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HEALING EFFECT OF THREE EXTRACTS FROM THE TRUNK BARK OF *TERMINALIA SUPERBA* ENGL. ET DIELS (COMBRETACEAE) ON ACETIC ACID INDUCED ULCER IN RATS

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ABSTRACT

Terminalia superba is a medicinal plant well known for its richness in phytochemicals compounds and its beneficial effects for the treatment of gastrointestinal disorders. This study investigated the healing effect of aqueous (AETs), hydro ethanol 70 % (HE 70 %) extracts and n-butanol fraction (BuF) from the trunk bark of *T. superba* on acetic acid induced ulcer in rats. Fasted rats were divided into thirteen groups (9 rats/group). Groups 1 (control 1) received orally distilled water at 1 ml/100 g b.w. while group 2 (Control 2) to 13 were given only acetic acid solution 20 % every day for three days at 1 ml/150 g b.w by oral route. After, groups 3 and 4 received cimetidine (12 mg/kg) and omeprazole (10 mg/kg) at 1 ml/100g respectively while groups 5 to 13 received AETs, HE 70 % (125, 250 and 500 mg/kg) and BuF (15, 30 and 60 mg/kg) respectively for 28 days. Sub-groups of three rats by groups were sacrificed weekely and ulcerous surface, mucus, ulceration index and inhibition percentage were examined. The results showed that AETs, HE 70 % and BuF significantly and dose dependently reduced surface aera, ulcer index and significantly increased the inhibition percentage and mucous in treated groups at 500 mg/kg (AETs and EH 70 %) and 60 mg/kg (BuF) compared to control 2 on the 28th. The three extracts induced gastric mucosal membrane re-epithelization. In conclusion, AETs, HE 70 % and BuF possessed healing effect against acetic acid induced ulcer in rats and could mainly be ascribable to their cytoprotective activity supplied with their anti-secretion effect.

KEYWORDS: *Terminalia superba*, healing effect, acid acetic, ulcer, rats.

INTRODUCTION

To keep its balance, human body is endowed with regulatory systems that help maintain the consistency of internal environment and proper functioning of organs. However, this balance is sometimes threatened. Indeed, according to,[1,2] in human body, H^+ ions concentration is million times higher in gastric lumen than in blood. Cytoprotection mechanisms are involves. Since stomach is provided with a protective mucous membrane, this tunica can sometimes be attacked by internal or external agents, which causes gastric ulcers which are superficial or deep open wounds in mucous membrane. These wounds result from an imbalance between stressors such as stomach acid, pepsin and defense factors which are mucus, bicarbonate, surface epithelium, mucosal vascularization and mucosa ability to oppose backscattering of H^+ ions and prostaglandins.[3] This disease is universal and does not spare any population.[4] Gastric ulcers are mainly caused by *Helicobacter pylori* infection in 75 to 80% of the cases.[5] In Côte d'Ivoire, according to several authors, gastric ulcer disease reported a prevalence of 7 to 16 % in 1999 and 2016, respectively.[6,7] Many treatments are used, but despite the diversity of modern drugs, this pathology has not yet been eradicated. In fact, these drugs have many known side effects. Treatment of pathologies such as gastric ulcers by plants becomes a necessity. *T. superba*, a plant known for a long time for its therapeutic virtues on gastric ulcer.[8] has been chosen. In Côte d'Ivoire, studies carried out with aqueous and hydroethanolic 70% extracts of the trunk bark of *T. superba*, revealed that this plant is endowed with a real preventive anti-ulcerogenic potential.[9,10] However, the plant's healing effect on gastric ulcers has yet to be scientifically proven. The present work was undertaken to evaluate the healing effect of three extracts (aqueous, hydroethanolic 70 % and n-butanol organic fraction extracts resulting from the partitioning of the hydroethanolic 70% extract of the trunk bark of *T. superba*) on acid acetic induced ulcer in rats.

MATERIAL AND METHODS

Plant material

Fresh trunk barks of *Terminalia superba* were collected locally from the forest of Ebillassokro village in the East of Côte d'Ivoire. Taxonomical identification of the trunk barks was established by botanists from the National floristic Center of University of Felix Houphouët Boigny, Cocody- Abidjan, Côte d'Ivoire, voucher n° 2456, *Terminalia superba* Engl. et Diels in June 4, 1954; n° 4207 in March 26, 1957; n° 10477, in February 26, 1969 and n° 416 in April 03, 1974 of Côte d'Ivoire national herbarium.

Preparation of the aqueous and hydroethanol 70 % extracts from the trunk bark of *Terminalia superba*

Fresh trunk barks of *Terminalia superba* were dried under shade and powdered with a machine (mark RETSCH, type SM 100, Germany). The extraction process was implemented according to the method described by.[11] Powder of trunk bark was extracted using aqueous infusion and ethanolic maceration separately.

One hundred grams of the trunk barks powder of *T. superba* were infused in one-liter hot distilled water for 15 min while another one hundred grams of the same powder of the same plant were macerated during 24 hours in one-liter ethanol-water (70:30 v/v) for 3 times until complete exhaustion. The aqueous (AETs) and hydroethanol 70 % (HE 70 %) extracts of the trunk bark of *T. superba* were then filtered (Whatman n°1) and concentrated under reduce pressure using a rotary evaporator (Büchi R110, type MKE 6540/2) at 45°C respectively. The concentrated extracts were stored in dessicators at 45°C.

Preparation of n-butanol organic fraction extract

Ten grams of the dried hydro ethanol 70 % extract were partitioned separately in *n*-butanol (Bu), chloroform (Ch), ethylacetate (Ea) and hexane (Hex)-water (50:50 v/v). Two fractions were obtained from each partition, organic and aqueous fractions after decantation, solvent evaporation and storage in dessicators at 45°C respectively. Organic fractions obtained from these partitions were BuF (3.208 g), ChF (3.118 g), EaF (3.018 g), HexF (3.213 g) and aqueous fractions were $Bu_{aq}F$ (6.387 g), $Ch_{aq}F$ (6.512 g), $Ea_{aq}F$ (6.213 g), $Hex_{aq}F$ (6.152 g). From the partitioned extracts of HE 70 % which were tested, the n-butanol organic fraction (BuF) was found to be the most interesting fraction because it produced more than 95 % ($P<0.05$) inhibition of ulcer induced by acetic acid 20 % during the preliminary tests and was retained for pharmacological tests.

Animals

Albino *Wistar* male rats weighing between 180 and 200 g and approximately12-16 weeks were selected for gastric anti-ulcer experiments. These animals came from the Animal House of Pastor Institute of Côte d'Ivoire located in Adiopodoumé (Abidjan) and have been put in reproduction in the Animal house of Physiology, Pharmacology and Pharmacopeia laboratory of Nangui Abrogoua University (Abidjan, Côte d'Ivoire) according to the principles for the care and use of laboratory animals of the Ethical Committee of the University (Nangui Abrogoua, Abidjan, Côte d'Ivoire). They were exposed to 12 h dark/light cycle at room temperature (22–25 °C) and given standard food for rats and water *ad libitum*.

1.3-Chemical substances

The following references substances used are: Ether (VWR International-Geldenaakfebaan464-B-3001 Leuven-Belgium), Omeprazole (Sanofi Aventis, France), Cimetidine (Sigma, USA), and Acid acetic (Sigma, USA).

Induction of gastric mucosal lesions with acetic acid necrotizing solution in rats

Gastric mucosal lesions were induced according to the method described by [12] with modifications. Fasted animals are divided into thirteen groups of nine rats each. Groups 1 served as control 1, received orally distilled water at 1 ml/100 g b.w. while groups 2 (Control 2) to 13 were given only acetic acid solution 20 % every day for three days at 1 ml/150 g b.w by oral route. Three days after mucosal damage appearances, groups 3 and 4 received cimetidine (12 mg/kg) and omeprazole (10 mg/kg) at 1 ml/100 g respectively while groups 5 to 13, corresponding to treated groups, received AETs and HE 70% extracts at doses ranging from 125 to 500 mg / kg b.w. and BuF at 15, 30 and 60 mg / kg bw respectively. Treatment was renewed each five days for 28 days. Sub-groups of three animals in all groups are sacrificed by over dose of ether every seven days. The removed stomach is opened along the greater curvature (cardia-pylorus) and examined. The mucosal damage was determined by measuring the area of the damages then it was scored. The sum of the areas was expressed as ulcer index (mm^2).[13,14] The scoring of stomach damage was established according to.[15] The percentage of inhibition (% I) was calculated using the following formula.[16]

$$\%I = \frac{(US_C - US_T)}{US_C} \times 100$$

US_C = ulcer surface area in control animals and US_T = ulcer surface area in treated animals. The mucus covering the gastric wall of each rat was collected and weighed. Histological assessment of ulcer healing was carried out.

Statistical analysis

Data were performed using Graph Pad Prism 5.01 software (San Diego, California, USA) and presented as mean ± standard error on mean (M ± SEM). Comparisons between treated groups and controls were made using Student's t test and one-way analysis of variance (ANOVA). Tukey–Kramer was used as post-

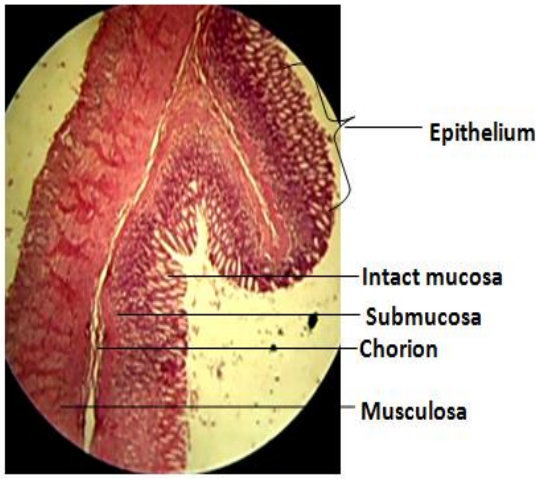
hoc test. Values were considered statistically significant when $p < 0.05$.

RESULTS

Healing effect of three extracts on gastric mucosal damage induced by acetic acid solution in rats

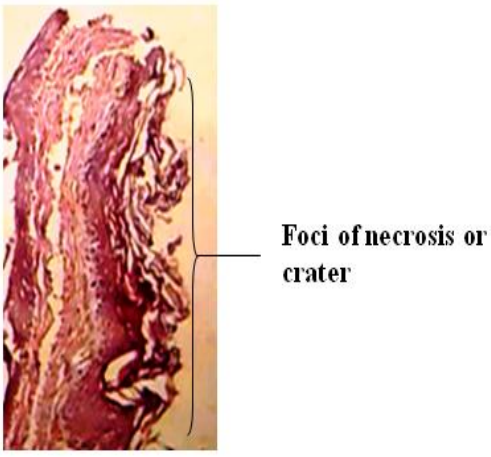
As shown in Figure 1-A, no damage in gastric mucosa was observed in control group 1 when no substances (AETs, HE 70 %, BuF, omeprazole, cimetidine and acetic acid 20 % solution) were given to rats. The gastric mucosa was intact and no migration of epithelial cells was observed due to crater absence and therefore lesions (Figure 1-A). A score and mucus recorded were 0 and 158.85 ± 4.20 mg respectively (Table 1). Oral administration of acetic acid necrotizing solution produced characteristic lesions in glandular part of stomach in control 2 giving a score 8. Observation of histological stomach sections revealed in control 2, multiple foci of necrosis extending to the entire thickness of mucosa (Figure 1-B). Cell lysis and degeneration were observed, reflecting severe acute erosive phenomena (Figure 1-B). From 7th to 14th day without any treatment, epithelial cells proliferated and migrated to crater dug in mucosa as a result of necrotizing action of acetic acid solution on mucosa (Figure 1-C). This results in start of mucosa reconstitution. Migration was accentuated on the 28th day, causing complete reconstitution of gastric mucosa (Figure 1-D). Ulcer index and ulceration area decreased significantly and respectively from 5.21 ± 0.1 to 1.1 ± 0.01 and from 145.67 ± 7.5 to 38.29 ± 0.5 mm^2 (Control 2). Mucus produced increased significantly ($p < 0.05$) compared to rats given acetic acid only (Control 2), and ranged from 168.47 ± 4.15 to 736.45 ± 6.30 mg (Table 1). Oral administration of AETs, HE 70% and BuF extracts to rats pretreated with acetic acid solution induced a decrease in score from 6 to 1, thus reflecting the progressive evolution of the healing process and dose-dependent inhibition on gastric ulceration from 41.27 (AETs, 125 mg/kg) to 98.17 % (AETs, 500 mg/kg), 50.14 (HE 70%, 125 mg/kg) to 98.35 % (HE 70 %, 500mg/kg) and 39.35(BuF, 15 mg/kg) to 99.87% (BuF, 60 mg/kg) (Table 1). From 7th to 14th day, cell exfoliation coupled with cells migration to injured area is greater compared to the control group 2 and results in significant ($p < 0.05$) inhibitions obtained from 63.08 (AETs, 125 mg/kg) to 80.33 % (AETs, 500 mg/kg), 75.37 (HE 70 %, 125 mg/kg) to 89.97% (HE 70 %, 500mg/kg) and 63.09 (BuF, 15 mg/kg) to 90.49 % (BuF, 60 mg/kg) (Table 1). At these studied doses, tissue regeneration is effective and healing is almost complete on the 28th day, ie at the end of the treatment (Figure 1-D). Animals treated with omeprazole and cimetidine, at10 and 12 mg/kg respectively, showed respective score ranging from 3 to 1 and an ulceration area which decreases from 7th to 28th day from 68.10 ± 2.16 to 1.12 ± 0.6 mm^2 (Omeprazole) and 71.23 ± 1.1 to 1.7 ± 1.1 mm^2 (Cimetidine) (Table 1). This decrease corresponds to inhibition variation from 53.25 to 97.07 % (Omeprazole) and 51.10 to 95.56 % (Cimetidine). AETs, HE 70 % and BuF induced significant ($p < 0.05$) decreased in ulceration area in treated groups from 85.55 ± 7.2 to 0.7 ± 0.1 mm^2 (AETs), from 72.63 ± 9.4 to 0.63 ± 0.02 mm^2 (EH 70%) and from 88.35 ± 2.2 to 0.05 ± 0.001 mm^2 (BuF) from 7th to 28th day of treatment (Table 1). AETs, HE 70% and BuF, induced a significant ($p < 0.05$) and dose-dependent increase in secreted mucus from 261.14 ± 0.21 to 1376.4 ± 19.31 mg (AETs), 443.38 ± 6.02 to 1493.01 ± 8.4 mg (HE 70 %) and 528.30 ± 6.12 to 1987.18 ± 8.5 mg (BuF) (Table 1) compared to control 2 where mucus produced increased significantly ($p < 0.05$) from 168.47 ± 4.15 to 736.45 ± 6.30 mg during the 28 days of treatment. This increase in mucus reached a maximum value at 60 mg / kg (BuF) and 500 mg/kg (AETs and HE 70 %) (Table 1). The pharmacological reference solutions (cimetidine and omeprazole), also caused a significant increase ($p < 0.05$) in secreted mucus with values ranging from 475.39 ± 3.1 to 1755.93 ± 9.7 mg (omeprazole) and from 363.41 ± 2.43 to 1689.41 ± 5.81 mg (cimetidine) compared to control 2.

From 7th to 14th day of treatment, cimetidine, omeprazole, AETs, HE 70% and BuF extracts considerably reduced crater formed by acetic acid 20 % necrotizing solution. The epithelial cells migrate further towards the crater and plug it up. Healing is reflected by the significant drop in ulceration indices ($p < 0.05$) which went from 5.21 ± 0.1 (acetic acid) to 0.06 ± 0.002 (AETs), 0.02 ± 0.004 (HE 70 %) and 0.01 ± 0.001 (BuF) on the 28th day of treatment.



Control group 1; X 40

Figure 1-A: Absence of crater



Control group 2; X 40

Figure 1-B: Action of acetic acid on gastric mucosa

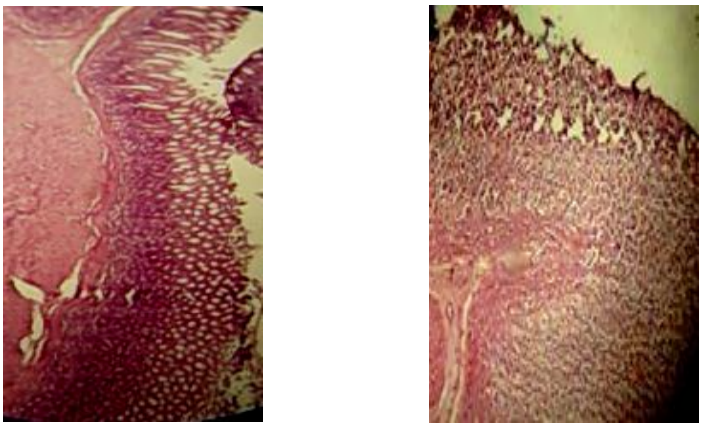


Figure 1: Photographs of histological sections of gastric mucosa after 28 days of treatment.

(n = 6 rats)**;** Hematoxylin / Eosin. Control 1 (Ggroup 1): rats given only distilled water (Control non-ulcerated rats showing normal healthy mucosa). Control 2 (Group 2): rats given only acetic acid solution 20 % (Control ulcerated rats showing well-defined ulcer crater). Ulcerated rats that were given cimetidine, omeprazole, AETs, HE 70 % and BuF extracts on the 28th day of treatment (ulcer craters are reduced due to gastric mucosal membrane re-epithelization and their cytoprotective activity supplied with their anti-secretion effect).

Table 1: Evolution of ulcer parameters in acetic acid-induced ulcers in rats.

Treatment	Dose (mg/kg)	US (mm^2)			UI			I %			Mucus (mg)		
		7 Days	14 Days	28 Days	7 Days	14 Days	28 Days	7 Days	14 Days	28 Days	7 Days	14 Days	28 Days
Group 1		-	-	-	-	-	-	-	-	-	158.47 ± 4.15^{m}	158.81 ± 3.24^{o}	158.85 ± 4.20^{c}
Group 2		145.67 ± 7.5^{h}	114.12 ± 3.1^{s}	38.29 ± 0.5^{k}	5.21 ± 0.1^{a}	$3.11\pm0,91^{j}$	1.1 ± 0.01^{sw}	-	-	-	168.47 ± 4.15^{r}	496.11 ± 3.24^{u}	736.45 ± 6.30^{q}
Omeprazole	10	68.10 ± 2.16^{q}	27.10 ± 1.3^{r}	1.12 ± 0.6^{q}	3.32 ± 0.41^{az}	1.01 ± 0.41^{sa}	0.1 ± 0.01^{y}	53.25	76.25	97.07	475.39 ± 3.1^{n}	989.93 ± 2.13^{h}	1755.93 ± 9.7^{w}
Cimetidine	12	71.23 ± 1.1^{v}	30.7 ± 0.1^{j}	1.7 ± 1.1^{a}	3.2 ± 0.11^{az}	1.03 ± 0.12^{sa}	0.13 ± 0.12^{sd}	51.10	73.10	95.56	363.41 ± 2.43^{z}	879.41 ± 2.01^{f}	1689.41 ± 5.81^{z}
	125	85.55 ± 7.2^{t}	37.67 ± 2.7^{f}	7.08 ± 1.01^{s}	3.17 ± 0.31^{az}	1.8 ± 0.05^{ij}	1.02 ± 0.01^{ss}	41.27	67	81.51	261.14 ± 0.21^{n}	521.41 ± 3.11^{a}	929.47 ± 0.3^{s}
AETs	250	77.22 ± 0.33^{k}	31.02 ± 1.6^{a}	4.19 ± 0.07^{y}	2.85 ± 0.47^{wq}	1.2 ± 0.2^{xx}	0.83 ± 0.01^{yb}	46.99	72.82	89.06	588.52 ± 5.3^{k}	982.77 ± 8.1^{x}	1182.03 ± 10.3^{k}
	500	53.78 ± 0.81^{x}	22.45 ± 0.23^{y}	0.7 ± 0.1^{i}	1.26 ± 0.91^{b}	0.8 ± 0.12^{x}	0.06 ± 0.002^{u}	63.08	80.33	98.17	968.68 ± 8.71^{ss}	1056.40 ± 11.1^{e}	$1376.4\pm19.31^{\mu}$
	125	72.63 ± 9.4^{l}	35.31 ± 0.6^{m}	5.3 ± 0.1^{b}	3.11 ± 0.44^{az}	3.01 ± 0.38^{np}	1.08 ± 0.38^{np}	50.14	69.06	86.16	443.38 ± 6.02^{nb}	777.21 ± 7.94^{tf}	974.51 ± 8.04^{la}
HE 70 %	250	61.05 ± 0.04^{b}	20.87 ± 0.9^{x}	3.21 ± 0.1^{z}	1.72 ± 0.82^{x}	1.11 ± 0.72^{w}	0.8 ± 0.72^{yb}	58.09	81.71	91.62	798.07 ± 7.06^{h}	928.33 ± 6.58^{j}	1289.7 ± 1.79^{g}
	500	35.88 ± 0.2^{d}	11.44 ± 0.14^{h}	0.63 ± 0.02^{v}	0.11 ± 0.07^{e}	0.08 ± 0.001^{t}	0.02 ± 0.004^{a}	75.37	89.97	98.35	$997.11\pm 5,07^{v}$	1197.13 ± 7.82^{u}	1493.01 ± 8.4^{x}
	15	88.35 ± 2.2^{p}	32.78 ± 3.2^{m}	3.87 ± 0.12^{x}	2.61 ± 0.4^{d}	1.6 ± 0.33^{aq}	1.16 ± 0.24^{j}	39.35	71.27	89.89	528.30 ± 6.12^{ij}	882.44 ± 8.10^{bo}	962.34 ± 2.17^{it}
BuF	30	66.75 ± 0.54^{g}	19.72 ± 0.4^{x}	1.7 ± 0.1^{i}	1.01 ± 0.25^{n}	0.9 ± 0.05^{x}	0.1 ± 0.02^{xq}	54.18	82.72	95.56	801.57 ± 7.1^{q}	981.83 ± 1.48^{z}	1101.82 ± 4.1^{h}
	60	53.77 ± 0.84^{e}	10.85 ± 0.3^{h}	0.05 ± 0.001^{r}	0.93 ± 0.01^{dr}	0.2 ± 0.01^{c}	0.01 ± 0.001^{u}	63.09	90.49	99.87	978.12 ± 9.40^{y}	1078.12 ± 6.4^{fu}	1987.18 ± 8.5^{t}

Values with the same letter in the same column are not statistically different at $p < 0.05$; n = 6. Control group 1: rats given only distilled water (Control non-ulcerated); Control group 2: rats given only acetic acid solution 20 % (Control ulcerated). AETs, HE 70% and BuF: Aqueous extract, hydro ethanol 70 % and n-butanol

organic fraction (BuF) from the trunk bark of *T. superba*, US: ulcerated surface; UI: Ulcer index; I%: inhibition percentage.

DISCUSSION

Ulcerations induced by acetic acid solution in rats resemble the human ulcer in location, pathology, severity and healing processes. Therefore, various authors have pointed out the relevance of this model for the study of the healing effects of extracts of medicinal plants and pharmacodynamic substances.[12] They have shown that various anti-secretory agents such as omeprazole, histaminergic H_2 receptor antagonists such as cimetidine.[17] and certain cytoprotectors such as sucralfate.[18] are effective in this model. Their effectiveness is attributable to their anti-secretory and cyto-protective effects. The results of this study indicate that the ulceration index and surface area are significantly reduced by *Terminalia superba* extracts. This decrease in ulcer index and ulceration area reflects healing. Ulcers healing is a complex process that involves the combination of wound retraction and re-epitheliasing of the gastric mucosa.[19,20] It depends on the regeneration of the glandular structure of the mucosa and the migration of epithelial cells to cover the crater dug in the gastric mucosa. Histopathological examination of the gastric mucosa has shown that treatment of rats with *T. superba* trunk bark extracts and pharmacological reference substances protect and promote regeneration of the mucous epithelium against damage caused by acetic acid. Studies with different plant extracts have shown that these protect the mucous epithelium against damage caused by necrotizing substances. This in agreement with.[21] who reported that *Ocimum sanctum* (Lamiaceae), in addition to effectively preventing gastric ulcers, cures them. Some authors indicate respectively that the ethanolic extract of *Rheum emodi* (Polygonaceae) rhizomes and the hydromethanolic crude extract of the leaf of *Urtica simensis* (Urticaceae) are endowed with cyto-protective and regenerative properties of the gastric mucosa on lesions induced by various necrotizing agents.[22,23] Researchers have also shown that the ethanolic extract of the leaves of *Ficus religiosa* (Moraceae) regenerates the gastric mucosa.[24] while other authors reported that the hydroalcoholic extract from *Green propolis*, protect and heal gastric ulcers induced by acetic acid solution in rats.[25] These actions occur through the increase in mucin production, the proliferation of mucosal cells. However, according to these authors, the real mechanism by which these extracts work is not yet clearly understood. The results of this *in vivo* study clearly indicate that the effect of the extracts is almost similar to that of omeprazole. This suggests that like omeprazole, these extracts would inhibit ion pumps by inducing almost complete suppression of acid secretion. The mechanism of omeprazole action is based on the inactivation of the H^+ / K^+-ATPase pump to which it binds very specifically at the level of the single subunit on the secretory surface of the parietal cell.[26] It reduces acid secretion regardless of the source of secretory stimulation. By increasing intragastric pH by inhibiting acid secretion, omeprazole prevents the activation of pepsin, which is an ulcerogenic agent.[27] Activation and infiltration of neutrophils appear to be involved in the process of damage to the gastric mucosa.[28] Furthermore,[29] have shown that oral administration of ethanol, by causing damage to the gastric mucosa, increases the infiltration of neutrophils into ulcerative tissues. Moreover, some authors demonstrated that reducing the infiltration of neutrophils into ulcerative gastric tissue helps prevent the formation of gastric ulcers in rats.[30] AETs, HE 70 % and BuF could act by this same mechanism. This hypothesis is all the more plausible as.[29] suggested that oral administration of herbal extracts significantly reduced the infiltration of neutrophils into the gastric mucosa. However, further experiments are needed to confirm or refute this hypothesis.

The anti-ulcer activity of some plants may be due to the presence of saponins, flavonoids, tannins, terpenoids, amino acids.[31,32] and p-coumaric acid isolated from *Baccharis dracunculifolia* which stimulates cell proliferation of murine fibroblasts cells and induces an increase in the mucin levels and reduction in the oxidative stress process.[33] Research has linked flavonoid-like molecules and saponins to the anti-inflammatory activity of certain plant extracts. Indeed, it has been established that baicalein and vogomine, flavonoids isolated from *Scutelleria baïcalensis* (Lamiaceae) have anti-inflammatory activity. The mechanism mentioned is the inhibition of prostaglandin synthesis by inhibition of cyclo-oxygenase and lipo-oxygenase.[34] Flavonoids also enhance capillary resistance thus preventing inflammation of the gastrointestinal mucosa.[35] Other studies have shown that flavonoids extracted from the leaves of *Anacardium occidentalis* (Anacardiaceae) are endowed with anti-ulcerogenic properties.[36,37] Researchers reported that ruscogenin [(1-beta, 3-beta, 25R)-Spirost-5-ene-1, 3-diol], a main steroid sapogenin of a traditional Chinese plant called *Ophiopogon japonicas* has been found to have notable anti-inflammatory and anti-thrombotic activities in different diseases.[38] Tannins with their astringent power, line the lining of the gastrointestinal mucosa while precipitating micro proteins in the areas of ulceration, which strengthens this mucosa and prevents any attack by proteolytic enzymes.[39] Thus, the presence of saponins, tannins, proteins, sterols and poly-terpenes and particularly flavonoids in the extracts used could explain, at least in part, these anti-ulcerogenic effects.

In total, the pharmacological effects of AETs, HE 70% and BuF from *T. superba* trunk bark have revealed that these extracts have real healing anti-ulcer potential. These extracts heal lesions of the gastric mucosa caused by acetic acid. This ability of the extracts to heal ulcers may be mainly due to a strengthening of the gastric mucosa by a strong production of mucus, correlated with

an anti-secretory effect and re-epithelization of the gastric mucosa.

CONCLUSION

The healing effect study, for its part, revealed that AETs, HE 70% and BuF promote re-epithelization of the gastric mucosa on lesions induced by acetic acid. This ulcer healing effect of these extracts may be mainly due to their cytoprotective activity along with their anti-secretory effect.

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