Original Research Article

Hepatoprotective effect of *Lippia multiflora* aqueous extract against ethanol-induced toxicity in wistar rats

Abstract

Aim: Usually called Tea of Gambia, *Lippia multiflora* is known for its sedative, relaxing, febrifuges, anti-flu-like, antispasmodic, hypotensive, antiinflammatory, anti-catarrhal, mucolytique, antiinfective, hepatoprotective properties. The aim of the present study was to evaluate the hepatoprotective effect of aqueous extract of *Lippia multiflora* (L.M.) on ethanol induced toxicity in rat livers.

Study design: Thirty- Wistar albino rats (weighing 100-162 g) were divided into six groups. Group 1 served as control and received only distilled water. Group 2 received only ethanol 15% (3ml/100g/day body weight). Group 3 served as standard group and received silymarin (70mg/kg B.W.). Group 4, 5 and 6 served as extract treatment groups and received 100, 300 and 900 mg/kg aqueous extract of L. multiflora. Ethanol 15% (3ml/100g/day B.W.) was administered 1h after treatment in group 3, 4, 5 and 6.

Place and Duration of Study: The study was carried out in Laboratory of Pharmacodymamy Biochemistry, Felix Houphouet-Boigny University of Cocody-Abidjan (Côte d'Ivoire) between september and november 2014.

Methodology: All treatment protocols followed 28 days and the serum levels of liver marker enzymes, biochemical analytes and hematological parameters were monitored.At the day 7, 14, 21 and 28 of experimental period, blood samples were collected from retroorbital venous plexus in nonheparinized tubes.Animals received daily doses for 28 days and were observed daily for psychomotor changes and other signs of toxicity including death throughout the period of study.

Results:*L. multiflora* extract (300 or 900 mg/kg b.w) provides significant protection against ethanol induced toxicity in liver of rats, revealed by reduction of enzymatic parameters activities (ALT, AST and GGT). Additionally, histopathological and hematological parameters revealed markedly ethanol-induced toxicity protection, by the extract of *L. multiflora*, on blood cells parameters and liver structure.

Conclusion: Our results prove that *L. multiflora* extract (300 or 900 mg/kg b.w) has protective effects against ethanol-induced toxicity and changes in parameters of blood cells and liver structure in rats.

Keywords: *Lippia multiflora,liver, ALT (alanine aminotransferase), AST (aspartate aminotransferase), GGT (gamma glutamyltransferase)*

1-INTRODUCTION

Lippia multiflora Moldenke also known as *Lippiaadoensis*Hochst is an herbaceous plant of the genus *Lippia.* It belongs to the family Verbanaceae, which is composed of 41 genera with approximately 220 species of herbs, shrubs and small trees[1,2,3]. *L. multiflora* is a stout woody, perennial and aromatic shrub mainly distributed throughout tropical Africa, South and Central American countries[4].The distribution range of *L. multiflora* has its major concentrations in Guinea Savannah, Forest Savannah

and Transitional and Coastal Savannah zones. This plant is commonly known as Lippia tea and commercially known as “Gambian Tea Bush” “Bush Tea”,and “Healer Herb” [5]. *L. multiflora* has been used in many traditional and herbal medicines to treat bronchial inflammation, malaria fever, conjunctivitis, gastro-intestinal disturbances, enteritis, coughs and colds[4], and possesses hypotensive, fatigue relieving, and diuretic properties[6]. Some rural dwellers cook the herbs and use it to relieve stress and enhance sleep [7]. The tea is also used traditionally against hypertension, conjunctivitis, treating venereal diseases and as a laxative [5]. Although, many scientific works had been conducted to investigate its pharmacological properties, there is no report concerning the effect of L. multiflora against liver injuries.

People in West and central African communities have used savannah tea like drinker for your aroma. The leaves of savannahteaare generally consumed in the form of hot drink. Through its values and commercialization in Côte d’Ivoire[8],the use of*L. multiflora* is drunk from rural and urban areas.

Herbal medicinal products play an important role in the management of liver diseases for the lack of satisfactory liver protective drugs in allopathic medical practices. Searching for hepatoprotective drugs with high efficacy and safety is of great need. In regard of the popular consumption of L. multiflora as a tea, the present work aimed to study the pharmacological properties of the aqueous extract of *Lippia multiflora* (L.M.) during liver damages induced with ethanol in rats. For this purpose some liver biochemical markers, hematological parameters and histopathological examination were investigated.

2-MATERIALS AND METHODS

2-1-Extraction methodology

The leaves were air-dried in shade and powdered with a mechanical grinder to obtain a coarse powder. One hundred (100g) powdered leaves of *L. multiflora* are boiled in 1L distilled water *for 15-20 min*. The aqueous extract was filtered through Whatmann filter and dried with a vacuum evaporator below 40 ^{0}C[9].

2-2-Administration of the treatment

Thirty-wistar rats were randomly distributed into six groups of five animals each. Group I served as the control and received only distilled water. Group 2 received only ethanol 15% (3ml/100g/day p.o). Group 3 served as standard group and received silymarine (70mg/kg p.o). Group 4, 5 and 6 served as extract treatment group and received 100,300 and 900 mg/kg aqueous extract of *L. multiflora*. Ethanol 15% (3ml/100g/day p.o) was administered 1h after treatment in group 3, 4, 5 and 6. Animals received daily doses for 28 days and were observed daily for psychomotor changes and other signs of toxicity including death throughout the period of study.

All the experimental procedures were approved by the Ethical Committee of Health Sciences, Felix Houphouet-Boigny University of Abidjan. These guidelines were in accordance with the European Council Legislation 87/607/EEC for the protection of experimental animals.

Body weights of rats in all groups weremeasured at the beginning, the day 7, day 14, day 21 and the end (day 28) of the experimentation. In addition, the weight gains were calculated using theses equations:

Weight gain (g) at day 7 = weight at day 7 - initial weight (day 0)
Weight gain (g) at day 14 = weight at day 14 - initial weight (day 7)
Weight gain (g) at day 14 = weight at day 14 - initial weight (day 7)
Weight gain (g) at day 28 = weight at day 28 - initial weight (day 14)

While the body weight changes (%) were calculated using the following equation:
Body weight change (%) = ((final bw - initial bw) / initial b w) x100.

2-3-Biochemical estimation

At the day 7, 14, 21 and 28 of experimental period, blood samples were collected from retroorbital venous plexus in nonheparinized tubes, centrifuged at 4,000 rpm for 10 min, and blood sera were collected and stored at 4^{o}C prior immediate determination of enzymatic parameters (ALT, AST, GGT) and substrates parameters (CRP and TG). All of these parameters were measured using Chemistry Analyser (SFRI BSA-300).

2-4-Hematological studies

At the end of the study (Day 28),blood samples from the experimental animals were collected in ethylene diamine tetra-acetic acid (EDTA) coated sample bottles for haematological analysis by the assessment of the number of red blood cells (RBCs), white blood cells (WBCs),and platelets, mean cell volume (MCV), according to standard methods using a Blood Counter (Urit Coulter).

2-5-Histopathological examination

Rats were sacrificed by cervical dislocation and liver was separated, washed in ringer's solution and soaked in filter paper. Immediately the liver was stored at –20°C and used later for histopathological studies. The hepatoprotective activity was confirmed through histopathological studies on liver of rats. For light microscopic examination, liver tissues from each group were fixed with 10% buffered formalin, embedded with paraffin. After routine processing, paraffin sections of each tissue were cut into 4 µm thickness and stained withhaematoxylin and eosin, and were observed with a light microscope [10].

2-6-Statistical analysis

All the data were expressed as mean±S.E.M and analyzed statistically using ANOVA followed by Tukey's Multiple Comparison. A value of $P<0.05$was considered significant.

3-RESULTS

3-1-Effects of treatmenton enzymatic parameters

Table 1shows serum ALT activities in rats treated at day 7, 14, 21, 28. The levels of ALT were significantly ($P<0.05$) elevate in ethanol group compared to the control group indicating induction of severe liver damage. Thereis not significant different enter ALT level of *L. multiflora* (100 and 300 g/kgb.w.) group and ethanol group at day 7. Differences occur the following two weeks.Otherwise,there were no significant changes in ethanol group compared to *L. multiflora* at dose of100 g/kg b.w. at day 28. Administration of *L. multiflora*(900 g/kg) and silymarin significantly ($P<0.05$) repressed hepatotoxicity induced by ethanol by reducing the levels of ALT during the fourth week.

Table 1: ALT activities in control and treated rats

GROUPS	ALT (UI/L)			
	DAY 7	DAY 14	DAY 21	DAY 28
Control	59,40±1,030^{a}	60,60±1,077^{a}	61,60±1,691^{a}	61,60±1,288^{a}
15% ethanol	124,5±1,708^{f}	127±0,9129^{f}	131,3±0,75^{f}	144±1,155^{f}
15% ethanol + Silymarin 70 mg/kg	96±1,414^{bc}	79±1,871^{b}	76,67±0,8819^{b}	75±1,732^{b}
15% ethanol + *L. multiflora* 100mg/kg	117±1,472^{def}	104,3±3,301^{de}	101,5±2,327^{e}	100±1,202^{e}
15% ethanol + *L. multiflora 3*00mg/kg	122±1,414^{ef}	104,8±1,315^{e}	93,75±1,250^{de}	90±2,082^{cd}
15% ethanol + *L. multiflora 9*00mg/kg	96,75±6,263^{c}	94,75±6,290^{cde}	93±6,042^{cde}	90±2,646^{d}

The values of ALT levels are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different ($P < 0.05$).
ALT=Alanine aminotransferase. S.E.: Standard error

Table 2 shows that, there was a significant elevation in the levels of serum AST content of ethanol intoxicated animals compared to the control group.However, pretreatment with *L. multiflora*(300 and 900 g/kg mg/kg, b.w.) and silymarin (70 mg/kg, b.w.) exhibited an ability to counteract the hepatotoxicity by decreasing serum AST.

Table 2: AST activities in control and treated rats

GROUPS	AST (UI/L)			
	DAY 7	DAY 14	DAY 21	DAY 28
Control	143±3,072[a]	143,6±2,909[a]	146±2,72[a]	145,8±3,262[a]
15% ethanol	251,8±3,816[cd]	297±6,868[f]	350,3±19,76[f]	381±6,658[f]
15% ethanol + Silymarin 70 mg/kg	228±0,7071[b]	217,4±7,414[b]	185±1,581[bc]	176,5±0,6455[b]
15% ethanol + *L. multiflora* 100mg/kg	305,7±1,764[f]	291,3±1,667[ef]	248,7±2,667[e]	237,7±3,180[e]
15% ethanol + *L. multiflora 3*00mg/kg	296,3±4,404[ef]	265,5±3,969[de]	236,5±2,630[de]	210±3,180[d]
15% ethanol + *L. multiflora 9*00mg/kg	262,8±3,184[d]	246±4,037[cd]	187,6±2,839[c]	207,2±5,190[cd]

The values of AST levels are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different ($P < 0.05$).
ALT=Aspartate aminotransferase. S.E.: Standard error.

Table 3 demonstrates that pretreatment with *L. multiflora* (at the doses of 300 and 900 g/kgb.w.) and silymarin (70 mg/kg, b.w.)hadproduced a highly significant increase in serum GGT activity compared to control group during 28 days.
Also, table 3 shows that, in the same groups receiving *L. multiflora* at the doses of 300 and 900 g/kg b.w. and silymarin (70 mg/kg, b.w.), these treatmentssignificantlyattenuated the elevation of serum GGT activity levels compared to ethanol group.On the other hand, no significant changeswere observed enter *L. multiflora* (100 g/kg b.w.) group and ethanol group.

Table 3: GGT activities in control and treated rats

GROUPS	GGT (UI/L)			
	DAY 7	DAY 14	DAY 21	DAY 28
Control	258,40±1,503[a]	258,60±1,030[a]	260±1,703[a]	263,80±2,083[a]
15% ethanol	368±2,16[f]	276±1,934[f]	284±2,677[f]	313,5±7,467[f]
15% ethanol + Silymarin 70mg/kg	277,8±1,744[b]	295,8±1,934[b]	310±5,666[b]	317,4±5,297[b]
15% ethanol + *L. multiflora* 100mg/kg	349,7±3,80[e]	362,7±4,055[ef]	377±1,155[ef]	388,3±4,10[e]
15% ethanol + *L. multiflora 3*00mg/kg	335±1,652[d]	344±2,273[d]	360,3±2,780[de]	375,5±2,102[de]
15% ethanol + *L. multiflora 9*00mg/kg	303,6±4,490[c]	318,6±4,632[c]	343,6±2,731[c]	354±1,393[c]

The values of GGT levels are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different ($P < 0.05$).
GGT = L-Gamma-glutamyltransferase. S.E.: Standard error mean

3-2-Effects of treatment on biochemical substrates

Table 4 shows that the treatments with different doses of *L. multiflora*had not significantly affected level ofTG of rats serumexceptfor day 14. At this day, there was a significant loweringof TG betweensilymarin (70 mg/kg, b.w.) groupscompared to ethanol group.

Table 4:TG levels in control and treated rats

GROUPS	TG (g/L)			
	DAY 7	DAY 14	DAY 21	DAY 28
Control	0,854±0,09315[a]	0,9240±0,05591[a]	0,8950±0,1024[a]	0,98±0,09[a]
15% ethanol	0,82±0,05132[a]	0,143±0,1419[a]	0,9±0,15[a]	1,230±0,14[a]
15% ethanol + Silymarin 70 mg/kg	0,752±0,08387[a]	0,7840±0,09511[a]	0,8060±0,09584[a]	1,135±0,1384[a]
15% ethanol + *L. multiflora* 100mg/kg	0,82±0,04[a]	1,355±0,055[ab]	1,06±0,01[a]	0,6±0,04[a]
15% ethanol + *L. multiflora 3*00mg/kg	0,7675±0,08910[a]	0,9325±0,1574[ab]	0,8933±0,08876[a]	1;030±0,2702[a]
15% ethanol + *L. multiflora 9*00mg/kg	0,9720±0,2409[a]	1,004±0,07737[b]	0,7825±0,6060[a]	0,81±1,223[a]

The values of TG levels are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different ($P < 0.05$).
TG = Triglycerides. S.E.: Standard error

In table 5, treatment of rats with *L. multiflora* (at the doses of 300 and 900 g/kgb.w.) and silymarin (70 mg/kg, b.w.) did not produce significant changes in serum levels of CRP ($P < 0.05$) compared with non-treated control animals. Moreover, there was a significant difference between *L. multiflora* (100 g/kgp.o.) treated group, for serum CRP levels, compared to positive control at day 28 ($P < 0.05$).

Table 5:CRP levels in control and treated rats

GROUPS	CRP (UI/L)	
	DAY 14	DAY 28
Control	0[a]	0[a]
15% ethanol	10,50±2,021[b]	12,25±1,750[c]
15% ethanol + Silymarin 70 mg/kg	0[a]	0[a]
15% ethanol +*L. multiflora* 100mg/kg	8,75±1,750[b]	7±0[b]
15% ethanol +*L. multiflora 3*00mg/kg	0[a]	0[a]
15% ethanol + *L. multiflora 9*00mg/kg	0[a]	0[a]

The values of CRP levels are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different ($P < 0.05$).
CRP= C ReactiveProtein.S.E.: Standard error

3-3-Hematological study

These observations were confirmed byincreased RBCs and platelets counts. However, a significant ($P< 0.05$) reduction in WBCs and MCV value were recorded in *L. multiflora* (900 g/kg) and silymarin-treated rats compared toethanol 15% group (Table 6).

Table 6:Some Hematological indices of rats at day28

GROUPS	SOME HEMATOLOGICAL PARAMETERS			
	RBC	WBC	PLATELET	MCV
Control	6,733±0,04807^{f}	6,4±0,6658^{a}	891±36,04^{e}	72,43±0,7219^{bcd}
15% ethanol	3,917±0,2489^{a}	15,97±0,5783^{d}	303±26,31^{a}	77,15±6,658^{e}
15% ethanol + Silymarin 70 mg/kg	6,460±0,1222^{ef}	6,333±0,2333^{a}	776,7±33,41^{de}	67,45±0,3617^{a}
15% ethanol + *L. multiflora* 100mg/kg	5,147±0,03180^{bc}	12,4±0,3786^{c}	450,3±35,69^{a}	75,75±1,65^{de}
15% ethanol + *L. multiflora 3*00mg/kg	5,303±0,1027^{cd}	9,067±0,2166^{b}	622,3±25,89^{bc}	73,15±0,85^{cde}
15% ethanol + *L. multiflora 9*00mg/kg	5,827±0,4667^{d}	7,225±0,08539^{a}	726±27,62^{dc}	69,05±0,05^{abc}

The values of hematological parameter are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different ($P < 0.05$).
RBC=Red Cell Count, WBC=White Blood Cell, MCV= Mean Cell Volume. S.E.: Standard error.

3-4-Body weight and liverweightstudy

The results of this study are shown in table (7,8 and 9). Compared to control (or normal group), all groups are not showed significantly different in rats body weight changes ($P< 0.05$), and in both absolute liver weight and relative liver weight. Except, the day 14, which ethanol group showed an increase, on the one hand, in rats body weight changes (6,16%±4,359^{b}) compared to normal group (1,01%±3,742^{a}),on the other hand , in weight liver (6,910±1,002^{b}) compared to normal group (3,96±0,1867^{a}).

Table 7: Effect of treatmenton weight variation of ethanol induced hepatotoxicity in rats.

GROUPS	WEIGHT (g)				
	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28
Control	117±5,385^{a}	118,6±4,523^{a}	118,6±4,915^{a}	124±4,103^{a}	126±6,110^{a}
15% ethanol	148,6±2,804^{a}	146±3,559^{d}	141,7±4,410^{bcd}	136,7±2,404^{ab}	135,3±1,453^{ab}
15% ethanol + Sylimarin 70 mg/kg	140±5,553^{a}	141,8±4,055^{bd}	142,8±5,093^{cd}	143±4,889^{ab}	143,2±7,490^{ab}
15% ethanol + *L. multiflora* 100mg/kg	132,3±2,417^{a}	132,3±3,180^{ad}	130,7±2,849^{ad}	128,7±3,333^{ab}	127±3,512^{a}
15% ethanol + *L. multiflora 3*00mg/kg	128,8±9,595^{a}	129,3±8,667^{ad}	131±2,933^{ad}	138,8±8,430^{ab}	139±13,08^{ab}
15% ethanol + *L. multiflora 9*00mg/kg	140,8±5,963^{a}	143,3±6,149^{cd}	147,2±4,954^{d}	149,6±4,895^{b}	154,6±3,326^{b}

The values of weight are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different ($P < 0.05$). S.E.: Standard error

Table 8: Effect of treatment on weight gain

GROUPS	Body weight change (%)

	Day 7 (week 1)	Day 14 (week 2)	Day 21 (week 3)	Day 28 (week 4)
Control	1,7±0,8367[a]	1,01±3,742[a]	1,26±0,2887[a]	4,667±1,856[a]
15% ethanol	3,03±1,443[a]	6,16±4,359[b]	3,53±2,517[a]	2,000±0,5774[a]
15% ethanol + Sylimarin 70 mg/kg	4,57±3,326[a]	1,27±0,9165[ab]	0,98±0,4000[a]	0,2000±0,2000[a]
15% ethanol + *L. multiflora* 100mg/kg	3,02±3,000[a]	1,007±0,333[ab]	1,78±0,3334[a]	1,000±0,5774[a]
15% ethanol + *L. multiflora 3*00mg/kg	4,66±2,082[a]	5,93±1,856[ab]	3,05±2,646[a]	6,33±1,764[a]
15% ethanol + *L. multiflora 9*00mg/kg	1,98±0,9595[a]	1,35±1,023[ab]	1,63±0,5099[a]	4,393±1,965[a]

The values of body weight change are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different (P< 0.05). S.E.: Standard error.

Table 9: Effect of treatmenton liver weight variation of ethanol induced hepatotoxicity in rats.

GROUPS	LIVER	
	WEIGHT	RELATIVE WEIGHT (%)
Control	3,96±0,1867[a]	3,100±0,2858[a]
15% ethanol	6,910±1,002[b]	5,120±0,7802[a]
15% ethanol + Silymarin 70 mg/kg	5,428±0,4374[ab]	3,810±0,3316[a]
15% ethanol + *L. multiflora* 100mg/kg	6,313±0,2567[ab]	4,980±0,2919[a]
15% ethanol + *L. multiflora 3*00mg/kg	5,545±0,7642[ab]	4,537±0,8952[a]
15% ethanol + *L. multiflora 9*00mg/kg	5,5±0,7151[ab]	3,508±0,3978[a]

The values of liver weight are expressed as Mean ± S.E. for five rats (n=5). In the same column values, the same letters are not significantly different (P< 0.05). S.E.: Standard error

3-5-Histopathological study

Histopathological examinations of the liver sections were carried out to further confirm the extent of the liver damage (Fig.1). However, no visible lesion was seen in the liver sections of the control group (Fig.1 A) while there was severe central venous and portal congestion as well as portal fibroplasias in the liver section of 15% ethanol treated rats(Fig.1 B). Normal hepatic parenchymal architecture with mild dilatation and congestion of the central vein and blood sinusoids was observed in 15% ethanol+ silymarin (70 mg/kg, B.W.) treatedrats(Fig. 1 C).On the other hand, diffuse hydropic degeneration and cellular infiltration by mononuclear cells was observed in liver section of 15% ethanol + *L. multiflora*extract 100 mg/kg treated rats (Fig.1 D). Thenormal hepatic architecture withdilated congested portal venules in the periportalwas less seenin 15% ethanol + *L. multiflora*extract 300 mg/kg(Fig.1E) than in 15% ethanol + *L. multiflora*extract900 mg/kg(Fig.1F) treated rats liver section.

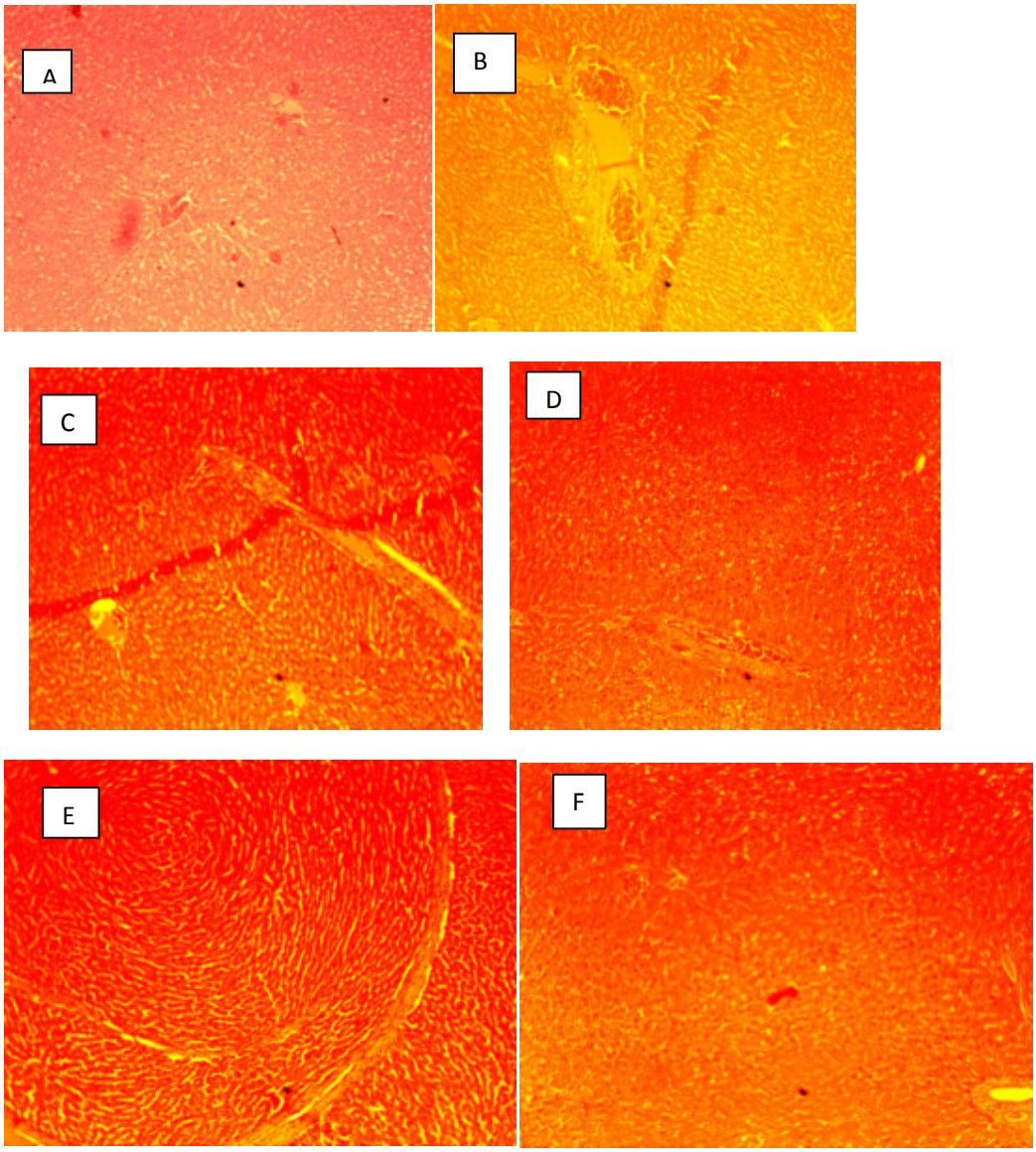

Figure 1: Representative of histological assessment of rat liver sections after 28 days of treatments. (A) Control, (B) ethanol, (C) ethanol + Silymarin70 mg/kg, (D) ethanol + *L. multiflora*100 mg/kg, (E) ethanol + *L. multiflora* 300 mg/kg, (F) ethanol + *L. multiflora* 900 mg/kg (x100).

DISCUSSION

Consumption of alcohol affects the liver and other organs and could contribute to the development of alcohol liver disease[11]. The elevation observed in serum levels of ALT and AST is an indication of the degree of the liver damages caused by ethanol [12, 13].The increase of ALT, AST and GGT in ethanol group reflects a cellular lesion, in particular at the hepatic level and certain cardiac cell [14, 15].Clinically, measurements of serum ALT, AST and GGT are widely used as markers in evaluating the degree of liver injury. ALT is the more specific measure of alcohol-induced liver injury because it is found predominantly in the liver, whereas AST is found in several organs, including the liver, heart, muscle, kidney, and brain [16].The reduction in the levels of ALT and AST by *L. multiflora* extracts at a dose of 300 or 900 mg/kg B.W. (a day 7, 14,21 and 28), during liver damages induced by ethanol, suggests that the extract was not toxic or damaging to the integrity of the liver but possibly hepatoprotective.

Worthy of note is the fact that ethanol administration led to a significant increase in the level of serum GGT, which was markedly reduced by the dose of silymarin and *L. multiflora* extract (300 or 900

mg/kg b.w.).Wang *et al*.[17] has suggested that*L. Multiflora*is one of themost widely consumed beverages in the world and more attention is paid toits health benefits effects notably in the prevention of cancer and cardiovascular diseases.Our work indicates that the beverage of *L. multiflora* may also protect liver from injuries, particularly those generated by ethanolconsumption.

The analysis of TG did not vary significantly. However, a significant increase CRP was able to be noticed in ethanol group indicating the inflammatory process in initiated by ethanol. The results also show that the inflammation is lowered by *L. multiflora* (300 and 900 mg/kg) as well as silymarin.

Effect of silymarin and*L. multiflora* extract (300 or 900 mg/kg b.w.)on blood parameterswas demonstrated by the significant reduction in WBC platelets counts and MCV compared to ethanol group.This result confirms MCV and GGT are important in the biological screening of the alcoholization[18].

As we mentioned before, we evaluated body weight gain,absolute and relative liver weights ratio of the laboratory rats. In general, obtained datashowed that the rats of all group haven't seen a significantly different in thebody weight gain and in both absolute and relative liver weight dosedependent, compared tonormal group of rats. Except,the day 14, whereethanol group is showed anincrease in both body weight gain and liver weight, compared to normal group.We found that ethanol treatment induced significant hepatic histopathological injuries. The increase ($p < 0.05$) in liver weight of the alcohol-treated rats can be due to theaccumulation of fats and water causing hepatocytic hypertrophy[19,20]**.**

In the present study, we used an animal model to reveal the protective role of *L. multifora* against ethanol-induced hepatic toxicity. The protection of liver by *L. multiflora* was detected by diagnostic indicators of liver damage (AST, GGT and ALT levels), and by histopathological analyses. The protection by *L. multiflora* in this study was reflected by the reductionhistological lesions both by weight gain and by liver weight.

CONCLUSION

Lippia multiflora was used in traditional middle to ill much pathology.The results showed that *L. multifora* aqueous extract couldameliorate hepatic damage caused by ethanol exposure in rat models.

ETHICAL APPROVAL

All authors hereby declare that all manipulations of animals were approved by the Ethical Committee of Health Sciences, Felix Houphouet-Boigny University of Abidjan. Moreover, all procedures used in animal experimentation complied with the European Council Legislation 87/607/EEC for the protection of experimental animals. All efforts were made to minimize the number of animals used and theirsuffering, and the study met the ethical standards of Chronobiology International.

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