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Cytoprotective Effect of The Total Aqueous Extract of The Stem Barks of *Terminalia mantaly* on Gastric Ulcer Induced by HCl/Ethanol, Stress and Aspirin in Rats

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ABSTRACT

Many studies today on certain medicinal plants have been carried out to show their potential effectiveness in the treatment of gastric ulcer. In Côte d'Ivoire, research into *Terminalia mantaly*, a plant used in traditional medicine to treat gastrointestinal disorders, falls within this framework. This work aimed to study the cytoprotective effect of the total aqueous extract of the stem barks of *Terminalia mantaly* (TAETm) in rats through three experimental models of induction of this pathology, namely the model HCl/Ethanol, stress and aspirin. The results showed that the treatment of rats with TAETm at 125 and 500 mg/kg bw, significantly ($P<0.05$) and dose-dependently reduced ulcerations observed in the treated groups compared to control group 2, untreated ulcer. This reduction is pronounced at 500 mg/kg bw. Thus, the inhibition percentages obtained at 500 mg/kg are 97.1; 96.76 and 94.74 % respectively in the HCl/Ethanol, aspirin and cold restraint stress models. TAETm also significantly ($P < 0.05$) increased mucus production in the treated groups compared to control group 2. These results suggest that TAETm exerts a cytoprotective effect on the stomach mucosa in rats. In conclusion, the treatment of gastric ulcer in traditional medicine in Côte d'Ivoire with *Terminalia mantaly* is therefore justified.

Keywords: *Terminalia mantaly*, gastric ulcer, rat, cytoprotective effect.

INTRODUCTION

Stomach has a protective lining. However, it happens that this tunic is attacked by internal or external agents, which causes gastric ulcers which are superficial or deep wounds open in the mucosa [1]. These wounds result in fact from an imbalance between agressive and defensive factors, such as mucus secretion, mucosal barrier, acid pepsin secretion, blood flow, cellular regeneration and endogenous protective agents such as prostaglandins [2]. This disease is universal and spares no population [3]. Different factors are involved in the pathogenesis of gastric ulcer in humans, such as chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs), stress, *Helicobacter pylori* (responsible for 75 to 80 % of cases) and alcohol consumption [4,5]. Gastric ulcer affects four million people worldwide each year and its lifetime prevalence is estimated between 5 and 10 % in the general population [3]. In Côte d'Ivoire, studies carried out in hospitals report a prevalence of 26.9 % of people suffering from gastric ulcer [6]. Although various types of medications namely H-2 receptor antagonists, proton pump inhibitors (PPIs), antacids and antimuscarinics [7]. are available to treat gastric ulcer, most of them cause side effects in patients, without ensuring complete recovery [8]. A recourse to traditional medicine is therefore necessary. However, the WHO [9] recommends that developing countries initiate programs for the identification, preparation, cultivation and conservation of medicinal plants but also and above all to evaluate the quality, effectiveness and the safety of these plant extracts using modern techniques. Thus, with these recommendations, the Laboratory of Physiology, Pharmacology and Pharmacopoeia of the Research Training-Unit of Sciences Nature of the NANGUI ABROGOUA University, Abidjan (Côte d'Ivoire) and the Polytechnic University of Man (Côte d'Ivoire) have initiated collaborations. For this purpose, *Terminalia mantaly* was chosen, with a view to promoting pharmacopoeia and traditional medicine, the importance of which no longer needs to be demonstrated. In Côte d'Ivoire, a decocted stem barks of *Terminalia mantaly* is used to treat gastrointestinal disorders [10]. However, the effect of the plant on gastric ulcers has not yet been scientifically proven. Furthermore, it is important to carry out a scientific evaluation of plants in order to obtain as much information as possible regarding their effectiveness. It is with this observation that this work has set itself the aim of studying the cytoprotective effect of the total aqueous extract of the stem barks of *Terminalia mantaly* through three experimental models of induction of gastric ulcer in rats, namely induction models by necrotizing HCl/Ethanol solution, aspirin and hypothermia stress.

1-Materials and methods

1.1-Material

1.1.1-Plant material

Stem barks of *Terminalia mantaly* were collected locally from the forest of NANGUI ABROGOUA University (Abidjan, Côte d"Ivoire). Taxonomical identification and authentication of those stem barks was established by botanist of v and the National Floristic Center (CNF) of the Félix Houphouët Boigny University of Cocody in Abidjan, voucher number 217 of May 23, 1995.

1.1.2-Animal material

Albino wistar rats of either sex weighing between 180 and 200 g and approximately 12 to 16 weeks old were selected for gastric antiulcer experiments. They were bred in Animal house of Physiology, Pharmacology and pharmacopeia laboratory of the University of NANGUI ABROGOUA (Abidjan, Côte d'Ivoire) according to the care and use the European Council of Legislation 87/609/EEC. They were fed with FACI® pellets, water *ad libitum* and acclimated in the cages for two weeks. They were exposed to 12 hours dark/light cycle and were subjected daily to ambient temperature 25 ± 2°C.

1.1.3-Chemical substances

The chemical substances used are: HCl/Ethanol (Sigma, USA), Acetylsalicylic acid (Aspirin^R, Sanofi Aventis, France), Cimetidine (Sigma, USA), Aluminum hydroxide (Maalox^R, Sanofi Aventis, France), Misoprostol (Cytotec^R, Pfizer, Germany), Ranitidine (Azantac^R, Bristol Myers Squibb, USA), Ether (VWR International-Geldenaakfebaan464-B-3001 Leuven-Belgium).

2-Methods

2.1-Preparation of the total aqueous extract of the stem bark of *Terminalia mantaly*

Stem barks of *Terminalia mantaly* were washed with distilled water, cut into small pieces and dried under shade for one week. They were finely powdered with electric machine mark RETSH, type SM 100 (Haan, Germany). One hundred grams of the stem barks powder were decocted for 15 min in one liter of distilled water. The aqueous solution obtained was filtered through hydrophilic cotton then through Whatman 3 mm filter paper. Half a liter of distilled water was added to the residual marc and left to decoction for 10 min. This solution was also filtered. The filtrates were concentrated under reduce pressure using a rotary evaporator (Büchi R110, type MKE 6540/2) at a temperature of 45°C. The concentrated extracts were stored in dessicators at 45°C. A powder (14.7 g) of black brown color which constitutes the total aqueous extract of the stem bark of *Terminalia mantaly* (TAETm) was obtained. The concentrations to be tested were prepared extemporaneously by dilution in saline solution (NaCl 9‰).

2.2-Induction of gastric lesions with the necrotizing HCl/Ethanol solution

Gastric lesions were induced according to the method described by Hara and Okabe [11]**.** The animals were divided into 7 groups of 6 animals each. Rats in groups 1 and 2 received distilled water at 1 ml/100 g of body weight (b.w.). Those in groups 3 and 4 received cimetidine (12 mg/kg) and maalox (50 mg/kg) respectively. As for groups 5 to 7, they received respectively TAETm at 125, 250 and 500 mg/kg bw. All treatments were administered orally. One hour after drug administration, 1 ml/150 g b.w. of the necrotizing solution of HCl/Ethanol (150 mM in HCl in 60 % v/v ethanol) was given orally to each rat except rats of group 1. One hour later, all animals were sacrificed by over dose of ether and the stomachs were incised along the greater curvature (cardia-pylorus). The stomach was grated. The collected mucus was then weighed. The mucosal erosion was determined by measuring the area of the lesions and then it was scored (points assigned to gastric lesions). The sum of the areas was expressed as ulcer index (mm^2). The scoring of stomach lesions was established according to the method described by Robert *et al.* [12]

0: normal mucosa; 1: hyperemic mucosa or up to 3 small ulcerated plaques; 2: 4 to 10 small patches of ulcerations; 3: more than 10 small or up to 3 medium-sized ulceration plaques; 4: 4 to 6 plaques of medium-sized ulcerations; 5: more than 6 medium or up to 3 large plaques of ulcerations; 6: from large ulceration plaques 4 to 6 mm in diameter; 7: 7 to 10 large patches of ulcerations; 8: more than 10 large or extensive necrotic areas.

The percentage of inhibition (%I) was calculated using the following formula:

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

Where US_C = ulcer surface area in control group 2 and US_T = ulcer surface area in pretreated animals.

2.3-Induction of gastric lesions with aspirin

Gastric lesions were induced using aspirin solution according to the method described by Hegde *et al.* ([13]. In this model, forty-two (42) rats were divided into seven groups of six rats each. Groups 1 and 2 received distilled water at 1 ml/100 g b.w. Groups 3 and 4 received respectively misoprostol (0.012 mg/kg) and maalox (50 mg/kg). As groups 5 to 7, they received TAETm at 125, 250 and 500 mg/kg bw. One hour after the administration of the different solutions, all the animals received aspirin (250 mg/kg bw) at 1 ml/100 g except rats in control group 1. All solutions were administered orally. Six hours later, all the animals were sacrificed by over dose of ether. The stomach was opened. The mucus was collected and weighed. The classification ("scores") of the lesions was carried out as described by Kulkarni. [14]: 0: absence of ulcer (normal mucosa); 0.5: dilation of blood vessels (presence of redness); 1: small ulcer marks; 1, 5: dilation of blood vessels and presence of ulcer marks, 2: ulcers ≥ 3 mm long ≤ 5 mm long; 3: large ulcers>5 mm long.

2.4-Gastric lesions induction by stress

Stress was created in this experiment by keeping rats in hypothermia on a 3 ± 1°C ice board. Forty-two rats were divided into seven groups of six rats each. Groups 1 and 2 received distilled water at 1ml/100g bw. Groups 3 and 4 received misoprostol (0.012 mg/kg bw) and ranitidine (50 mg/kg bw) respectively at a rate of 1 ml/100 g of p.c. Groups 5 to 7, received TAETm at 125, 250 and 500 mg/kg bw. One hour after the administration of the different solutions orally, animals from groups 2 to 7 were kept on a board. ice for 1 h 30 min according to Gupta *et al.*, [15]:. Once removed from the ice board, animals were sacrificed by cervical dislocation. The stomach was opened, mucus was collected and weighed. The different stomachs were examined for ulceration and severity of intraluminal hemorrhage according to the classification established by Chiu *et al*. [16].

0: absence of ulcer (normal mucosa); 1: thin layer of blood following the ridges; 2: thick blood following the ridges; 3: thick blood following ridges and blood clots in some areas; 4: large extent of gastric mucosal surface with thick blood.

2.5-Macroscopic evaluation of gastric ulcers

After spreading the stomachs, photos were taken using a digital camera and the surfaces were determined using Image J software. Once the measurements were made, the ulceration index and the percentage of inhibition of ulcerations were calculated by the formulas described by Nguelefack *et al.* [17]:

2.6-Statistical analyzes

Statistical analysis of the data was carried out using GraphPad Prism 8.0.1 software (San Diego, California, USA). Results were given as the mean followed by the standard error of the mean (M ± SEM). The one-way analysis of variance test (ANOVA1) was carried out to check the normality of the variables. When significant differences were revealed between the tested means, ANOVA 1 was completed with multiple comparisons of the mean values of the different parameters using the Turkey-Kramer test. The significance threshold was set at $P<0.05$ for the expression of the results.

3-Results

3.1-Effect of different pretreatments on gastric lesions induced by the necrotizing HCl/ethanol solution

3.1.1- Effect of different pretreatments on the stomach of rats

Figure 1 represents the effect of the different pretreatments on gastric lesions induced by the HCl/ethanol solution on the stomach of rats. In ulcerated rats from group 2, the necrotizing HCl/ethanol solution induced characteristic hemorrhagic lesions in the glandular part of the stomach (Figure 1-B). As for the rats in control group 1 which received distilled water, no lesions were observed in the gastric mucosa (Figure 1-A). However, in rats pretreated with TAETm at 125, 250 and 500 mg/kg b.w., one hour before the administration of HCl/Ethanol solution, the gastric mucosa was considerably protected and in a dose-dependent manner compared to those of the control group 2. The mucosa of the rats which received the extract at 250 and 500 mg/kg bw (Figures 1-F and G) presented an almost normal appearance similar to that of control group 1 in comparison to control group 2. On the other hand, a

lesser effect for the dose of 125 mg/kg bw (Figures 1-E) was observed showing the persistence of ulceration foci. Maalox at 50 mg/kg bw and cimetidine at 12 mg/kg bw, considerably reduced ulceration (Figure 1-C and D), so as to restore the normal appearance of the stomach compared to control group 2.

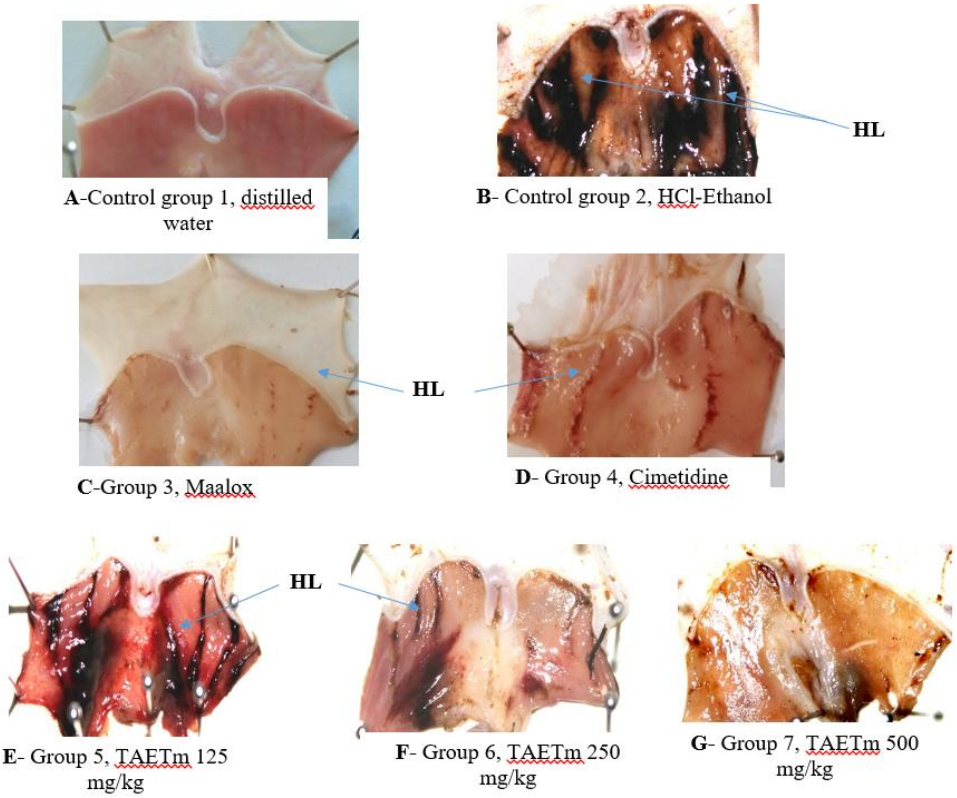

Figure 1: Photograph of rat stomachs according to the different pretreatments on gastric lesions induced by the necrotizing HCl/ethanol solution

TAETm: Total aqueous extract of the stem bark of *Terminalia mantaly*

HL: Hemorrhagic lesion

3.1.2- Effect of different pretreatments on macroscopic parameters

Rats from control group 1 presented a zero score, surface area and ulceration index. However, mucus production worth 157.17 ± 2.12 mg was recorded. This secretion of mucus produced decreases significantly ($P<0.01$) in the ulcerated rats of control group 2 which received the necrotizing HCl/ethanol solution compared to control group 1 and it corresponds to 107.43 ± 7.53 mg (Table 1). A score of 7.20 ± 0.98 was observed with an ulceration surface and an ulceration index which were respectively 202.11 ± 5.07 mm^2 and 6.22 ± 0.15 in these animals treated only with the necrotizing HCl/ethanol solution.

In rats pretreated with TAETm, a significantly ($P<0.01$) decreased ulceration area from 130.45 ± 2.12 to 5.77 ± 0.15 mm^2 and a dose-dependent inhibition of gastric ulceration of 35.45 to 97.14 % for doses between 125 and 500 mg/kg bw were recorded in comparison to rats from control group 2. Cimetidine and maalox, administered by gavage to rats at respective doses of 12 and 50 mg/kg bw, resulted in an ulceration surface of 65.63 ± 6.21 mm^2 (Cimetidine) and 121.31±4.28 mm^2 (Maalox), which corresponded to 67.53 and 39.98 % inhibition, respectively (Table 1). TAETm significantly ($P<0.05$) and dose-dependently increased mucus secretion from 165.54 ± 8.67 to 390.32 ± 10.12 mg (Table 1) compared to control group 2 where this quantity of mucus is 157.17±2.12 mg. This increase in secreted mucus was accompanied by a significant reduction ($P<0.05$) in the ulceration index which went from 6.22 ± 0.15 (Control group 2) to 0.13 ± 0.01 at 500 mg/kg bw of TAETm. As for the reference pharmacological solutions (Cimetidine and Maalox), they also induce a significant increase ($P<0.001$) in mucus secreted with values of 158.02±3.88 mg and 171.42±4.16 mg respectively for the cimetidine and maalox.

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Table 1: Effect of different pretreatments on gastric lesions induced by the necrotizing HCl/ethanol solution in rats

Pretreatment	Dose (mg/kg)	US (mm^2)	UI	Score	% I	Mucous (mg)
Control group 1	10	00,00±0,00	00,00±0,00	00,00±0,00	-	157,17±2,12
Control group 2	10	202,11±5,07 ###	6,22±0,15 ###	7,20 ± 0,98 ###	-	107,43±7,3 ###
Group 3	12	65,63±6,21***	2,89±0,26***	2,03±0,25***	67,53	158,02±3,88**
Group 4	50	121,31±4,28***	3,93±0,51***	3,65±0,50***	39,98	171,42±4,16***
Group 5	125	130,45±2,12***	3,11±0,71***	4,06 ± 0,21***	35,45	165,54± 8,67**
Group 6	250	49,09±1,72***	1,84±0,55***	2,12 ± 0,15***	75,71	283,89±7,08***
Group 7	500	5,77±0,15***	0,13±0,01***	0,96 ± 0,32***	97,14	390,32±10,12***

###P < 0.001: Significant difference between the values of control group 1 (non-ulcerous) and those of control group 2 (ulcerous), for the same parameter; **P < 0.01; ***P < 0.001: Significant difference between the values of control group 2 (ulcerative) and those of the test groups, for the same parameter; US: ulceration surface; UI: ulceration index; % I: percentage of inhibition, TAETm: Total aqueous extract of the stem bark of *Terminalia mantaly*, n=6 rats per group. Control group 1: rats received only distilled water at 1 ml/100 g of body weight (b.w.); Control goup 2: rats pretreated with the necrotizing solution of HCl/Ethanol and received only distilled water at 1 ml/100 g of body weight (b.w.); Groups 3 and 4: rats pretreated with the necrotizing solution of HCl/Ethanol and received cimetidine (12 mg/kg) and maalox (50 mg/kg) respectively; Groups 5 to 7: rats pretreated with the necrotizing solution of HCl/Ethanol and received TAETm at 125, 250 and 500 mg/kg bw respectively.

3.2-Effect of different substances on gastric lesions induced by Aspirin

3.2.1- Effect of different pretreatments on the stomach of rats

Rats from control group 2, with ulcers, developed characteristic ulcerations in the glandular portion of the stomach. These ulcerations are in the form of red spots present in the gastric mucosa (Figure 2-B). On the other hand, in rats from control group 1, non-ulcerative, pretreated with distilled water, the stomach presents a normal appearance compared to control group 2 (Figure 2-A). Misoprostol (0.012 mg/kg bw) and Maalox (50 mg/kg bw) significantly reduced ulcerations in rats making the appearance of the gastric mucosa almost normal (Figure 2-C and D). Rats pretreated with TAETm at doses of 125, 250 and 500 mg kg bw, led to a reduction in visible gastric lesions with respect to the damage produced by aspirin in comparison to those of the rats from control group 2, ulcerative and untreated (Figure 2-E, F and G).

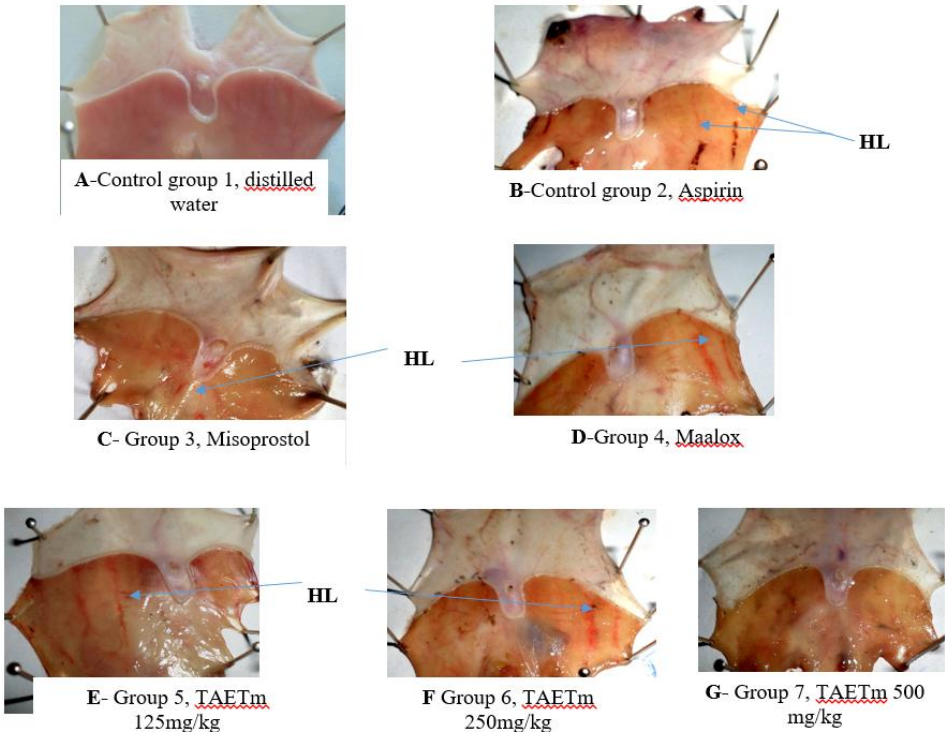

Figure 2: Photograph of aspirin-induced gastric lesions of rats after pretreatment

TAETm: Total aqueous extract of the stem bark of *Terminalia mantaly*

HL: Hemorrhagic lesion

3.2.2- Effect of different treatments on macroscopic parameters

Aspirin administered by gavage caused characteristic lesions in the gastric mucosa of ulcerative control group 2 rats, with an ulceration area and ulceration index of 178.26 ± 5.41 mm^2 and 4.9 ± 1.03 respectively and a score of 2.50 ± 0.63. An amount of mucus of 81.78 ± 3.91 mg was collected. The administration of distilled water to rats did not induce any damage to the gastric mucosa, which corresponds to a score of 0. A secretion of mucus worth 157.17 ± 2.12 mg is recorded. However, lesions were significantly (P<0.001) reduced in rats pretreated with TAETm at doses between 125 and 500 mg/kg bw with an ulceration area ranging from 24.83 ± 1.05 to 2.53 ± 1.03 mm^2 was recorded compared to control group 2 (Table 2). These surfaces correspond to an inhibition percentage which varies from 68.27 to 96.58 %. This reduction in lesions of the gastric mucosa by TAETm is accompanied by a significant (P<0.001) and dose-dependent increase in secreted mucus which varies from 113.43 ± 5.42 to 196.22 ± 6.12 mg compared to the control group 2, where this quantity of mucus was 81.78 ± 3.91 mg. Furthermore, pretreatment of rats with misoprostol (0.012 mg/kg bw) and maalox (50 mg/kg bw), respectively induced a score of 0.60±0.20 (Misoprostol) and 0.83±0, 16 (Maalox). Inhibitions of 91.36% (Misoprostol) and 86.25% (Maalox) accompanied by an ulceration area of 6.76 ± 0.92 (Misoprostol) and 10.77 ± 1.84 mm2 (Maalox) were been recorded.

Table 2: Effect of different pretreatments on aspirin-induced gastric lesions

Pretreatment	Dose (mg/kg)	US (mm^2)	UI	Score	% I	Mucous (mg)
Control group 1	10	00,00±0,00	00,00±0,00	00,00±0,00	-	157,17±2,12
Control group 2	10	78,26±5,41$^{###}$	4,9 ±1,03$^{###}$	2,50±0,63$^{###}$	-	81,78±3,91$^{###}$
Group 3	0,012	6,76±1,92***	0,38 ± 0,22***	0,60±0,20***	91,36	152,44±2,11***
Group 4	50	10,77±1,84***	1,43 ± 0,51***	0,83±0,16***	86,23	126,73 ±8,37***
Group 5	125	24,83± 1,05***	2,9 ± 0, 22***	1,33 ± 0,22***	68,27	113,43±5,42**
Group 6	250	8,97±1,01***	1,2 ± 0,02***	0,96±0,44***	88,54	187,61±4,33***
Group 7	500	2,53±1,03***	0,35 ± 0,01***	0,69±0,32***	96,76	196,22±6,12***

###P < 0.001: Significant difference between the values of control group 1 (non-ulcerous) and those of control group 2 (ulcerous), for the same parameter; **P < 0.01; ***P < 0.001: Significant difference between the values of control group 2 (ulcerative) and those of the test groups, for the same parameter; US: ulceration surface; UI: ulceration index; % I: percentage of inhibition, TAETm: Total aqueous extract of the stem bark of *Terminalia mantaly*, n=6 rats per group. Control group 1: rats received only distilled water at 1 ml/100 g of body weight (b.w.); Control group 2: rats pretreated with aspirin received only distilled water at 1 ml/100 g of body weight (b.w.); Groups 3 and 4: rats pretreated with aspirin and received misoprostol (0.012 mg/kg) and maalox (50 mg/kg) respectively; Groups 5 to 7: rats pretreated with aspirin and received r TAETm at 125, 250 and 500 mg/kg bw respectively.

3.3-Effect of different substances on stress-induced gastric lesions in hypothermic rats

3.3.1- Effect of different pretreatments on the stomach of rats

Rats from control group 1, non-ulcerated, pretreated with distilled water showed normal gastric mucosa without ulceration (Figure 3-A). However, rats from control group 2, pretreated with distilled water and put in hypothermia on an ice board showed large areas of thick blood on the surface of the gastric mucosa (Figure 3-B). Pretreatment of rats with misoprostol (0.012 mg/kg bw) and ranitidine (50 mg/kg bw) decreased ulcerations in rats making the appearance of the gastric mucosa almost normal (Figure 3-C and D). Furthermore, in rats pretreated with TAETm at doses between 125 to 500 mg/kg bw, a reduction in ulcerations produced compared to those of rats from control group 2, ulcerous was observed (Figure 3-E, F and G).

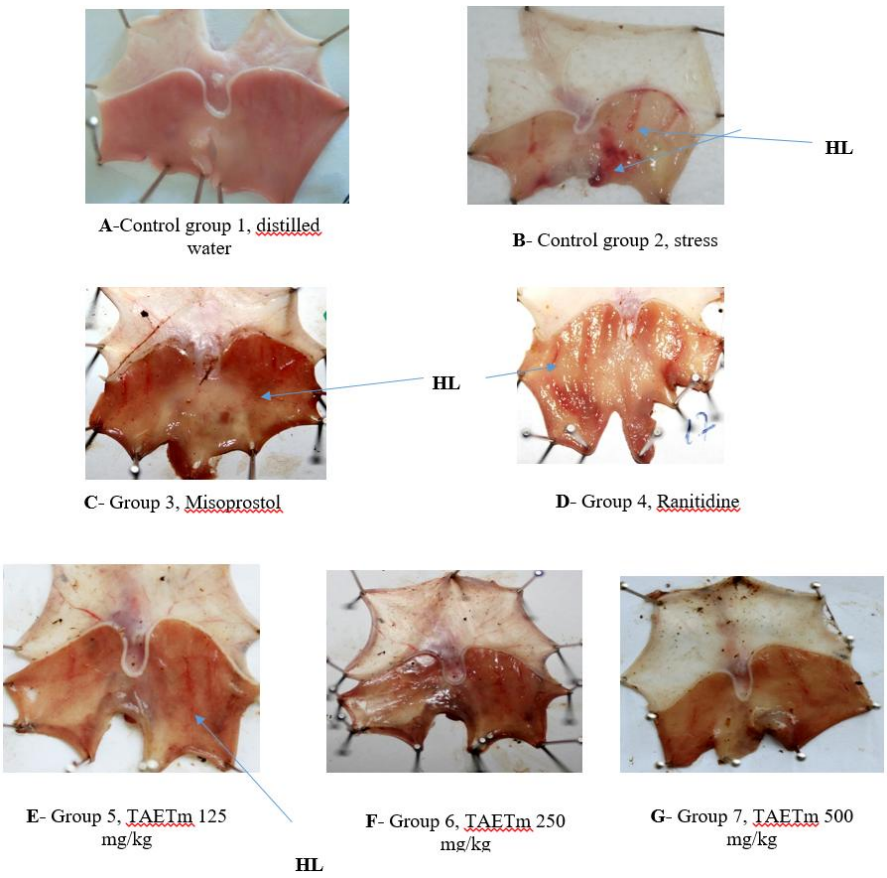

Figure 3: Photograph of stress-induced gastric lesions in rats

TAETm: Total aqueous extract of the stem bark of *Terminalia mantaly*

HL: Hemorrhagic lesion

3.3.2- Effect of different pretreatments on macroscopic parameters

In rats that are not hypothermic and receive only distilled water, the gastric mucosa is not damaged, corresponding to zero score, index and ulceration. The secreted mucus is worth 157.17 ± 2.12 mg. In rats in hypothermia and which do not receive extract, the ulceration surface and the ulceration index are respectively 50.47 ± 1.73 mm^2 and 6.07 ± 0.36, which corresponds to a score of 3.46 ± 0.82 (Table 3). The amount of mucus produced decreased significantly ($P<0.001$) and was worth 55.77 ±2.85 mg compared to rats which received only distilled water (157.17 ±2.12 mg).

The induction of cold stress in rats pretreated with TAETm for doses between 125 and 500 mg/kg bw causes a reduction in the ulceration surface and the ulceration index compared to control group 2 (stress) to reach respectively 2.65 ± 0.01 mm^2 and 0.15 ± 0.01 at 500 mg/kg bw. A score between 1.60 ± 0.25 and 0.52 ± 0.12 and a significant ($P<0.001$) and dose-dependent decrease in ulceration of the stomach mucosa were observed. This inhibition varies from 73.62 to 94.74 % for doses between 125 and 500 mg/kg bw (Table 3). Pretreatment of animals with ranitidine, misoprostol and TAETm induces an increase in mucus which reaches 148.16 ± 1.54 mg for TAETm at 500 mg/kg bw compared to control group 2 where this quantity of mucus secreted is 55.77 ± 0.85 mg (Table 3).

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Table 3: Effect of different pretreatments on stress-induced gastric lesions in hypothermic rats

Pretreatment	Dose (mg/kg)	US (mm^2)	UI	Score	% I	Mucous (mg)
Control group 1	10	00,00±0,00	00,00±0,00	00,00±0,00	-	157,17±2,12
Control group 2	10	50,47 ± 1,73$^{###}$	6,07±0,36$^{###}$	3,46±0,82$^{###}$	-	55,77±2,85$^{###}$
Group 3	0,012	4,92±0,3***	2,73±0,11***	0,82±0,20***	90,25	98,47±4,74***
Group 4	50	5,91±1,21***	3,87±0,64***	0,50 ± 0,10***	88,29	95,51±3,62***
Group 5	125	13,31 ± 1,04***	3,17±0,05***	1,60 ± 0,25***	73,62	83,02±1,39 **
Group 6	250	6,40 ± 1,11***	1,33 ± 0,02***	0,90±0,32**	87,31	96,43±1,27 ***
Group 7	500	2,65 ± 0,01***	0,15 ± 0,01***	0,52±0,12***	94,74	148,16±1,54***

###P < 0.001: Significant difference between the values of control group 1 (non-ulcerous) and those of control group 2 (ulcerous), for the same parameter; **P < 0.01; ***P < 0.001: Significant difference between the values of control group 2 (ulcerative) and those of the test groups, for the same parameter; US: ulceration surface; UI: ulceration index; % I: percentage of inhibition, TAETm: Total aqueous extract of the stem bark of *Terminalia mantaly*, n=6 rats per group. Control group 1: rats received only distilled water at 1 ml/100 g of body weight (b.w.); Control group 2: rats pretreated only with distilled water at 1 ml/100 g of body weight (b.w.) in hypothermia; Groups 3 and 4: rats pretreated only with misoprostol (0.012 mg/kg) and ranitidine (50 mg/kg) in hypothermia respectively; Groups 5 to 7: rats pretreated with TAETm at 125, 250 and 500 mg/kg bw in hypothermia respectively.

4-Discussion

The pharmacological effects of the total aqueous extract of the stem bark of *Terminalia mantaly* (TAETm) revealed that this extract prevents lesions of the gastric mucosa caused by hydrochloric acid/Ethanol, aspirin and stress, three experimental models used to evaluate the effects of TAETm on induced gastric ulcer in rats. This protection of the gastric mucosa results from the cytoprotective and anti-secretory effect of this extract. These results are similar to those obtained with the 70 % hydro-ethanol extract of the stem bark of *Terminalia superba* [18], the aqueous extract of the leaves of *Macaranga barteri* [19], Indeed, these authors showed that these medicinal plant extracts remarkably reduced experimentally induced ulcers in rats while protecting the gastric mucosa against necrotizing agents.

It is known that ethanol disrupts the barrier of the gastric mucosa and causes profound changes with strong vaso-constriction accompanied by dilation responsible for arteriolar and capillary engorgement of the mucous membranes [20]. This causes necrosis of the superficial epithelial cells of the stomach lining, leading to their erosion [21]. This would be the cause of the very large surface of ulceration observed in control group 2 which received the necrotizing HCl/ethanol solution. According to Goel and Bhattacharya [22], ulcer medications inhibit acid secretion, *Helicobacter pylori* and protect the gastric mucosa. Various authors have also reported that the effectiveness of a substance in preventing or curing ulcers is attributable to its anti-secretory and cytoprotective effect [23]. The protection of the gastric mucosa is due to the neutralization of gastric acidity. This hypothesis is all the more plausible since the results showed that the stem bark extract of *Terminalia mantaly* reduced the secretion of gastric acid or improved the defense of the wall of the gastric mucosa through a strong production of gastric mucus. The ulcerative activity of aspirin is due to the induction of lesions of the gastric mucosa by reduction of prostaglandin levels or by inhibition of prostaglandin synthesis [24, 25]. In order to understand the effect of the extract of the stem bark of *Terminalia mantaly* on cyclooxygenase, an enzyme which activates the secretion of gastroduodenal bicarbonate and the biosynthesis of endogenous prostaglandins, the effects of TAETm were studied on models of ulcers induced by aspirin, a specific inhibitor of this enzyme.

The results of this study indicate that the ulceration index and surface area are significantly reduced by the TAETm extract. This extract also increases mucus secretion in the pretreated groups and in a dose-dependent manner compared to the control group 2. These results suggest that TAETm could act on cyclooxygenation to accentuate the protective mechanisms of the gastric mucosa. Although the enzyme is inhibited, an absence of ulceration is observed in the presence of the extract. This effect could be attributed to the probable presence of compounds in this extract whose effect is similar to that of endogenous prostaglandins. This result is similar to that obtained by Vinothapooshan and Sunda [26]. Indeed, these authors showed that the methanolic extract of *Mimosa pudica* exerts its cytoprotective and anti-inflammatory activity by stimulating the production of prostaglandins. According to Davenport *et al.* [27], the defense mechanisms may be due to epithelial cells of the gastric mucosa which are impermeable to hydrogen. Thus, the antiulcer agent can protect the gastric mucosa from the effects of acid by selectively increasing the production of prostaglandin PGF2 [28]. Wilson [29] also state that prostaglandins improve mucosal resistance by perhaps increasing the secretion of mucus and bicarbonates. The pathogenesis of gastric mucosal damage includes the generation of special reactive oxygen (SRO) which appears to play an essential role in the formation of lipid peroxides, accompanied by the antioxidant enzymatic activity of cells under stress [30].

To confirm the ability of the extract studied to prevent this self-destruction of the gastrointestinal mucosa and its anti-secretory activity, its effect in models of ulcer induction by stress experimentally induced by cold was evaluated. The results of this study show that TAETm significantly reduces lesions while at the same time promoting an increase in mucus production. These results are similar to those of Rakesh *et al*., [31]. Indeed, according to these authors, the cytoprotection of *Rheum ribes* extracts is due to its free radical scavenging effect and its mucus production. The anti-ulcerogenic effect of TAETm in these ulcer induction models could be due to the trapping of free radicals, therefore to their antioxidant effect or to their action on nervous pathways. This allows the control of acid secretion in order to strengthen the physiological capacities of the animals to reduce stress and consequently ulcers as reported by Hoogerwerf and Pasricha [32]. However, further studies are needed to confirm this hypothesis.

Conclusion

The present study indicates that the total aqueous extract of *Terminalia mantaly* stem bark has £real antiulcer potential. This extract prevents lesions of the gastric mucosa induced by HCl/ethanol, aspirin and stress. This ability of TAETm to prevent ulcers may be mainly attributable to a strengthening of the gastric mucosa through strong mucus production correlated with an anti-secretory effect. The use of this plant in traditional medicine for the treatment of gastric ulcer finds its explanation here.

Conflict of interests

The authors have not declared any conflict of interests.

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REFERENCES

[1] Rau W, Hohaus C, Jessen EA, Differential approach to form and site of peptic ulcer. *Scientific Reports,* 2019; 9 (1):8683**.**
[2] Laine L, Takeuchi K, Tarnawski A. Gastric mucosal defense and cytoprotection: bench to bedside. *Gastroenterology*, 2008, 135(1): 41-60.
[3] Abbasi-Kangevari M., Ahmadi N., Fattahi N., Rezaei N., Malekpour M.R., Ghamari S.H., Moghaddam S.S., Azadnajafabad S., Esfahani Z., Kolahi A.A., Roshani S., Rezazadeh-Khadem S., Gorgani F., Naleini S.N., Naderimagham S., Larijani B., Farzadfar F. Quality of care of peptic ulcer disease worldwide: A systematic analysis for the global burden of disease study 1990-2019. *PLoS One*,2022; 17(8): e0271284.
[4] Lanas Á., Carrera-Lasfuentes P., Arguedas Y., García S., Bujanda L., Calvet X., Ponce J., Perez-Aísa Á., Castro M., Muñoz M., Sostres C., García-Rodríguez, L.A. Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. *Clinical Gastroenterology and Hepatology*,2015, 13(5). 906-912.
[5] Narayanan M., Reddy K.M., Marsicano E. Peptic ulcer disease and *Helicobacter pylori* infection. *Missouri Medicine*, 2018, 115(3): 219-224.
[6] Doffou A.S., Kouamé G.D., Bangoura A.D., Yaogo A.M., Mamonman K.H., Alassan M.K., Yao-Bathaix F.M., Attia K.A. Prevalence of gastroduodenal ulcers and precancerous gastric lesions in chronic *Helicobacter Pylori* gastritis according to the Sydney system: about 52 Cases, *Health Sciences and Diseases*, 2020, 21(3):16-25.
[7] Wallace J.L., Granger D. The cellular and molecular basis of gastric mucosal defense. *FASEB Journal*;1996, 10(7): 731-734.
[8] Rates S.M. Plants as source of drugs. Toxicon, 2001,39 (5): 603-613.
[9] WHO, "WHO traditional medicine strategy 2002–2005", WHO/EDM/TRM, Geneva, p 65, 2002.
[10] Yaye Y.G., Kra A. K. M., Ackah J. A. A. B., Djaman A. J. Evaluation of antifungal activity and purification test of active ingredients of extracts of *Terminalia mantaly* H.perrier, a combretaceae, on the in vitro growth of candida albicans. *Bulletin of the Royal Society of Sciences of Liège*,2021, 80(7):953-964.
[11] Hara N., Okabe S., Effects of Gefanate on acute lesions in rats. *Folia Pharma*, 1985, 85:443-448.
[12] Robert A., Nezamis J.E., Lancaster C., Davis J.P., Field S.O., Hanchar A.J. Mild irritants prevent gastric necrosis through 'adaptive cytoprotection mediated by prostaglandins. *American Journal of Physiology,*1983, 245(1): G113–G121.
[13] Hegde D.A., Khosa R.L., Goel R.K. Antiulcer and cytoprotective action of *Wedelia calendulacea*", *Ancient Science of Life*, 1994, 14(1):77-81.
[14] Kulkarni S. K.,. "Hand book of experimental pharmacology", Vallabh Prakashan, New Delhi, India, 3rd edition, 2002.
[15] Gupta M.B., Nath R., Gupta G.P., Bhargava K.P. A study of the antiulcer activity of diazepan and other tranquillose datives in albinos rats. *Clinical and Experimental Pharmacology and Physiology,* 1985,12(1):61-66.

[16] Chiu P.J.S., Gerhart C., Brown A.D., Barnett A. Effects of a gastric antisecretory cytprotetor 2-methyl-8–(phenylmethoxy) imidazo (1,2a) -pyridine-3-acetonitrine (Sch28080) on cyteamine, reserpine and stress ulcers in rat. *Arzneimittelforschung*,1984, 34 (7):783-786.
[17] Nguelefack T.B.,Watcho P., Nguelta M.M., Wansi S.L, Kamanyi A. Effects of the methanol leaf extract of *Alchornea cordifolia* (SchumetThonn.) Muell. Arg. on different gastric ulcer models in rats, *Cameroon Journal of Experimental Biology,*1(1): 54-56.
[18] Goze N.B., Kouakou K.L., Bléyéré N.M., Amonkan K.A., Konan B.A., Abo K. J.C., Yapo A.P., Ehilé E.E. Anti-ulcerogenic effects of a hydroethanol 70% extract from stem bark of *Terminalia superba* Engl. et Diels (Combretaceae) in rats and phytochemical screening., *International Journal of Science Innovations and Discoveries*, 2013,3(5): 539-550.
[19] Ehilé E.H., Goze N. B., Kouakou K. L., Yapo A. P., Ehilé E. E. Acute toxicity and gastric anti-ulcer activity of an aqueous extract of the leaves of *Macaranga barteri* Müll.Arg (Euphorbiaceae) on rat models. *Journal of medicinal plants research*, 2018, 12(9): 96-105.
[20] Chang W., Bai J., Tian S., Ma M., Li W., Yin Y., Deng R., Cui J., Li J., Wang G., Zhang P., Tao K. Autophagy protects gastric mucosal epithelial cells from ethanol-induced oxidative damage via mTOR signaling pathway. *Experimental Biology and Medicine* (Maywood), 2017. 242(10):1025-1033.
[21] Oates P.J., Kakkinen J.P. Studies on the mechanism of ethanol induced gastric damage in rats. *Gastroenterology*,1988, 94(1):10-21.
[22] Goel R. K., Bhattacharya S.K. Gastroduodenal mucosal defense and mucosal protective agents. *Indian Journal of Experimental Biology*,1991, 29(8): 701-714.
[23] Tsukimi Y., Nozue C., Okabe S. Effects of leminoprazole, omeprazole and sucralfateon indomethacin-induced delayed healing of kissing gastric ulcers in rats. *The Journal of Gastroenterology and Hepatology,*1996, 11(4):335-340.
[24] Cryer B., Mahaffey K.W. Gastrointestinal ulcers, role of aspirin, and clinical outcomes: pathobiology, diagnosis, and treatment. *Journal of Multidisciplinary Healthcare,*2014,(3)7: 137-146.
[25] Olaleye S.B., Farombi E.O. Attenuation of indomethacin and HCI/ ethanol induced oxitative gastric mucosa damage in rats by Kolaviron: A natural biflavonoid of *Garcina kola* seed. *Phytotherapy Research*, 2006, 20(1): 14-20.
[26] Vinothapooshan G., Sundar K. Anti-ulcer activity of *Mimosa pudica* leaves against gastric ulcer in rats. *Research Journal of Pharmaceutical, Biological and Chemical Sciences;*2010 (1): 4: 606-6014.
[27] Davenport H. W., Warner H. A., Code C.F. Functional significance of gastric mucosal barrier to sodium. *Gastroenterology*, 1964, 47(2):142-152.
[28] Lauritsen K., Hansen J., Bytzer P., Bukhave K., J.Rask-Madsen. Effects of sulphasalazine and disodium azodisalicylate on colonic PGE_2 concentrations determined by equilibrium *in vivo* dialysis of faeces in patients with ulcerative colitis and healthy controls. *Gut*, 1984, 24: 1271-1278.
[29] Wilson DE. Role of prostaglandins in gastroduodenal mucosal protection. *Journal of Clinical Gastroenterology*,1991, 13(1): S65-S71.
[30] Kwiecien S., Jasnos K., Magierowski M., Sliwowski Z., Pajdo R., Brzozowski B., Mach T., Wojcik D, Brzozowski T. Lipid peroxidation, reactive oxygen species and antioxidative factors in the pathogenesis of gastric mucosal lesions and mechanism of protection against oxidative stress induced gastric injury. *Journal of Physiology and Pharmacology*, 2014,65, (5): 613-622.
[31] Rakesh K.S., Pradeep K., Jagdeep K., Ashok K., Sandeep A., Investigations into the anti-ulcer activity of *Rheum ribes* L. leave extracts. *International Journal of Pharmacy and Pharmaceutical Sciences,* 2010, 2(4): 90-93.
[32] Schubert M.L., Peura D.A. Control of gastric acid secretion in health and disease, *Gastroenterology*,134, (7): 1842-1860.

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