and Superoxide dismutase (SOD) activities

Group	Treatment	lipid peroxidation (LPO)	superoxide dismutase (SOD)	catalase (CAT)
Ι	Control	0.70 ± 0.03	220.3 ± 9.3	19.3 ± 1.7
II	standard	0.51 ± 0.03**	96.5 ± 7.3**	35.3 ±1.8**
III	EOBH (100 mg/kg)	0.68 ± 0.05	189.2 ± 1.2	21.7 ± 0.9
IV	EOBH (200 mg/kg)	$0.60 \pm 0.01^{**}$	149.0 ± 2.1**	$26.2 \pm 1.9^{*}$
V	EOBH (300 mg/kg)	$0.54 \pm 0.03^{**}$	116.2 ± 1.7**	39.7 ± 1.7**

Values are mean \pm SEM * P < 0.05, ** P < 0.01 compared to respective control group

Histopathology of gastric tissue on 6th day acetic acid- induced chronic ulcers

Histopathology of the gastric tissue of the control showed focal ulceration and necrosis within the gastric mucosa. The mucosal layer was infiltrated by mixed inflammatory cells. The sub mucosal layer showed scattered inflammatory infiltration along with some congested vascular spaces and areas of hemorrhage. The muscular and serosal layers however appeared within normal limits. Animals treated with EOCB (200mg/kg) showed gastric mucosa with intact lining epithelium. The submucosal slayer showed some congested vascular spaces. The muscular and serosal layers appeared within normal limits. Animals treated with EOCB (200mg/kg) showed some congested vascular spaces. The muscular and serosal layers appeared within normal limits. Animals treated with EOCB (200mg/kg) shows gastric mucosa with intact lining epithelium[20-23]. The mucosal layer and submucosal layer were infiltrated by scattered mononuclear inflammatory cells predominantly compare with ranitidine as standard. The muscularly layer appeared with in normal range.



EOCB (200mg/kg)

EOCB (300mg/kg)

Figure 9: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on 6th day acetic acid- induced chronic ulcers on Histopathology of gastric tissue

Histopathology of the gastric tissue of the control animals showed focal ulceration and few areas of necrosis within the gastric mucosa. The mucosal layer was infiltrated by mixed inflammatory cells. The sub mucosal layer showed scattered inflammatory infiltration along with some congested vascular spaces and areas of hemorrhage. The muscular and serosal layers however appeared within normal limits. Animals treated with

200 mg/kg of EOBH showed gastric mucosa with intact lining epithelium. The submucosal slayer showed some congested vascular spaces. The muscular and serosal layers appeared within normal limits. Animals treated with 300 mg/kg of EOBH the extracts shows gastric mucosa with intact lining epithelium. The mucosal layer and submucosal layer were infiltrated by scant scattered mononuclear inflammatory cells predominantly compare with ranitidine as standard. The muscularly layer appeared with in normal range[24-28].

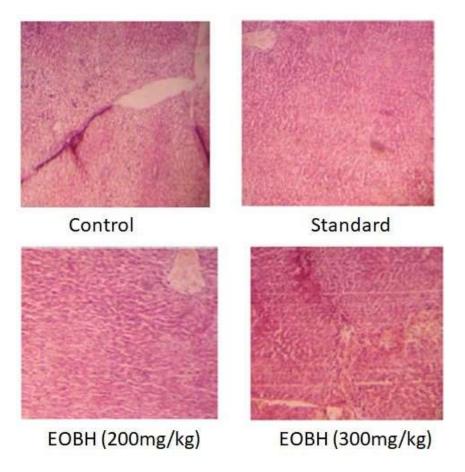


Figure 10: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on 6th day acetic acid- induced chronic ulcers on Histopathology of gastric tissue

The rats of control group treated with HCl–ethanol showed histopathological changes in the gastric mucosa by loss of glandular architecture, oedema and erosions of the epithelial layer, this infiltration by inflammatory cells. The animals treated with the EOCP (200mg/kg) and EOCP (300mg/kg) showed significant healing of gastric tissue.

Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) and Benincasa hispida fruit (EOBH) on HCl- ethanol induced ulcer

Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on HCl- ethanol induced ulcer

The result obtained when animals were subjected with HCl–ethanol induced ulcer and pretreated with Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) at doses of 100, 200 and 300 mg/kg. The 200 mg/kg and 300 mg/kg were showed inhibitory effect in ulcer index while 100 mg/kg did not show any significant effect in ulcer index[29-32].

Table 13:	Effect	of	ethanolic	extract	of	Cucurbita	pepo	fruit	(EOCP)	on HCl-
ethanol in	duced u	lce	r							

Group	Treatment	Ulcer (mm²/rat)	index Percent protection
Ι	Control	17.2 ± 2.2	-
II	standard	3.6 ± 1.1 ^{**}	80.31
III	EOCP (100 mg/kg)	12.5 ± 1.9	30.21
IV	EOCP (200 mg/kg)	$7.9 \pm 1.4^{*}$	58.34
V	EOCP (300 mg/kg)	$4.0 \pm 1.9^{**}$	76.21

Values are mean \pm SEM ^{*} P < 0.05, ^{**} P < 0.01 compared to respective control group Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on HCl- ethanol induced ulcer

Effect of ethanolic extract of Benincasa hispida fruit (EOBH) at a dose of 100, 200 and 300 mg/kg against HCl-ethanol induced ulcer. The dose of 200 mg/kg & 300 mg/kg and standard were showed inhibitory effect in ulcer index when compared from control.

Table 14: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on HCl-
ethanol induced ulcer

Group	Treatment	Ulcer in (mm²/rat)	ndexPercent protection
Ι	Control	17.2 ± 2.2	-
II	standard	3.6 ± 1.1**	80.31
III	EOBH (100 mg/kg)	12.9 ± 2.1	28.54
IV	EOBH (200 mg/kg)	$8.4 \pm 1.7^{*}$	56.21
V	EOBH (300 mg/kg)	$4.7 \pm 1.7^{**}$	72.21

Values are mean \pm SEM * P < 0.05, ** P < 0.01 compared to respective control group

Histopathology of Cucurbita pepo fruit (EOCP) and Benincasa hispida fruit (EOBH) on HCl - ethanol induced ulcer:

The rats of control group treated with HCl–ethanol showed histopathological changes in the gastric mucosa by loss of glandular architecture, oedema and erosions of the epithelial layer, this infiltration by inflammatory cells. The animals treated with the EOCP (200mg/kg) and EOCP (300mg/kg) showed significant healing of gastric tissue[33].

Section A-Research paper

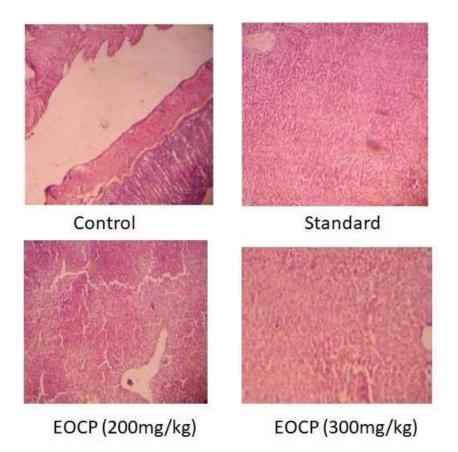
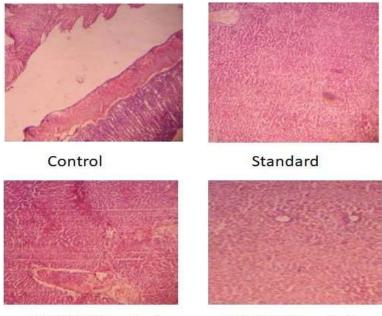


Figure 11: Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) on HCl ethanol induced ulcer on Histopathology of gastric tissue

The rats of control group treated with HCl–ethanol showed histopathological changes in the gastric mucosa by loss of glandular architecture, oedema and erosions of the epithelial layer. This was showed due to infiltration by inflammatory cells. The rats treated with the Benincasa hispida fruit (EOBH) at a dose of 200, 300 mg/kg the result showed significant regenerative changes[34-35].

Section A-Research paper



EOBH (200mg/kg)

EOBH (300mg/kg)

Figure 12: Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on HCl ethanol induced ulcer on Histopathology of gastric tissue

Increased mucus secretion by the gastric mucosal cells can prevent gastric ulceration by several mechanisms, including lessening of stomach wall friction during peristalsis and gastric contractions, improving the buffering of acid in gastric juice and by acting as an effective barrier to back diffusion of H+ ions. Both the plant extract EOCP and EOBH at dose 200mg/kg and 300 mg/kg were found to augment the mucin secretion as evidenced from the increase in concentration of the individual as well as total carbohydrate levels. The drugs also increased the TC:P ratio, which reflects the functional integrity of the mucosal barrier and has been accepted as a reliable index of mucin secretion. The increase in protein content of the gastric juice resulting in a decrease in the TC:P. ratio in the Aspirin+PL animals indicates damage of the gastric mucosa, as a result of which the plasma proteins may leak into the gastric juice. Effect of extract on secretory parameters like total and free acidity, total acid output, gastric volume and ulcer index. From the results, it is clear that the drugs exhibited significant antisecretory activity by reducing the secretory parameters when compared with the control group. As the EOCP and EOBH treatment significantly reduced the protein[36]

concentration and increased the total carbohydrate content, it may be suggested that the extract EOCP and EOBH may act by strengthening the mucosal barrier of the gastric mucosa. The EOCP and EOBH, 300 mg/kg p.o. showed activity that is comparable to the standard drug, Ranitidine. The presence of polysachharises in EOCB and EOBH may be responsible for the mucoprotective action in the specified ulcer model. The antiulcer activity of various polysaccharides in experimental ulcers has also been reported (Sun et al., 1992; Matsumoto et al., 2002). The antiulcerogenic potential of EOCP and EOBH was further evidenced by the histopathological studies.In conclusion, both EOCP and EOBH, 300 mg/kg p.o. exhibited antiulcerogenic activity, which may be attributed to the presence of mucilaginous polysaccharides.

Ethanol extracts of selected plants have exhibited significant gastroprotective activity. The ethanol extract of cucurbita pepo at a dose of 200 and 300 mg/kg b.w has showed significant gastroprotective activity than ethanol extract of benincasa hispida at a dose of 200, 300mg/kg b.w. Gastroprotective action of certain phytoconstituents like flavonoids, alkaloids, Tannins Have been well documented in the literature. The above mentioned phytoconstituents alone or in combination may be resposible for the gastroprotective activity of the selected plants[37].

SUMMRY AND CONCLUSION

Pharmacognostic study helps in confirmation and determination of identity, purity and quality of a crude drug. Morphological characterization of *Cucurbita pepo* reveals that it is a sprawling vine with yellow fruit-bearing flowers. The of Cucurbita pepo have a mild flavor. Size and weight of fruit may vary.

Benincasa hispida is a large climbing or trailing herb with stout hispid stems. Fruits are 30 to 45 cm long broadly, cylindric, not ribbed hairy, ultimately covered with a waxy bloom. Fruit is covered in a fuzzy coating of fine hairs when young. The immature melon has thick white flesh that tastes sweet. By maturity, the fruit loses its hairs and develops a waxy coating, giving rise to the name wax gourd. The fruit may grow as large as 80 cm in length. It has yellow flowers and broad leaves.

Total ash of Cucurbita pepo fruit was found 6.4%. Water soluble ash was found 2.91 % whereas 0.91% was acid insoluble ash. The ethanol soluble extractive values were found

to be 9.6% and water- soluble extractive values were found to be 13.8 %. The moisture content of the powder estimated as percentage loss on drying (LOD) was found to be 29.2 % w/w. Total ash of Benincasa hispida fruit was found 5.7%. Water soluble ash was found 2.68 % whereas 0.98% was acid insoluble ash. The ethanol soluble extractive values were found to be 8.3 % and water- soluble extractive values were found to be 10.9% and loss on drying (LOD) was found to be 27.86% w/w.

The coarse powder of the fruit of *Cucurbita pepo* and *Benincasa hispida* were subjected to successive solvent extraction using solvents of ascending polarity. After extraction the percentage yield of each extract was calculated with reference to the air dried drug used for the study. The qualitative phytochemical screening of the tubers for the presence of alkaloids, carbohydrate ,reducing sugars, glycosides like anthraquinones, flavanoids, saponins, tannins, phenolic compounds, fixed oils, fats, proteins, amino acids and sterols in petroleum ether, ethyl acetate and ethanol extracts of the fruit of *Cucurbita pepo* and *Benincasa hispida* were carried out.

Analysis of the free radical scavenging activities of the selected *Cucurbita pepo* fruit and *Benincasa hispida* fruits extracts revealed a concentration dependent free radical scavenging activity resulting from reduction of DPPH, NO, Hydroxyl radical and superoxide radical radical to non-radical form. The scavenging activity of Ascorbic acid,

a known antioxidant used as positive control, was however higher[38-40].

DPPH radical is considered to be a model for a lipophilic radical. A chain in lipophilic radicals was intiated by the lipid autoxidation. DPPH is a stable free radical at room temperature and accepts an electron or hydrogen radical to become a stable diamagnetic molecule. The reduction capacity of DPPH was determined by the decrease in its absorbance at 517nm, which is induced by antioxidant. Positive DPPH test suggests that the samples were free radical scavengers. The scavenging effect of 1-Ascorbic acid, and plant extracts increased gradually with increase in concentration. In case of cucurbita pepo extracts the order of reduction potential was: Ascorbic acid> EOCP > EACP> PECP.

Percentage Inhibition of in vitro anti oxidant result of various Benincasa hispida fruit extracts by DPPH Method and ascorbic acid as standard at various concentrations were tested. In case of Benincasa hispida extracts the order of reduction potential was: Ascorbic acid> EOBH >EABH >PEBH. Nitric oxide plays an important role in various types of inflammatory processes in the body. In the present study the fruit extracts of selected cucurbita pepo and Benincasa hispida checked for its inhibitory effect on Nitric oxide production. Nitric oxide radical generated for sodium nitroprusside at physiological pH was found to be inhibited by the extracts.

The ethanol extract of cucurbita pepo at varied concentrations showed remarkable inhibitory effect of nitric oxide radical scavenging activity compared to other extract. Results revealed that all the tested extracts showed the percentage of inhibition in a dose dependent manner.

The inhibitory effect of Benincasa hispida fruits extracts on Nitric oxide radical scavenging model was tested. The ethanol extract of Benincasa hispida at varied concentrations showed remarkable inhibitory effect of nitric oxide radical scavenging activity compared to other extract. The ethanol extract of cucurbita pepo at varied concentrations showed remarkable inhibitory effect of nitric oxide radical scavenging activity compared to other extract. The ethanol extract of cucurbita pepo at varied concentrations showed remarkable inhibitory effect of nitric oxide radical scavenging activity compared to other extract. The ethanol extract of cucurbita pepo showed more activity than ethanol extract of Benincasa hispida[41-44].

The hydroxyl radical is an extremely reactive free radical formed in biological systems and has been implicated as a highly damaging species in free radical pathology, capable of damaging almost every molecule found in living cells. This radical has the capacity to join nucleotides in DNA and cause strand breakage, which contributes to carcinogenesis, mutagenesis and cytotoxicity. Hydroxyl radical scavenging capacity of an extract is directly related to its antioxidant activity. The highly reactive hydroxyl radicals can cause oxidative damage to DNA, lipids and proteins. The effect of the selected plant extracts were assessed by means of the iron (II)- dependent DNA damage assay. The fentone reaction generated hydroxyl radicals (OH) which degrade DNA deoxy ribose, using Fe 2+ salts as an important catalytic component. Oxygen radicals may attack DNA either at the sugar or the base, giving rise to a large number of products. All the results showed hydroxyl radical scavenging activity in a dose dependent manner.

The ethanol extract of cucurbita pepo at varied concentrations showed remarkable

inhibitory effect of Hydroxyl radical scavenging activity compared to petroleum ether and ethyl acetate extract. The ethanol extract of cucurbita pepo showed more inhibitory effect of Hydroxyl radical scavenging activity compared ethanol extract of Benincasa hispida. The ethanol extract of Benincasa hispida at varied concentrations showed remarkable inhibitory effect of Hydroxyl radical scavenging activity compared to petroleum ether and ethyl acetate extract.

Superoxide is a reactive oxygen species, which can cause damage to the cells and DNA leading to various diseases. It was therefore proposed to measure the comparative interceptive ability of the antioxidant extracts to scavenge the superoxide radical. Several In vitro methods are available for generation of super oxide radicals. In the present study the superoxide radicals were generated by auto-oxidation of hydroxylamine in the presence of NBT (Nitro blue tetrazolium). The reduction of NBT in presence of antioxidants was measured. The decrease of absorbance at 560 nm with antioxidants thus indicates the consumption of superoxide anion in the reaction mixture. The ethanol extract of Benincasa hispida at varied concentrations showed remarkable inhibitory effect of superoxide radical activity scavenging compared to petroleum ether and ethyl acetate extract. The ethanol extract of cucurbita pepo at varied concentrations showed[45-48]

remarkable inhibitory effect of superoxide radical scavenging activity compared to petroleum ether and ethyl acetate extract.

The ethanol extract of *Benincasa hispida* at varied concentrations showed remarkable inhibitory effect of superoxide radical activity scavenging compared to petroleum ether and ethyl acetate extract. From this work we conclude that all the extracts were exhibiting significant scavenging activity towards 1, 1-di phenyl picryl hydrazyl, Nitric oxide, Hydroxyl, Super oxide radicals. The activity was found to be concentration dependent. In DPPH model the free radical scavenging capacity was found to be highly significant when compare other three models. In all the three selected plants Ethanol extract was found to have high scavenging activity than Ethyl acetate and petroleum ether extracts. Scavenging activity of ethanol extracts may be due to presence of the flavonoids and phenolic. Acute toxicity studies were performed for extracts of selected three plants according to the toxic classic method as per guidelines 423 prescribed by OECD. Acute toxicity studies of extracts of *Cucurbita pepo* and *Benincasa hispida* fruit were performed in animals at dose levels of 50, 300 and 2000 mg/kg as per OECD guide lines. No mortality was observed in animals dosed with the extracts of *Cucurbita pepo* and *Benincasa hispida* fruits at dose levels of 50, 300 and 2000 mg/kg (p.o). The treated animals did not demonstrate any significant changes in behavioral pattern and exhibited normal activity. Also there were no clinical signs of tremors, convulsions, exophthalmos, salivation, diarrhea and lethargy. There was no significant difference in the mean body weights between treated groups and control group and the rats exhibited normal body weight gain during the study. No lethal effects or mortality was observed in animals throughout the test period following single oral administration at all selected dose levels of all extracts. The animals were examined for long term toxicity (14 days).. None of these extracts showed any mortality even at the dose of 2000mg/kg. From the results of acute toxicity studies $1/10^{\text{th}}$, $1/20^{\text{th}}$ doses were selected for the experimental study[49-54].

Gastro Protective Activity of extract of Cucurbita pepo fruit and Benincasa hispida fruits were performed on various ulcer induce model including aspirin + Pylorus ligation induced, acetic acid induced chronic ulcer, HCl- ethanol induced ulcer. Ethanol extracts of Cucurbita pepo fruit and Benincasa hispida fruits were found more potent in antioxidant activity so ethanol extract were selected for further gastroprotective activity. Ethanol extracts of both plant at dose of 100 200 and 300 mg/kg were tested for gastroprotective activity using above ulcer model.

Aspirin+pylorus ligation-induced gastric ulcer model is a useful model to induce severe ulceration in experimental animals. Aspirin causes mucosal damage by interfering with prostaglandin synthesis, increasing acid secretion and back diffusion of H+ ions. The inhibition of mucosal prostaglandin production occurs rapidly following oral administration of aspirin. This is correlated with the rapid absorption of these drugs through the mucos. In pylorus ligation, the digestive effect of accumulated gastric juice and interference of gastric blood circulation are responsible for the induction of ulceration

Aspirin causes mucosal damage by interfering with prostaglandin synthesis, increasing acid secretion and back diffusion of H+ ions. In pyloric ligation, the digestive effect of accumulated gastric juice and interference of gastric blood circulation are responsible for the induction of ulceration. Aspirin was administered to PL rats; thus, aspirin further aggravated the acidity and the resistance of the gastric mucosa was decreased thereby causing extensive damage to the glandular regions of the stomach.

Ethanol extracts of Cucurbita pepo fruit and Benincasa hispida fruits at a dose of 100 200 and 300 mg/kg b.w., were tested for gastroprotective activity using pyloric ligation rat model. Peptic ulcer is results from an imbalance between aggressive factors and the maintenance of mucosal integrity through the endogenous defense mechanisms. To regain the balance, different therapeutic agents are used to inhibit the gastric acid secretion or to boost the mucosal defense mechanisms by increasing mucosal production, stabilizing the surface epithelial cells or interfering with the prostaglandin synthesis. The causes of gastric ulcer pyloric ligation are believed to be due to stress induced increase in gastric hydrochloric acid secretion and/or stasis of acid and the volume of secretion is also an important factor in the formation of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid[55].

Antiulcer study has been performed using 100, 200 and 300 mg/kg of ethanol extract of Cucurbita pepo fruit against aspirin + Pylorus ligation gastric ulcer models. The ethanol extract were administered to various groups, orally, twice a day as described earlier. The result indicated a dose-dependent antiulcerogenic activity of extract EOCP. The best effect observed was at dose of 300 mg/kg onwards with EOCP. So for further studies on other biochemical parameters of gastric secretion or mucosal studies, a dose of 300 mg/kg was selected.

The ethanolic extract of Benincasa hispida fruit against aspirin + Pylorus ligation gastric ulcer models. The result indicated that extract of fruits decrease ulcer index in dose dependent manner. The maximum effect observed was at dose of 300 mg/kg. So for biochemical parameters of gastric secretion and mucosal studies, a dose of 300 mg/kg was selected.

The effect of ethanol extract of Cucurbita pepo fruit (300 mg/kg) when administered

orally, twice daily for 5 days was studied for their effect on volume, acid and pepsin secretion in aspirin + 4hrs pylorus ligation rats. The EOCP showed a trend to decrease in volume, acid-pepsin concentration and output. The result EOCP were caused significant decrease on volume, acid and pepsin concentration and acid output comparable to standard[56-58].

Mucoprotein was estimated in the 90% alcoholic precipitate of the gastric juice in aspirin + 4hrs pylorus ligation rats treated with ethanol extract of *Cucurbita pepo* fruit. Treated group with EOCP showed enhance the concentration of total carbohydrates and individual carbohydrates like total hexoses, hexosaamine, fucose and sialic acid with a tendency to decrease protein content leading to a significant incease in TC: P ratio, indicating an increasing in mucin secretion which was comparable with the effect of ranitidine.

Gastric mucosal glycoproteins were studied in the 90% alcoholic precipitate of the homogenates of gastric mucosal scraping of the rats. Treated group with EOCP showed enhance the concentration of individual carbohydrates or total carbohydrates with a little change in protein level leading to an increase in total carbohydrate: protein ratio and thus, mucosal glycoprotein in the treated groups.

Group I (Aspirin+PL) rats, there was significant increase in protein concentration, but decrease in individual as well as total carbohydrate levels. The drug treatment significantly decreased the protein level and increased the total carbohydrate (TC) level. The index of mucin activity TC:P was found to be decreased in the Aspirin+PL rats. The EOCP and EOBH at the tested dose levels significantly increased the TC:P ratio when compared with control group.

The effect of ethanolic extract of Benincasa hispida fruit (EOBH) at a dose of 300 mg/kg on volume, acid and pepsin secretion showed a tendency to decrease in said parameter, while standard drug ranitidine (50mg/kg) also showed significant decrease on volume, acid and pepsin concentration and acid output.

Mucoprotein was estimated in gastric juice of a spirin + 4 hrs pylorus ligation rats treated with EOBH. It was showed a tendency to increase the concentration of total carbohydrates and individual carbohydrates like total hexoses, hexosamine, fucose and sialic acid with a tendency to decrease protein content indicated that secretion of mucin increased.

The Gastric mucosal study of glycoproteins result indicated a tendency to increase in the concentration of individual carbohydrates and total carbohydrates with a change in protein level increase in glycoprotein content.

The study of healing property of ethanolic extract of Cucurbita pepo fruit (EOCP) on acetic acid induced ulceration has been done using dose of 100, 200 and 300 mg/kg and the healing effect was indicated a dose-dependent antiulcerogenic activity of ethanolic extract. The ulcer area was reduced after 5 day treatment respectively at a dose of 200 and 300 mg/kg while 100 mg/kg did not show significant reduction of ulcer.

The effect of Benincasa hispida fruit (EOBH) on 6th day acetic acid-induced chronic ulcers indicated that the ulcer area was reduced. 200 mg/kg and 300 mg/kg dose levels showed a highly significant when compare with control (p<0.01) decrease in ulcer area.

The results of the present study on free radical-mediated Lipid peroxidation and alteration in circulating enzymatic antioxidants, CAT and SOD, indicate the involvement of these enzymes in ulcer.

Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on in vivo antioxidant parameters like LPO and SOD level decreases respectively when compare with control (P < 0.001) at a dose level 100, 200, 300 mg/kg while increased CAT Level (P < 0.01). The level of these enzymes indicates the involvement in ulcer.

Histopathology of gastric tissue on 6th day acetic acid- induced chronic ulcers revealed that gastric tissue of the control showed focal ulceration and necrosis within the gastric mucosa. The mucosal layer was infiltrated by mixed inflammatory cells. The sub mucosal layer showed scattered inflammatory infiltration along with some congested vascular spaces and areas of hemorrhage. The muscular and serosal layers however appeared within normal limits. Animals treated with EOCB (200mg/kg) showed gastric mucosa spaces. The muscular and serosal slayer showed some congested vascular spaces. The muscular and serosal slayer showed some congested vascular spaces. The muscular and serosal slayer showed some congested vascular spaces. The muscular and serosal layers appeared within normal limits. Animals treated with EOCB (200mg/kg) shows gastric mucosa with intact lining epithelium. The submucosal slayer showed some congested vascular spaces. The muscular and serosal layers appeared within normal limits. Animals treated with EOCB (200mg/kg) shows gastric mucosa with intact lining epithelium. The submucosal slayer showed some congested vascular spaces.

layer and submucosal layer were infiltrated by scattered mononuclear inflammatory cells predominantly compare with ranitidine as standard. The muscularly layer appeared with in normal range[59].

Histopathology of the gastric tissue of the control animals showed focal ulceration and few areas of necrosis within the gastric mucosa. The mucosal layer was infiltrated by mixed inflammatory cells. The sub mucosal layer showed scattered inflammatory infiltration along with some congested vascular spaces and areas of hemorrhage. The muscular and serosal layers however appeared within normal limits. Animals treated with 200 mg/kg of EOBH showed gastric mucosa with intact lining epithelium. The submucosal slayer showed some congested vascular spaces. The muscular and serosal layers appeared within normal limits. Animals treated with 200 mg/kg of EOBH showed some congested vascular spaces. The muscular and serosal layers appeared within normal limits. Animals treated with 300 mg/kg of EOBH the extracts shows gastric mucosa with intact lining epithelium. The mucosal layer were infiltrated by scant scattered mononuclear inflammatory cells predominantly compare with ranitidine as standard. The muscularly layer appeared with in normal range.

Effect of ethanolic extract of Benincasa hispida fruit (EOBH) on 6th day acetic acidinduced chronic ulcers on Histopathology of gastric tissue revealed that control group treated with HCl–ethanol showed histopathological changes in the gastric mucosa by loss of glandular architecture, oedema and erosions of the epithelial layer, this infiltration by inflammatory cells. The animals treated with the EOCP (200mg/kg) and EOCP (300mg/kg) showed significant healing of gastric tissue.

The result obtained when animals were subjected with HCl–ethanol induced ulcer and pretreated with Effect of ethanolic extract of Cucurbita pepo fruit (EOCP) at doses of 100, 200 and 300 mg/kg. The 200 mg/kg and 300 mg/kg were showed inhibitory effect in ulcer index while 100 mg/kg did not show any significant effect in ulcer index.

Effect of ethanolic extract of Benincasa hispida fruit (EOBH) at a dose of 100, 200 and 300 mg/kg against HCl-ethanol induced ulcer. The dose of 200 mg/kg & 300 mg/kg and standard were showed inhibitory effect in ulcer index when compared from control.

The rats of control group treated with HCl-ethanol showed histopathological changes in

the gastric mucosa by loss of glandular architecture, oedema and erosions of the epithelial layer, this infiltration by inflammatory cells. The animals treated with the EOCP (200mg/kg) and EOCP (300mg/kg) showed significant healing of gastric tissue.

The rats of control group treated with HCl–ethanol showed histopathological changes in the gastric mucosa by loss of glandular architecture, oedema and erosions of the epithelial layer. This was showed due to infiltration by inflammatory cells. The rats treated with the Benincasa hispida fruit (EOBH) at a dose of 200, 300 mg/kg the result showed significant regenerative changes.

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evidenced by the histopathological studies. In conclusion, both EOCP and EOBH, 300 mg/kg p.o. exhibited antiulcerogenic activity, which may be attributed to the presence of mucilaginous polysaccharides.

Ethanol extracts of selected plants have exhibited significant gastroprotective activity. The ethanol extract of cucurbita pepo at a dose of 200 and 300 mg/kg b.w has showed significant gastroprotective activity than ethanol extract of benincasa hispida at a dose of 200, 300mg/kg b.w. Gastroprotective action of certain phytoconstituents like flavonoids, alkaloids, Tannins Have been well documented in the literature. The above mentioned phytoconstituents alone or in combination may be resposible for the gastroprotective activity of the selected plants[60-67].

References

- Akuodor GC, Essien AD, David-Oku E, Chilaka KC, Akpan JL, Ezeokpo B, Ezeonwumelu JO. Gastroprotective effect of the aqueous leaf extract of Guiera senegalensis in Albino rats. Asian Pac J Trop Med. 2013 Oct;6(10):771-5.
- Alvarez A, Pamar F and Seveilla M A. Gastric antisecretory and anti ulcer activities of an ethanolic extract of *Bidens pilosa*. Var. *Radiata Schult. J EthanoPharmacol*.1999; 67:333-340.
- Ardiles A, Barrientos R, Simirgiotis MJ, Bórquez J, Sepúlveda B, Areche C. Gastroprotective Activity of *Parastrephia quadrangularis* (Meyen), Cabrera from the Atacama Desert. Molecules. 2018 Sep 15;23(9):2361.
- Arunachalam, K.; Balogun, S.O.; Pavan, E.; Almeida, G.V.B.; Oliveira, R.G.; Wagner, T.; Filho, V.C.; Martins, D.O. Chemical characterization, toxicology and mechanism of gastric antiulcer action of essential oil from Gallesia integrifolia (spreng.) harms in the in vitro and in vivo experimental models. Biomed. Pharmacother. 2017, 94, 292–306
- Ayaz M, Junaid M, Ullah F, Sadiq A, Shahid M, Ahmad W, Ullah I, Ahmad A, Syed NI. GC-MS Analysis and Gastroprotective Evaluations of Crude Extracts, Isolated Saponins, and Essential Oil from *Polygonum hydropiper* L. Front Chem. 2017 Aug 2;5:58.
- 6. Bharti SK, Kumar A, Sharma NK, Prakash BO, Jaiswal SK, et al. (2013) Tocopherol from seeds of Cucurbitapepo against diabetes: Validation by in vivo experiments supported by

computational docking. J Formosan Med Assoc 112: 676-690.

- Biano LS, Oliveira AS, Palmeira DN, Silva LA, de Albuquerque-Junior RLC, Duarte MC, Correa CB, Grespan R, Batista JS, Camargo EA. Gastroprotective action of the ethanol extract of Leonurus sibiricus L. (Lamiaceae) in mice. J Ethnopharmacol. 2022 Feb 10;284:114792.
- 8. Bigoniya, P.; Singh, K. Ulcer protective potential of standardized hesperidin, a citrus flavonoid isolated from Citrus sinensis. Rev. Bras. Farmacogn. 2014, 24, 330–334.
- Biondo, T.M.A.; Tanae, M.M.; Della Coletta, E.; Lima-Landman, M.T.R.; Lapa, A.J.; Souccar, C. Antisecretory actions of Baccharis trimera (Less.) DC aqueous extract and isolated compounds: Analysis of underlying mechanisms. J. Ethnopharmacol. 2011, 136, 368–373.
- 10. Blaskovich MA, Sun J, Cantor A, Turkson J, Jove R, et al. (2003) Discovery of JSI-124 (cucurbitacin I), a selective Janus kinase/signal transducer and activatorof transcription 3 signaling pathway inhibitor with potent antitumor activity against human and murine cancer cells in mice. Cancer Res 63: 1270-1279.
- 11. Boeing T, Mariano LNB, Dos Santos AC, Tolentino B, Vargas AC, de Souza P, Nesello LAN, da Silva LM. Gastroprotective effect of the alkaloid boldine: Involvement of non-protein sulfhydryl groups, prostanoids and reduction on oxidative stress. Chem Biol Interact. 2020 Aug 25;327:109166.
- 12. Boeing T, Mejía JAA, Ccana-Ccapatinta GV, Mariott M, Melo Vilhena de Andrade Fonseca Da Silva RC, de Souza P, Mariano LNB, Oliveira GR, da Rocha IM, da Costa GA, de Andrade SF, da Silva LM, Bastos JK. The gastroprotective effect of red propolis extract from Northeastern Brazil and the role of its isolated compounds. J Ethnopharmacol. 2021 Mar 1;267:113623.
- Boeing, T.; da Silva, L.M.; Somensi, L.B.; Cury, B.J.; Costa, A.P.M.; Petreanu, M.; Niero, R.; de Andrade, S.F. Antiulcer mechanisms of Vernonia condensata Baker: A medicinal plant used in the treatment of gastritis and gastric ulcer. J. Ethnopharmacol. 2016, 184, 196–207.
- 14. Boligon, A.A.; de Freitas, R.B.; de Brum, T.F.; Waczuk, E.P.; Klimaczewski, C.V.; de

Ávila, D.S.; Athayde, M.L.; de Freitas Bauermann, L. Antiulcerogenic activity of Scutia buxifolia on gastric ulcers induced by ethanol in rats. Acta Pharm. Sinica B 2014, 4, 358–367

- 15. Brand-Williams W, Cuvelier M E and Berset C. Use of free radical method to evaluate antioxidant activity. *Lebensm Wiss Technol.* 1995; 28: 25-30.
- 16. Breviglieri E, Mota da Silva L, Boeing T, Somensi LB, Cury BJ, Gimenez A, Cechinel Filho V, de Andrade SF. Gastroprotective and anti-secretory mechanisms of 2phenylquinoline, an alkaloid isolated from Galipea longiflora. Phytomedicine. 2017 Feb 15;25:61-70.
- 17. Brito SMO, Martins AOBPB, de Oliveira MRC, Vidal CS, de Lacerda Neto LJ, Ramos AGB, da Cruz LP, Nascimento EA, da Costa JGM, Coutinho HDM, Quintans-Junior LJ, de Menezes IRA. Gastroprotective and cicatrizing activity of the Ziziphus joazeiro Mart. leaf hydroalcoholic extract. J Physiol Pharmacol.2020 Jun;71(3).
- Campos-Vidal Y, Herrera-Ruiz M, Trejo-Tapia G, Gonzalez-Cortazar M, Aparicio AJ, Zamilpa A. Gastroprotective activity of kaempferol glycosides from Malvaviscus arboreus Cav. J Ethnopharmacol. 2021 Mar 25;268:113633.
- Carrasco, V.; Pinto, L.A.; Cordeiro, K.W.; Cardoso, C.A.; Freitas Kde, C. Antiulcer activities of the hydroethanolic extract of Sedum dendroideum Moc et Sesse ex DC. (balsam). J. Ethnopharmacol. 2014, 158 (Pt A), 345–351.
- Chevallier. A. *The Encyclopedia of Medicinal Plants* Dorling Kindersley. London 1996 ISBN 9-780751-303148.
- 21. Choi H.Y., Park Y.K., et al. Donguibogam. Yeogang Press, Seoul, 2001; 374-202.
- 22. Chopra R. N., Nayar S. L. and Chopra I. C. *Glossary of Indian Medicinal Plants* (*Including the Supplement*). Council of Scientific and Industrial Research, New Delhi. 1986.
- 23. Choudhary, M.K.; Bodakhe, S.H.; Gupta, S.K. Assessment of the antiulcer potential of Moringa oleifera root-bark extract in rats. J. Acupunct. MeridianStud. 2013, 6, 214–220.
- 24. da Rosa RL, de Almeida CL, Somensi LB, Boeing T, Mariano LNB, de Medeiros Amorim

Krueger C, de Souza P, Filho VC, da Silva LM, de Andrade SF. Chrysophyllum cainito (apple-star): a fruit with gastroprotective activity in experimental ulcer models. Inflammopharmacology. 2019 Oct;27(5):985-996.

- 25. da Silva Monteiro CE, Franco ÁX, Sousa JAO, Matos VEA, de Souza EP, Fraga CAM, Barreiro EJ, de Souza MHLP, Soares PMG, Barbosa ALR. Gastroprotective effects of Nacylarylhydrazone derivatives on ethanol-induced gastric lesions in mice are dependent on the NO/cGMP/K_{ATP} pathway. Biochem Pharmacol. 2019 Nov;169:113629.
- 26. Da Silva, L.M.; Allemand, A.; Mendes, D.A.G.; dos Santos, A.C.; André, E.; de Souza, L.M.; Cipriani, T.R.; Dartora, N.; Marques, M.C.A.; Baggio, C.H. Ethanolic extract of roots from Arctium lappa L. accelerates the healing of acetic acid-induced gastric ulcer in rats: Involvement of the antioxidant system. Food Chem. Toxicol. 2013, 51, 179–187.
- 27. Dajani, E.; Trotman, B. Drugs for treatment of peptic ulcers. J. Assoc. Acad.Minority Physic. Official Publ. Asso. Acad. Minority Physic. 1992, 3, 78–88.
- 28. De Barros, M.; da Silva, L.M.; Boeing, T.; Somensi, L.B.; Cury, B.J.; Burci, L.D.; Santin, J.R.; de Andrade, S.F.; Delle Monache, F.; Cechinel, V. Pharmacological reports about gastroprotective effects of methanolic extract from leaves of Solidago chilensis (Brazilian arnica) and its components quercitrin and afzelin in rodents. N-S Arch. Pharmacol. 2016, 389, 403–417.
- 29. Dey, A.; Mukherjeex, A.; Chaudhury, M. Alkaloids from apocynaceae: Origin, pharmacotherapeutic properties, and structureactivity studies. In Studies in Natural Products Chemistry; Atta-ur-Rahman; Elsevier: Amsterdam, The Netherlands, 2017; Volume 52, pp. 376–478.
- 30. Evans W.C., Trease., "Text Book of Pharmacognosy", 15th ed.; ELBS London: 2002.
- 31. Falcao Hde S, Maia GL, Bonamin F, Kushima H, Moraes TM, Hiruma Lima CA, Takayama C, Ferreira AL, Souza Brito AR, Agra Mde F, Barbosa Filho JM, Batista LM. Gastroprotective mechanisms of the chloroform and ethyl acetate phases of Praxelis clematidea (Griseb.) R.M.King & H.Robinson (Asteraceae). J Nat Med. 2013 Jul;67(3):480-91.
- 32. Gill NS, Bali M (2011) Type triterpenoid from the seeds of Cucurbitapepo. Res J Phytochemistry 5: 70-79.

- 33. Girdhar Shikha, et al. Evaluation of Anti-compulsive effect of methanolic extract of *Benincasahispida* Cogn fruit in mice. ActaPoloniae Pharmaceutical Drug Research, 2010;
 67 : (4) 417-421.
- 34. Glew RH, Glew RS, Chuang LT, Huang YS, Millson M, et al. (2006) Amino acid, mineral and fatty acid content of pumpkin seeds (Cucurbitaspp) and Cyperu: esculentlls nuts in the Republic of Niger. Plant Foods Hum Nut 61: 51-56.
- 35. Goel, R.K., Gupta, S., Shankar, R., Sanyal, A.K., 1986. Antiulcerogenic effect of banana powder (Musa sapientum var paradisica) and its effect on mucosal resistance. J. Ethnopharmacol. 18, 33–44.
- 36. Gohil, K.J.; Patel, J.A.; Gajjar, A.K. Pharmacological review on centella asiatica: A potential herbal cure-all. Indian J. Pharm. Sci. 2010, 72, 546–556.
- Babu, A. K., Kumar, M. P., Krupavaram, B., Mandadi, S. R., Lakshmi, Manikandhan, R., Haque, M. A., & Sultana, R. (2022). Diabetic foot ulcer, antimicrobial remedies and emerging strategies for the treatment: An overview. International Journal of Health Sciences, 6(S3), 2835–2850.
- 38. Goulart da Silva G, de Oliveira Braga LE, Souza de Oliveira EC, Valério Tinti S, de Carvalho JE, Goldoni Lazarini J, Rosalen PL, Dionísio AP, Tasca Gois Ruiz AL. Cashew apple byproduct: Gastroprotective effects of standardized extract. J Ethnopharmacol. 2021 Apr 6;269:113744.
- Goyal C., Ahuja M., Sharma S.K., "Preparation and evaluation of anti- inflammatory activity of gugulipid-loaded Proniosomal gel", *Acta Poloniae Pharmaceutica - Drug Res.*, 2011, 68, 147-150.
- 40. Graham, D.Y. Changing patterns of peptic ulcer, gastrooesophageal reflux disease and Helicobacter pylori: A unifying hypothesis. Eur. J. Gastroen. Hepat. 2003, 15,571–572.
- 41. Grover J.K., Adiga G., et al. Extracts of *Benincasahispida* prevent development of experimental ulcers. Journal of Ethnophamacology 2001; 78: 159–164.
- 42. Gupta A.K., "Physical constant: Evaluation of crude drug" Quality Standard of Indian medicinal plant, Indian council of Medical Research, New Delhi, 2003, 1, 236-237.
- 43. Guth P H and Hall P. Microcirculatotory and mast cell change in restraint –induced gastric ulcer. Gastroenter.1960; 50: 562-569.

- 44. Hafez HM, Morsy MA, Mohamed MZ, Zenhom NM. Mechanisms underlying gastroprotective effect of paeonol against indomethacin-induced ulcer in rats. Hum Exp Toxicol. 2019 May;38(5):510-518.
- 45. Halliwell B, Aeschbach R, Loliger J and Aruom O I. The characterization of antioxidants. J of Food chem. Toxicol. 1995; 33:601-617.
- 46. Hamedi, S.; Arian, A.A.; Farzaei, M.H. Gastroprotective effect of aqueous stem bark extract of ziziphus jujuba l. Against hcl/ethanol-induced gastric mucosal injury in rats. J. Tradit. Chin. Med. 2015, 35, 666–670.
- 47. Houracia T and Guillmmoschimulla. Effect of *Tanaetum Vulgare* on experimental gastric ulcers in rats. *J Pharm pharmacol*. 1999; 51(2):128.
- 48. Jamal A, Siddiqui A, Tajuddin Jafri MA. 2006. A review on gastric ulcer remedies used in Unani System of Medicine. Nat Prod Radiance. 5:153–159.
- Keyong-HoLeea, Hye-Ran Choib, Chang-Han Kimb. Anti-angiogenic effect of the seed extract of *Benincasahispida* Cogniaux. Journal of Ethno pharmacology, 2005; 97: 509– 513.
- 50. Khandelwal K.R., "Practical Pharmacognosy", Nirali Prakashan, Pune, 1998, 146-160.
- 51. Kikuchi T, Ando H, Maekawa K, Arie H, Yamada T, et al. (2015) Two new entkauranetype diterpene glycosides from zucchini (Cucurbitapepo L.) seeds. Fitoterapia 107: 69-76.
- 52. Kim SE, Memon A, Kim BY, Jeon H, Lee WK, Kang SC. Gastroprotective effect of phytoncide extract from Pinus koraiensis pinecone in Helicobacter pylori infection. Sci Rep. 2020 Jun 12;10(1):9547.
- 53. Kim YS, Nam Y, Song J, Kim H. Gastroprotective and Healing Effects of *Polygonum cuspidatum* Root on Experimentally Induced Gastric Ulcers in Rats. Nutrients.
- 54. Kokate C.K., "Practical Pharmacognosy", Vallabh Prakashan, Delhi, 4th ed., 1994, 148.
- 55. Kumar A., Nirmala V., Nootropic activity of methanol extract of Benincasahispida fruit. Indian Journal of Pharmacol.2003; 35: 128-136.

- 56. kumar Anil D., Ramu P. Effect of methanolic extract of Benincasahispida against histamine and acetylcholine induced Bronchospasm in Guinea pigs. Indian Journal of Pharmacol.2002; 34: 365-366.
- 57. Kumazawa Y., Nakatsuru Y., et al. Immunopotentiator separated from hot water extract of the seed of *Benincasacerifera* Savi (Tohgashi). Cancer Immunology and Immunotherapy 1985; 19: 79–84.
- Kuruuzum-Uz, A.; Suleyman, H.; Cadirci, E.; Guvenalp, Z.; Demirezer, L.O. Investigation on anti-inflammatory and antiulcer activities of Anchusa azurea extracts and their major constituent rosmarinic acid. Zeitschrift fur Naturforschung. C. J. Biosci. 2012, 67, 360– 366. [CrossRef]
- 59. Laloo D, Prasad SK, Sairam K, Hemalatha S. Gastroprotective activity of polyphenolicrich extract of Potentilla mooniana. Pharm Biol. 2014 Dec;52(12):1532-42.
- 60. Li M, Lv R, Xu X, Ge Q, Lin S. *Tricholoma matsutake*-Derived Peptides Show Gastroprotective Effects against Ethanol-Induced Acute Gastric Injury. J Agric Food Chem. 2021 Dec 15;69(49):14985-14994.
- 61. Li W, Koike K, Tatsuzaki M, Koide A, Nikaido T (2005) Cucurbitosides F-M, acylated phenolic glycosides from the seeds of Cucurbitapepo. J Nat Prod 68: 1754-1757.
- 62. López-Rodríguez R, Herrera-Ruiz M, Trejo-Tapia G, Domínguez-Mendoza BE, González-Cortazar M, Zamilpa A. In Vivo Gastroprotective and Antidepressant Effects of Iridoids, Verbascoside and Tenuifloroside from *Castilleja tenuiflora* Benth.Molecules. 2019 Apr 2;24(7):1292.
- 63. Malfertheiner, P.; Chan, F.K.; McColl, K.E. Peptic ulcer disease. Lancet 2009, 374, 1449– 1461.
- 64. Mandal U., Nandi D., et al, Remedial effect of aqueous extract of whole plant of FumariavaillantiiLoisel and ripe fruit of BenincasahispidaThunb in ranitidine inducedhypochlorhydric male rat. International Journal of Applied Research in Natural Products. 2010; 3(1): 37-47.