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ANALGESIC, ANTI-INFLAMMATORY AND ANTI-ULCER ACTIVITY OF ETHANOL AND ETHYL ACETATE EXTRACTS OF *TECOMARIA CAPENSIS* LEAVES

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ABSTRACT
In the present study ethyl acetate and ethanol extracts of leaves of *Tecomaria capensis* were screened for analgesic, anti-inflammatory and anti-ulcer activity. The analgesic activity was performed by two thermal models. One is hot plate method and another one is tail flick method. The two extracts of *Tecomaria capensis* leaves have showed analgesic activity in both methods. The anti-inflammatory activity was investigated by two methods. One is carrageenan induced paw edema method (*in-vivo*) and other is HRBC stabilization method (*in-vitro*). In both methods ethyl acetate and ethanol extracts showed anti-inflammatory activity. Anti-ulcer activity was done by aspirin induced method. In this, various biochemical parameters like ulcer index, gastric juice, pH, free acidity, total acidity and percentage protection has been investigated. Further, histopathological studies have also been examined. Ethyl acetate and ethanol extracts have showed anti-ulcer activity. In all the activities ethyl acetate showed a comparable activity to that of standard.
Keywords: *Tecomaria capensis,* Bignoniaceae, analgesic, anti-inflammatory and anti-ulcer

INTRODUCTION

Tecomaria capensis (family:Bignoniaceae) also known as Cape-honeysuckle is a fast growing, scrambling shrub which may grow up to 2-3m high and spread more than 2.5m. *Tecomaria capensis* is an evergreen plant in warm climate areas but loses its leaves in colder areas. It has pinnately compound leaves that have oval leaflets with blunt teeth. Flowering time for this shrub is very erratic and often it flowers all year round. Flowers are orange in color. Plant is used as a traditional medicine to relieve pain and sleeplessness. Dried powdered bark infusions are taken for sleeplessness[1] and reported to induce sleep [2]. It is included in the list of African plants evaluated for in vitro antiplasmodial activity[3].

MATERIALS AND METHODS
Plant materials and Preparation of Extracts
The leaves of *Tecomaria capensis* were collected from Guntur, Andhra Pradesh. It was authenticated by professor Dr.S.M.Khasim, Department ofBotony and Microbiology, Acharya Nagarjuna University, Nagarjuna nagar, Guntur, India. The leaf part of *Tecomaria capensis* was dried at room temperature and grounded into powder and passed through 60# sieve. The powder (500gm) was extracted successively in soxhlet by ethanol and ethyl acetate. The sediments were filtered and the filtrate was dried at 40°C in an oven to get dried product. The different fractions obtained were used for further study.

Acute oral toxicity study and selection of doses
Acute Toxicity Study
Healthy Wistar albino rats of both sexes weighing between 120-150 g maintained under standard laboratory conditions were used for the acute toxicity test according

to the Organization for Economic Cooperation and Development (OECD) guidelines 423 (OECD guideline, 2002). A total of ten animals of equal numbers of male and female rats were used and each received a single oral-dose of 2000 mg kg-1 body weight of ethyl acetate and ethanol extracts of *Tecomaria capensis*. Animals were kept overnight fasting prior to drug administration by oral gavage. After administration of drug sample, food was withheld for further 3-4 hour. Animals were observed individually at least once during first 30 min after dosing, periodically during first 24 hour (with special attention during the first 4 h) and daily thereafter for a period of 7 days. Daily observations on the changes in skin and fur, eyes and mucus membrane (nasal), respiratory rate, circulatory signs (heart rate and blood pressure), autonomic effects (salivation, lacrimation, perspiration, piloerection, urinary incontinence and defecation) and central nervous system (ptosis, drowsiness, gait, tremors and convulsion) changes were noted (OECD, 2002) [4]. Experimental protocol was approved by the institutional animal ethics committee IAEC PROTOCOL.NO: 8/IAEC/VPC/pharma/RES/2011-2012.

Analgesic Activity
Hot plate method
Mice of either sex weighing between 20-25gm were kept on hot plate (55±1⁰C), the time for fore paw licking or jumping was taken as reaction time. Mice showing reaction time before 5 seconds were selected. Animals not responding in this period were discarded. Analgesia was assessed with Eddy's hot plate apparatus (Analgesiometer). The basal reaction time was measured initially and another set of three measures were taken as

30, 60 and 120 minutes interval. A cut-off period of 15 seconds was observed to avoid damage of paws[5,6].

Tail flick method

Before the study, Swiss albino mice (20-25g) were screened for sensitivity test by placing the tip of the tail on the radiant heat source. Any animal that held to withdraw its tail in 5 seconds was rejected from the study. The selected animals were divided into six groups. Each animals of the groups received one of the following 2%w/v of Gum acacia (2ml/kg) in normal saline,pentazocine (30mg/kg),Ethyl acetate extract(100mg/kg and 200mg/kg) and ethanol extract (100mg/kg and 200mg/kg) intraperitoneally. Analgesia was assessed with the tail flick apparatus (Analgesiometer). The basal reaction time was measured initially and another set of three measures were taken as 30, 60 and 120 minutes interval and the reaction of animals consider as the post-drug reaction time. A cut of period of 10 seconds was observed to prevent tissue damage of the tail of the animals [7,8]

Anti-inflammatory Activity
Carrageenan induced hind paw edema

Either sex of albino rats weighing (150-200g) was divided into six groups of six animals each. Group 1 was treated as control, group 2 was treated as standard, group 3 was treated as ethyl acetate extract low dose, group 4 was treated as ethyl acetate extract high dose, group 5 was treated as ethanol extract low dose and group 6 was treated as ethanol extract high dose. Paw edema was induced by 0.1ml of 1% carrageenan in physiological saline into sub plantar tissues of the left hind paw of each rat in each group. Diclofenac sodium (5mg/kg), ethyl acetate extracts (100mg/kg and 200mg/kg) and ethanol extracts (100mg/kg and 200mg/kg) were administered orally 30 minutes prior to carrageenan administration. Paw volume was measured at 1, 2, 3 and 6 hours by the mercury displacement method using a plethysmograph. The percentage inhibition of paw volume in drug treated group was compared with the control group[9,10].

% inhibition = Control (% increase in paw volume in 3rd hour) - Test (% increase in paw volume in 3rd hour) / Control (% increase in paw volume in 3rd hour) X100

HRBC membrane stabilization method

The anti-inflammatory activity of leaves extract of *Tecomaria capensis* was determined by HRBC membrane stabilization method. Blood was collected from healthy volunteers. The collected blood was mixed with equal volume of (2% dextrose, 0.8% sodium citrate, 0.05% citric acid & 0.42% sodium chloride in water). The blood was centrifuged at 3000 rpm and packed cells were washed with isosaline (0.85%, pH 7.2) and 10% v/v suspension was made with isosaline. The assay mixture contained the drug 1ml phosphate buffer (0.15M, pH7.4), 2ml of hyposaline (0.36%) and 0.5 ml of HRBC suspension. Diclofenac was used as the reference drug. Instead of hyposaline, 2ml of distilled water was used as control. All the assay mixtures were incubated at 37^{0}c for 30 minutes and centrifuged. The haemoglobin content in the supernant solution was estimated using colorimeter at 560 nm. The percentage haemolysis was calculated by assuming the haemolysis produced in the presence of distilled water as 100%. The percentage of HRBC membrane stabilization or protection was calculated using the following formula [11].

% Protection =
100 - Optical density of drug treated sample / Optical density of control
x 100

Anti-ulcer Activity
Aspirin induced ulcer method

Animals were divided into six groups having six Wister rats each. Group 1 (control group) received distilled water orally. Group 2 (standard group) received ranitidine (20mg/kg) b.w. orally. Group 3 and 4 received ethyl acetate extract (100mg/kg and 200mg/kg) b.w. respectively and group 5 and 6 received ethanol extract (100mg/kg and 200mg/kg) b.w. All groups of animals were kept for overnight fasting fed only with the tap water. Both sexes of rats are used ranging from 150-200g. After one hour of last administration of extracts and ranitidine treatment, aspirin was administered in the dose of 200mg/kg. The animals were sacrificed 4 hours later by cervical dislocation. Animal was dissected and stomach was then excised and cut by grater curvature and the mucosa was exposed for evaluation then stomach was washed carefully with 5ml of 0.9% NaCl. Then ulcers were scored by macroscopically. Mean ulcer score for each animal was expressed as ulcer index. The percentage production was determined as follows[12].

Ulcer index =
No. of ulcer positive animals / Total number of animals x 2

% Protection =
Control mean ulcer index – Test mean ulcer index / Control mean ulcer index x 100

Acidity =
Volume of NaOH x Normality of NaOH / 0.1 N x 100 mEq/L/100g

Free and total acidity

Free and total acidity were determined by titrating with 0.01N NaOH using Topfer's reagent and phenapthalene as indicator. The free and total acidity were expressed as mEq/L.

Histopathological evaluation

The gastric tissue samples were fixed in neutral buffered formalin for 24hrs. Sections of tissue from stomach were examined histopathologically to study the ulcerogenic or anti-ulcerogenic activity of *Tecomaria capensis*. The tissues were fixed in 10% buffered formalin and were processed using a tissue processor. The processed tissues were embedded in paraffin blocks and about 5-µm thick sections were cut using a rotary microtome. These sections were stained with hematoxylin and eosin using routine procedures. The slides were examined microscopically for pathomorphological changes such as congestion, haemorrhage, oedema and erosions using an arbitrary scale for the assessment of severity of these changes.

Table 1: Effect of ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves by Eddy's hot plate method

Treatment	Dose	Mean latency time (seconds)			
		Before	After administration of drug		
			30 min	60 min	120 min
Control (2%w/v gum acacia)	2ml/kg	2.11 ± 0.03	2.19 ± 0.07	2.19 ± 0.07	2.15 ± 0.03
Standard (Pentazocine)	10 mg/kg	2.14 ± 0.55	5.53 ± 0.05**	8.14 ± 0.06**	11.78 ±0.10**
EA (LD)	100 mg/kg	2.18 ± 0.04	3.13 ± 0.05**	5.83 ± 0.05**	5.39 ± 0.04**
EA (HD)	200 mg/kg	2.12 ± 0.03	4.13 ± 0.04**	7.43 ± 0.07**	7.16 ± 0.06**
E (LD)	100 mg/kg	2.5 ± 0.3	2.8 ± 0.1	4.33 ±0.33**	4.8 ± 0.7**
E (HD)	200 mg/kg	2.18 ± 0.04	3.96 ± 0.04**	5.32 ± 0.07**	6.12 ± 0.08**

Mean ± S.E.M of 6 animals (one-way ANOVA). **$P<0.05$ when compared to control.

Table 2: Effect of ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves by tail flick method

Treatment	Dose	Basal reaction time (seconds)			
		Before	After administration of drug		
			30 min	60 min	120 min
Control (2% w/v gum acacia)	2ml/kg	2.50 ± 0.33	2.80 ± 0.21	2.90 ± 0.21	3.10 ± 0.19
Standard (Pentazocine)	10 mg/kg	2.60 ± 0.28	5.50 ± 0.39**	6.93 ± 0.72**	8.26 ± 0.59**
EA (LD)	100 mg/kg	2.80 ± 0.23	4.60 ± 0.20*	5.70 ± 0.54**	7.26 ± 0.49**
EA (HD)	200 mg/kg	2.40 ± 0.25	5.00 ± 0.23**	6.20 ± 0.43**	7.60 ± 0.56**
E (LD)	100 mg/kg	2.33 ± 0.19	3.5 ± 0.20*	4.5 ± 0.39*	5.83 ± 0.54**
E (HD)	200 mg/kg	2.66 ± 0.19	3.83 ± 0.33*	5.0 ± 0.23**	6.33 ± 0.38**

Mean ± S.E.M. of 6 animals (one-way ANOVA). *$p<0.01$, **$p<0.001$, when compared with control.

Table 3: Effect of ethanol and ethyl acetate extracts of *Tecomaria capensis* leaves by carrageenan-induced hind paw edema

Group	Dose	Edema Volume in ml				
		0hr	1hr	2hr	3hr	6hr
Control	2ml/kg	0.38±0.01	0.37±0.02	0.40±0.01	0.38±0.01	0.38±0.01
Standard (Diclofenac)	5mg/kg	0.37±0.02	0.16±0.01*	0.15±0.01*	0.13±0.01*	0.11±0.01*
EA LD	100 mg/kg	0.40±0.01	0.24±0.01*	0.20±0.01*	0.18±0.01*	0.16±0.01*
EA HD	200 mg/kg	0.37±0.02	0.19±0.01*	0.16±0.01*	0.15±0.01*	0.14±0.004*
E LD	100 mg/kg	0.38±0.01	0.25±0.01*	0.23±0.01*	0.17±0.01*	0.16±0.004*
E HD	200 mg/kg	0.37±0.02	0.21±0.01*	0.17±0.01*	0.16±0.01*	0.14±0.01*

Mean ± S.E.M of 6 animals (one-way ANOVA), statistically significant from control*$p<0.001$

Table 4: Effect of ethanol and ethyl acetate extracts of *Tecomaria capensis* leaves by HRBC membrane stabilization method

Concentration µg/ ml	Standard		Ethyl acetate		Ethanol	
	OD value	% Protection	OD value	% Protection	OD value	% Protection
50	0.31± 0.08	55.8± 1.23	0.43± 0.02	45.9± 2.86	0.432± 0.02	45.9± 1.7
100	0.26±0.011	59.8± 0.92	0.40± 0.01	48.1± 0.92	0.392± 0.01	49.1± 0.9
150	0.21±0.072	63.9± 1.3	0.35± 0.02	52.5± 1.89	0.225± 0.04	62.7± 0.7
200	0.14±0.104	69.5± 1.6	0.15± 0.009	68.6± 1.24	0.208± 0.02	64.0± 0.65
250	0.04±0.130	75.24± 0.42	0.07± 0.006	74.7± 0.92	0.203± 0.02	64.4± 0.61

Mean ± S.E.M, **$P<0.001$ considered significant, n=3

Table 5: Effects of ethyl acetate and ethanolic extracts of *Tecomaria capensis* leaves on various biochemical parameters in rats with aspirin induced ulcer method

Parameters	Control (Normal saline 2ml/kg)	Standard (Ranitidine 20mg/kg)	Ethyl acetate low dose (100mg/kg)	Ethyl acetate high dose (200mg/kg)	Ethanol low dose (100mg/kg)	Ethanol high dose (200mg/kg)
Ulcer index	3.68±0.56	0.71±0.14	2.34±0.24	1.10±0.29	2.62±0.36	1.52±0.44
Gastric juice	4.02±0.11	1.94±0.06	3.66±0.16	2.40±0.14	3.79±0.016	3.28±0.21
pH	1.84±0.14	4.96±0.18	3.12±0.14	4.56±0.18	3.20±0.14	3.88±0.14
Free acidity	26.84±0.08	10.42± 0.02	21.18 ±0.05	11.76± 0.06	22.96± 0.08	13.68± 0.02
Total acidity	70.16±0.30	22.24±0.18	52.14±0.38	30.62±0.26	60.48±0.24	35.45±0.33
% Protection	- - - - -	80.70***	36.41*	70.10***	28.80*	58.69**

Mean ± S.E.M of 6 animals (one-way ANOVA) coupled with student 't' test *$P<0.05$,**$P<0.01$,
***$P<0.001$were consider statistically significant when compared to control group.

RESULTS
Acute toxicity study results
In the acute toxicity study with both extracts (Ethanol and Ethyl acetate) treatment, no related mortalities were recorded in animals treated with a single dose of 2000mg/kg body weight. Therefore, the approximate lethal dose (LD_{50}) of both extracts in the experimental rats was higher than 2000 mg/kg. There was no clinical signs in the skin and fur, eyes and mucus membrane (nasal), respiratory rate, circulatory signs (heart rate and blood pressure), autonomic effects (salivation, perspiration, piloerection, urinary incontinence and defecation) and central nervous system (ptosis, drowsiness, gait, tremors and convulsion) among rats administered 2000 mg kg-1 body weight of both extracts (Ethanol and Ethyl acetate). According to organization for economic cooperation and development (OECD) guidelines for acute oral toxicity, an LD_{50} dose of 2000mg/kg and above is categorized as unclassified and hence the drug is found to be safe.

Analgesic activity
Hot plate method
Analgesic activity of ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves were found to be significant (P < 0.05) when compared with control and standard. Comparing the ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves, ethyl acetate extract showed better action. Both extracts exhibited marked central analgesic effect as evidence by significant increase in mean latency time comparable to control. Results are tabulated in Table 1.

Tail flick method
Analgesic activity of ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves were found to be significant (P < 0.001) when compared with control and standard. Comparing the ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves, ethyl acetate extract showed better results. Both extracts exhibited marked central analgesic effect as evidence by significant increase in basal reaction time comparable to control. Results are tabulated in Table 2.

Anti-inflammatory activity
Carrageenan induced hind paw edema method
Anti-inflammatory activity was performed based on the folklore information using two methods. Carrageenan-induced rat paw edema is used widely as a working model of inflammation in the search for new anti-inflammatory drug. The development of edema in the paw of the rat after the injection of Carrageenan is due to release of histamine, serotonin and prostaglandin like substances. The significant ameliorative activity of the ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves and standard drug were observed. Results are tabulated in Table 3.

HRBC membrane stabilizing method
HRBC method was selected for *in vitro* evaluation of anti-inflammatory property because the erythrocyte membrane is analogous to the lysosomal membrane and its stabilization implies that the extract may stabilize lysosomal membranes. Stabilization of lysosomal membrane is important in limiting the inflammatory response by preventing the release of lysosomal constituents of activated neutrophil, such as bactericidal enzymes and proteases, which cause further tissue inflammation and damage upon extra cellular release.
The results indicated that the ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves at various concentrations has significant anti-inflammatory property. The lysosomal enzymes released during inflammation produce a variety of disorders. The extra cellular activity of these enzymes was said to be related to acute or chronic inflammation. The non-steroidal drugs act either by inhibiting these lysosomal enzymes or by stabilizing the lysosomal membrane[24]. Since HRBC membrane components are similar to lysosomal membrane components the prevention of hypo tonicity induced HRBC membrane lysis was taken as a measure of anti-inflammatory activity of drugs. The results were reported in Table 4.

Anti-ulcer activity
In the present study, ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves was evaluated for its anti-ulcer activity against NSAIDs induced gastric ulcer model. Observation showed a significant gastro protective action. Animals treated with standard (Ranitidine 20mg/kg), ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves at 100mg/kg and 200mg/kg respectively. The percentages of inhibition of ulcers were 36.41% and 70.10% for the group treated with 100 mg/kg and 200 mg/kg of ethyl acetate extract of *Tecomaria capensis* leaves, for ethanol extracts of *Tecomaria capensis* leaves 100mg/kg and 200mg/kg were 28.80% and 58.69% and for standard group. It was 80.70% respectively. Ulcer index score, gastric juice, pH, free acidity of ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves treated and standard group are summarized in Table 5.

DISCUSSION
Pain is centrally modulated *via* number of complex processes including opioid, dopaminergic, descending noradrenergic and serotonergic systems[13,14]. The hot-plate and tail flick tests were useful in elucidating centrally mediated anti-nociceptive responses, which focuses mainly on changes above the spinal cord level[15,16]. The hot-plate method and tail flick test are considered to be selective to examine compounds acting through opioid receptor. Narcotic analgesics inhibit both peripheral and central mechanism of pain, while non-steroidal anti-inflammatory drugs inhibit only peripheral pain[17,18]. It also reported that the inhibition of pain could arise not only from the presence of opioids and/or opiodiomimetics but could also arise from the presence of phenolic constituents[19] and also steroidal constituents[20]. It may be due to the similar type of constituents present in the *Tecomaria Capensis* leaves extracts which exhibited the analgesic activity. The phytoconstituents like flavonoids, tannins, alkaloids have been reported in several analgesic literatures as possible to produce analgesic effect. Due to presence of flavonoids in ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves may contribute for

the analgesic activity. Ethyl acetate and Ethanolic extracts of *Tecomaria Capensis* leaves increased mean basal latency which indicates that it may act *via* centrally mediated analgesic mechanism.

The percentage reduction in the paw volume in the group of animals treated with ethyl acetate extract 100mg/kg was 52.63 % and for 200mg/kg was 60.52 %, ethanol extract 100mg/kg was 55.26 % and 200mg/kg was 57.89 % and for standard diclofenac was 71.05% at 3 hours. It may be due to inhibition of the mediators of inflammation such as histamine, serotonin and prostaglandin. These results indicate that the extracts act in later phases in dose dependent manner. This anti-inflammatory effect of the extracts observed might be due to the presence of flavonoids in the plant. The edema and inflammation induced by Carrageenan was shown to be mediated by histamine and serotonin during first 1 hour. after which increased vascular permeability is maintained by the release of kinins up to 2 hours 30 minutes, followed by the release of kinins and finally through the release of bradykinin, prostaglandin and lysosomes from 2 hours 30 minutes to 6 hours. The later phase was reported to be sensitive to the most of the clinically effective anti-inflammatory agents. The mediators appear to be prostaglandins, the release of which was closely associated with migration of leucocytes into the inflamed site[21].The Carrageenan induced paw edema model in rats was known to be sensitive to cyclooxygenase (COX) inhibitors and had been used to evaluate the effect of non-steroidal anti-inflammatory agents[22,23]. Though Ethyl acetate and Ethanol extracts of *Tecomaria capensis* significantly reduced the paw edema in rats but the effect was of less intensity, when compared with diclofenac (5 mg/kg, p.o).

In HRBC membrane stabilizing method, from the observation the percentage protection of lysis for Diclofenac 50μg was 55.8%, 100μg was 59.8%, 150μg was 63.9%, 200μg was 69.5%, 250μg was 75.24%, for ethyl acetate extract 50μg was 45.9%, ethyl acetate extract 100μg was 48.1%, 150μg was 52.5%, ethyl acetate extract 200μg was 68.6%,ethyl acetate extract 250μg was 74.7% and ethanol extract 50μg was 45.9%, ethanol extract 100μg was 49.1%, ethanol extract 150μg was 62.7%, ethanol extract 200μg was 64.4% and ethanol extract 250μg was 64.4%. The ethyl acetate extract of *Tecomaria capensis* had shown better membrane stabilization, in comparison to ethanol extract of *Tecomaria capensis* leaves. The results were comparable to that of the standard drug Diclofenac. The anti-inflammatory activity of the extracts were concentration dependent, with the increased concentration the activity was also increased. The *Tecomaria capensis* exhibited membrane stabilization effect by inhibiting hypo-tonicity induced lysis of erythrocyte membrane. The erythrocyte membrane is analogous to the lysosomal membrane and its stabilization implies that the extract may stabilize lysosomal membranes[24,25]. Stabilization of lysosomal membrane is important in limiting the inflammatory response by preventing the release of lysosomal constituents of activated neutrophil such as bactericidal enzymes and proteases, which cause further tissue inflammation and damage upon extra cellular release[26].

Flavonoids and steroids show remarkable anti-inflammatory activity by inhibiting the cox and lox systems. Presence of flavonoids are responsible for membrane stabilizing ability, the anti-inflammatory effect of ethyl acetate and ethanol extracts may be attributed due to presence of flavonoids. The main action of anti-inflammatory agent is by inhibition of the cyclooxygenase systems, which is responsible for prostaglandins. The Carrageenan assay is a good method for the comparative bioassay of anti-inflammatory agents.

Aspirin induced ulcers develop due to the decrease in mucous production and increased proton back diffusion. Peptic ulcer and gastritis had been associated with multi pathogenic factors and could be due to disturbances in natural balances between the aggressive factors (eg: acid, bicarbonate, pepsin) and maintenance of the mucosal integrity through the endogenous defense mechanism (e.g.: defensive mechanisms of mucus, mucosal turnover and blood supply to mucosal barrier)[27]. Generally various non-specific methods were used to restore these imbalances including regular food intake, adequate rest and avoidance of ulcerogenic agents (e.g.: Tobacco, Alcohol and Coffee). Their aims were to attenuate and possibly block the gastric acid secretion or to enhance the mucosal defense mechanisms[28]. The latter can be achieved through increasing mucus production, stabilizing the surface epithelial cells or interfering with the prostaglandin synthesis. In addition, there are also drugs, such as proton pump inhibitors, histamine (H2)-antagonists, anti-cholinergic and antacids used in the treatment of ulcer[29]. Despite the availability of many pharmaceutical products for the treatment of gastric ulcers in the market as mentioned above, their success were limited by presence of several adverse effects (e.g.: Anaphylaxis reactions, Gynacomastia, Hematopoietic changes, Thrombocytopenia, Acute interstitial nephritis, Nephrotoxicity and Hepatotoxicity)[30,31]. Due to the reported side effects of available antiulcer drugs, the focus had been shifted towards natural products as the new sources of antiulcer agents. With the increasingly growing interest in natural medicine, various plants had been studied based on the traditional knowledge for their pharmacological properties and confirmed to be useful in treating and managing ulcer. Furthermore, medicinal plants had been known to be amongst the most attractive sources of new drugs, and had been giving promising results in treatment of various diseases including gastric and duodenal ulcers[32,33].

Chronic use of anti-inflammatory drugs and stress were some of the main causes of gastric ulcers[34] and since ethanol and ethyl acetate extracts exerted significant antiulcer activity under experimental models that mimic those conditions. These results suggested that ethanol and ethyl acetate extracts possesses anti-secretory potency as well as acid neutralizing effect. Furthermore, based on findings by Ubaka *et al,*[35], the anti-secretory effect was suggested to be one of the mechanisms through which the extracts were able to protect the stomach mucosa from NSAIDs (aspirin) induced damage. It was well known that inhibition of prostaglandin synthesis, which is essential for mucosal integrity and regeneration, will trigger the mucosal lining damage. It was also believed

that the extracts exert its antiulcer activity by increasing the synthesis of endogenous prostaglandins, which in turn promotes mucus secretion and enhances the mucosal barrier against the actions of various damaging agents[36]. Other than that, leukotrienes antagonist and 5-lipoxygenase inhibitors had been demonstrated to inhibit NSAIDs induced gastric ulceration in rats. Hence, the observed anti-ulcer activity of *T.capensis* could also be suggested that due to inhibition of 5-lipoxygenase pathway or by leukotriene's antagonistic activity. In recent experiments, it had been found that heat shock proteins (HSPs), specifically HSP70 and HSP47 were involved in the gastric protection. The HSC70 (a constitutive form of HSP70) was co-precipitated with COX-1 and the neuronal form of nitric oxide synthase after treatment with a mild irritant (20% ethanol). A positive relationship between enhanced interaction of HSC70 either with Cyclooxygenase-1 or nitric oxide synthase and mucosal defense mechanisms and ulcer healing, most probably through protecting key enzymes is related to cytoprotection[37].

From the observation, comparing the ethyl acetate and ethanol extract of *Tecomaria capensis,* ethyl acetate extract showed better activity results were comparable to that of the standard. The phytoconstituents like flavonoids, tannins, terpenoids and saponin have been reported in several anti-ulcer literatures which reveal that they are responsible for the gastro protective activity. As the above mentioned phytoconstituents are present in ethyl acetate and ethanol extracts of *Tecomaria capensis* leaves which may elicit the anti-ulcer activity.

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