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Effects of *Sarcocephalus latifolius* Fruits Extract on Paracetamol-Induced Liver Damage in Wistar Rats

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Abstract

Background and Aim: *Sarcocephalus latifolius* is a medicinal plant commonly used in traditional medicine to treat various diseases. The aim of the present study is to evaluate the hepatoprotective activity of *Sarcocephalus latifolius* fruits aqueous extract against paracetamol-induced liver damage in rats. **Material and Methods:** Aqueous extract of *Sarcocephalus latifolius* fruits at doses of 100, 250 and 500 mg/kg were administered orally to rats with paracetamol-induced hepatotoxicity (1 g/kg). The treatment with the extract and paracetamol lasted 7 days. *Silymarin* (50 mg/kg) was given as reference control. All tested drugs were administered orally. **Results:** Our results show that the *Sarcocephalus latifolius* fruits extract induced a significant reduction ($p < 0.05$) of serum enzymes alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), alkaline phosphatase (PAL) and total bilirubin (TB). Then, the extract at the dose of 500 mg/kg showed a better protection ($p < 0.001$) of hepatocytes with a percentage of protection of 43.59% ± 2.03%; 59.43% ± 4.12%; 73.29% ± 5.72% and 62.55% ± 7.48% for ALAT, ASAT, PAL and TB, respectively. The histology of livers exposed to paracetamol shows an inflammation of the hepatocytes. In addition, there was a significant alteration of the liver parenchyma. The 500 mg/kg extract showed a resorption of the inflammation. Histopathological examination showed that the extract regenerated paracetamol-induced liver damage. **Conclusion:** Aqueous extract of *Sarcocephalus latifolius* fruits has hepatoprotective activity against paracetamol-induced hepatotoxicity in rats. But it would be important to evaluate the activity of aqueous extract of *Sarcocephalus latifolius*

fruits on oxidative stress parameters *in vivo* in rats.

Keywords

Rats, Paracetamol, Hepatotoxicity, *Sarcocephalus latifolius*, *Silymarin*

1. Introduction

The liver is an auxiliary organ of the digestive tract. It fulfills many functions that are essential to life. It participates in the process of digestion through biliary secretion. All substances introduced into the body reach the bloodstream to be transformed before being excreted. Thus, the liver is exposed to various aggressions which sometimes have serious damages on the organism. It has been estimated in recent reports that 10% of world population is affected with liver diseases including hepatitis. Morbidity and mortality resulting from liver diseases is a major public health problem worldwide [1].

Drug-induced hepatitis is manifested by inflammatory processes. These data show that liver disease is a public health problem in the world. It is important that some to improve the prevention and treatment of liver disease through scientific research. The availability of a varied plants repertoire with hepatotropic action in the traditional medicine of Burkina Faso [2] and the hepatic damage linked to Paracetamol exposure motivated this study. *Sarcocephalus latifolius* is a medicinal plant whose different parts are used to treat various diseases in Burkina Faso. The fruits are edible and remain an excellent source of nutrients in vitamins, minerals as well as carbohydrates [3]. Likewise, fruit of *Sarcocephalus latifolius* is used in traditional medicine for the treatment of many diseases [4]. These roots and fruits are used to treat liver disease and jaundice [5]. The objective of the study was to evaluate the hepatoprotective activity of the aqueous extract of the fruits of *Sarcocephalus latifolius* on paracetamol-induced hepatotoxicity in rats.

2. Materiel and Methods

2.1. Plant Collection

The fruits of the *Sarcocephalus latifolius* plant were collected in the South West region of Burkina Faso. A specimen (18,028) was deposited in the Herbarium of the Département de Botanique de l'Université Joseph KI ZERBO, Ouagadougou (Burkina Faso). The collected fruits were washed with water, cut into small parts and dried in the shade without dust for a week and pulverized.

2.2. Plant Extraction

These dried fruits were pulverized and 400 g of this powder were macerated in 1000 ml of distilled water for 24 hours. The filtrate was centrifuged at 2000 rpm for 10 min. The supernatant was frozen at −23˚C and lyophilized. Aqueous ex-

tract of *Sarcocephalus latifolius* fruits (EASL) obtained, was stored at −4˚C. The extraction yield was 24.23%.

2.3. Experimental Animals

Thirty male Wistar rats weighing between 150 and 200 g were randomized into six groups of five rats. Rats were maintained under standard laboratory conditions (temperature: 22˚C ± 3˚C, relative humidity: 50% ± 10% and light/dark cycle: 12/24h). Food pellets and water were provided *ad libitum*. The animals were used in accordance with the local ethic committee of Université Joseph KI-ZERBO.

2.4. Paracetamol-Induced Hepatotoxicity in Rat

Rats were randomized into six groups of rats including five rats for each group. The treatments were achieved according to the experiment design described by [6] [7]:

Group I (Vehicle): Rats received 0.9% NaCl solution at 0.5 mL/rat with normal diet.

Group II (Negative control): Rats received paracetamol at 1 g/kg bw (*p.o.*)

Group III (Positive control): Rats received *Silymarin* at 50 mg/kg bw (*p.o.*)

Group IV: Rats received paracetamol 1 g/kg bw, (*p.o.*) and aqueous extract of *Sarcocephalus latifolius* fruit 100 mg/kg bw (*p.o.*)

Group V: Rats received paracetamol 1 g/kg bw, (*p.o.*) and aqueous extract of *Sarcocephalus latifolius* fruit 250 mg/kg bw (*p.o.*)

Group VI: Rats received paracetamol 1 g/kg bw, (*p.o.*) and aqueous extract of *Sarcocephalus latifolius* fruit 500 mg/kg bw (*p.o.*)

2.5. Biochemical and Histopathology Studies

On day 8, rats were anesthetized with ether, sacrificed, and blood was collected centrifuged at 3000 rpm during 15 minutes for serum separation. Serum was stored at −20˚C until biochemical studies. The change in aspartate amino transferase (ASAT), alanine amino transferase (ALAT), alkaline phosphatase (PAL), and total bilirubin (TB) levels were measured for biochemical investigations. Atlas diagnostic product kits were used for these investigations.

Then animals were sacrified and livers were removed weighed. The liver samples were washed with saline, fixed in 70% ethanol and were processed for paraffin embedding following the microtome technique. The sections were taken at 5 µm thickness processed in alcohol-xylene series and were stained with alum-haematoxylin and eosin. The sections were examined microscopically for the evaluation of histopathological changes.

2.6. Statistical Analysis

Results were expressed as Mean ± SEM, (n = 5). Statistical analyses were performed with one-way analysis of variance (ANOVA I) followed by Tukey's multiple comparison test by using Graph Pad Prism Software. $P < 0.05$ was considered to be statistically significant.

3. Results and Discussion

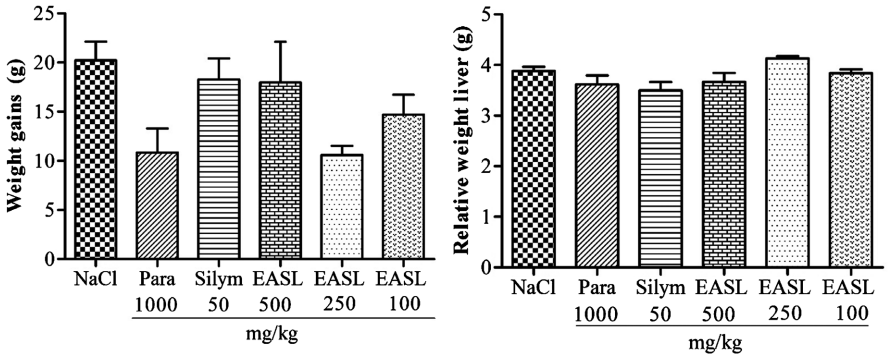
3.1. Results

3.1.1. Effect of Aqueous Extract of *Sarcocephalus latifolius* Fruit on the Body Weight Gain and Liver Weight in Paracetamol-Induced Hepatotoxicity in Rats

Extract caused a non-significant ($p > 0.05$) weight gain in the rats compared to the negative control. The extract did not cause a significant ($p > 0.05$) change in liver weight compared to the control (Figure 1).

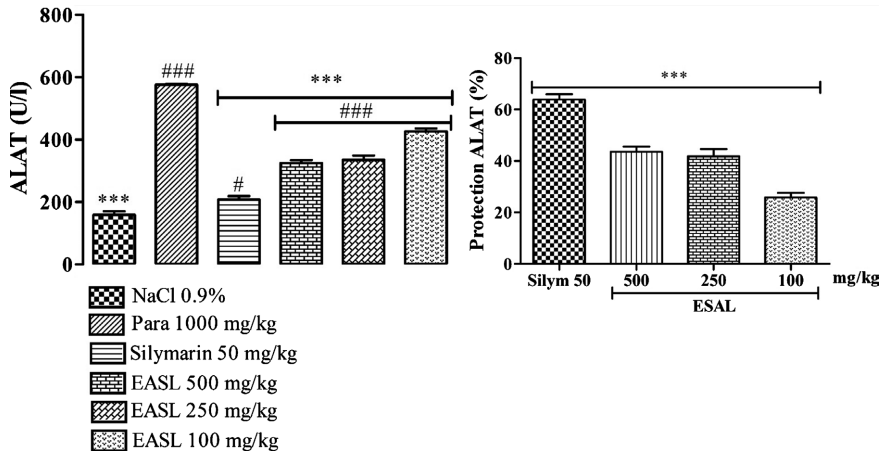
3.1.2. Effect of Aqueous Extract of *Sarcocephalus latifolius* Fruit on Transaminases Levels in Paracetamol-Induced Hepatotoxicity in Rats

The extract at all doses significantly ($p < 0.05$) decreased ALAT level compared to the negative control. Extract at the dose of 500 mg/kg had the best percentage protection against paracetamol-induced hepatotoxicity. It was about 44% (Figure 2).



Key: Para: Paracetamol; Silym: Silymarin.

Figure 1. Effect of aqueous extract of *Sarcocephalus latifolius* fruit on the body weight gain and liver weight in paracetamol-induced hepatotoxicity in rats.



Key: Para: Paracetamol; Silym: Silymarin. #: Comparison of the different groups with the neutral control (NaCl 0.9%). *: Comparison of the different groups with the negative control (Para 1000 mg/kg).

Figure 2. Effect of aqueous extract of *Sarcocephalus latifolius* fruit on ALAT level in paracetamol-induced hepatotoxicity in rats.

Paracetamol induced a significant ($p < 0.05$) increase in ASAT levels compared to neutral control. Extract at all doses induced a significant decrease in the level of this enzyme compared to the negative control. Extract 500 mg/kg showed a better percentage of hepatocyte protection (Figure 3).

3.1.3. Effect of Aqueous Extract of *Sarcocephalus latifolius* Fruit on Total Bilirubin Level in Paracetamol-Induced Hepatotoxicity in Rats

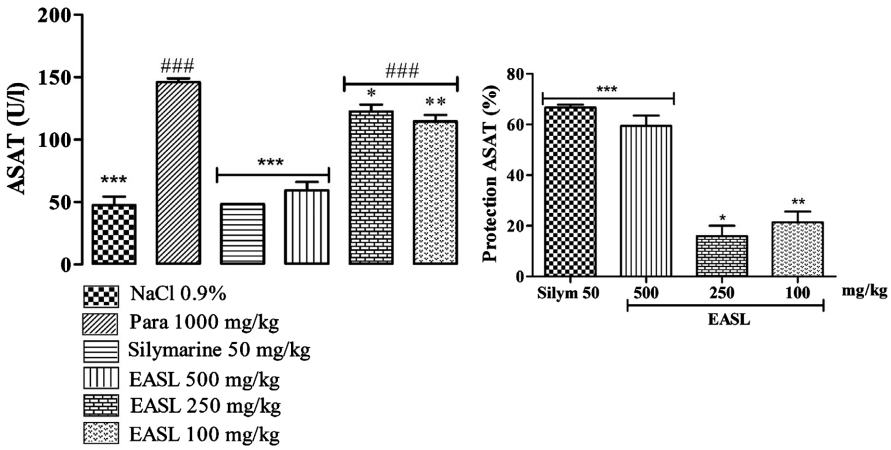
Paracetamol induced a significant ($p < 0.001$) increase in total bilirubin levels compared to the neutral control. Extract at all doses induced a significant ($p < 0.001$) decrease in bilirubin level compared to the negative control. The extract protected liver cells at 45%; 40% and 63% for the doses of 100, 250 and 500 mg/kg, respectively (Figure 4).

3.1.4. Effect of Aqueous Extract of *Sarcocephalus latifolius* Fruit on Alkaline Phosphatase Level in Paracetamol-Induced Hepatotoxicity in Rats

Paracetamol induced a significant ($p < 0.001$) increase in alkaline phosphatase levels compared to the neutral control. Extract at all doses induced a significant ($p < 0.001$) decrease in alkaline phosphatase level compared to the negative control. The extract protected liver cells at 66%, 70% and 73% for the doses of 100, 250 and 500 mg/kg, respectively (Figure 5).

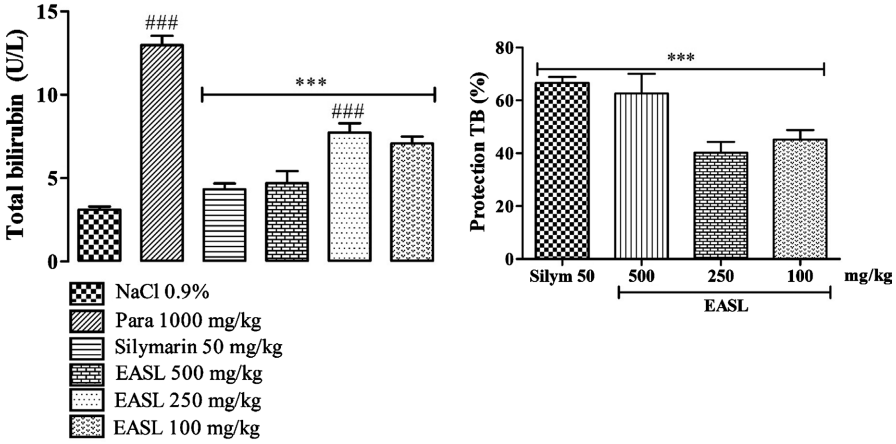
3.1.5. Histopathological Evaluation of the Effect of *Sarcocephalus latifolius* and Vehicles Groups in Paracetamol-Induced Hepatic Injury in Rats

Histopathological profiles showed a hepatoprotective activity of the aqueous extract of *Sarcocephalus latifolius* fruits at all doses. However, animals only treated with paracetamol showed hepatocellular and centrilobular necrosis. This necrosis was accompanied by leukocyte infiltration in the liver. There were also



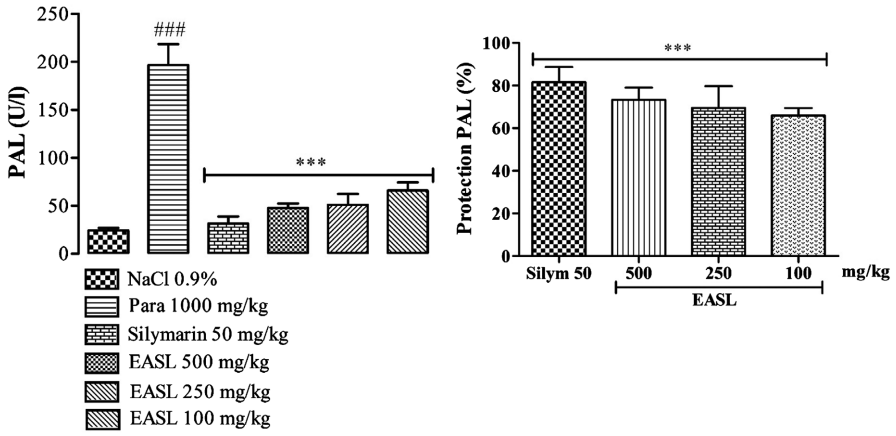
Key: Para: Paracetamol; Silym: Silymarin. #: Comparison of the different groups with the neutral control (NaCl 0.9%). *: Comparison of the different groups with the negative control (Para 1000 mg/kg).

Figure 3. Effect of aqueous extract of *Sarcocephalus latifolius* fruit on ASAT level in paracetamol-induced hepatotoxicity in rats.



Key: Para: Paracetamol; Silym: Silymarin. #: Comparison of the different groups with the neutral control (NaCl 0.9%). *: Comparison of the different groups with the negative control (Para 1000 mg/kg).

Figure 4. Effect of aqueous extract of *Sarcocephalus latifolius* fruit on total bilirubin level in paracetamol-induced hepatotoxicity in rats.



Key: Para: Paracetamol; Silym: Silymarin. #: Comparison of the different groups with the neutral control (NaCl 0.9%). *: Comparison of the different groups with the negative control (Para 1000 mg/kg).

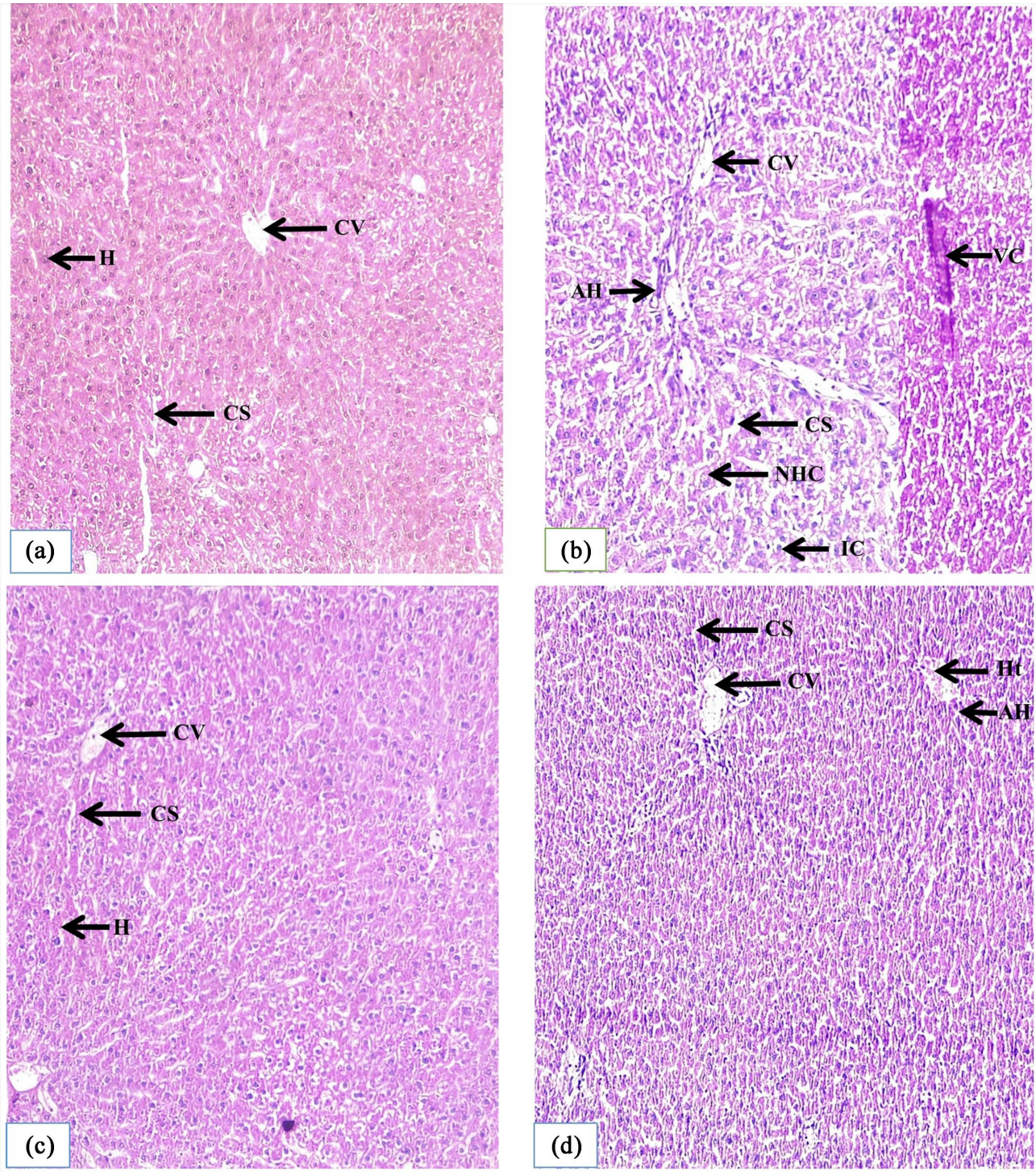
Figure 5. Effect of aqueous extract of *Sarcocephalus latifolius* fruit on alkaline phosphatase level in paracetamol-induced hepatotoxicity in rats.

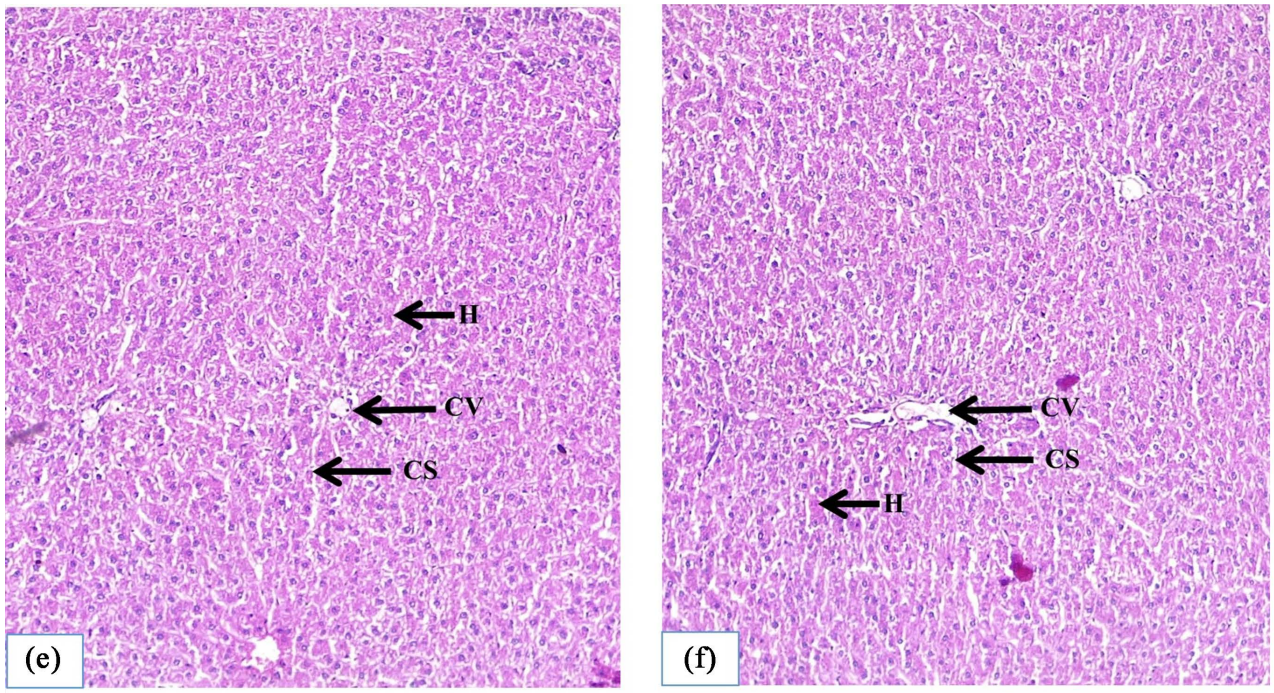
vascular congestion leading to destruction of the sinusoidal canaliculi and hepatic arteries. The inflammation of the hepatocytes was less severe or even reduced in the groups treated with the 500 mg/kg extract, as well as in the groups treated with *Silymarin* 50 mg/kg (**Figure 6**).

3.2. Discussion

Paracetamol is sometimes used as an analgesic and antipyretic. When taken in overdose (at least 200 mg/kg), Paracetamol can produce significant hepatotoxic effects [8]. In the liver, there is a protective mechanism involving glutathione in the regression of cellular damage [9]. But when paracetamol is used in high doses, the glutathione level is not sufficient to conjugate N-acetyl-*p*-benzoquinoneimine

(NAPQI). Therefore, NAPQI alkylates the proteins present in the biomembranes of microsomes and mitochondria, producing hepatic necrosis [10] [11] [12]. Therefore, macromolecules such as enzymes will pass from the damaged tissues into the bloodstream [13] and the study of the activity of these enzymes in plasma is very important for the assessment of liver injury [14]. Increased ASAT and ALAT level indicates cellular damage and loss of functional integrity of hepatocytes [15].





Key: CV: central vein; HA: hepatic artery, H: hepatocytes; VC: vascular congestion; CS: sinusoidal canaliculus, NHC: hepatocellular necrosis; IC: inflammation cell, Ht: hematite.

Figure 6. Histopathological evaluation of the effect of *Sarcocephalus latifolius* and vehicles groups in paracetamol-induced hepatic injury in rats (*H & E* × *400*). (a) treated with normal saline; (b) treated with Paracetamol; (c) treated with *Silymarin* 50 mg/kg; (d) treated with aqueous extract of *Sarcocephalus latifolius* fruit (100 mg/kg); (e) treated with aqueous extract of *Sarcocephalus latifolius* fruit (250 mg/kg); (f) treated with aqueous extract of *Sarcocephalus latifolius* fruit (500 mg/kg).

Increased PAL in liver disease reflects pathological alteration of bile flow [16].

The abnormally high serum level of ALAT, ASAT, PAL and total bilirubin observed in the negative control group is a consequence of paracetamol-induced liver dysfunction and indicates liver cell damage. The extract at doses of 100,250, and 500 mg/kg significantly ($p < 0.01$) decreased the activity of ASAT and ALAT compared with the negative control. The increase in serum PAL could be due to its high synthesis following high bile pressure. The extract at all doses showed a highly significant reduction in PAL and bilirubin levels in the test groups. These results were comparable to those of the standard drug, *Silymarin*. The extract appears to offer protection and maintain liver cell function. Extract of *Sarcocephalus latifolius* fruits possesses flavonoids and tannins recognized for their hepatoprotective action. Saponins, alkaloids, flavonoids, phytates and triterpenoids are phytochemical constituents of *Sarcocephalus latifolius* with antioxidant, free radical scavenging and peroxidant inhibition capacity and inhibition of lipid peroxidation. These results are comparable to those of [7] [17] [18] [19]. *Silymarin* isolated from *Silybum marianum* has a protective effect on the plasma membrane of hepatocytes and has multiple inhibitory effects against different hepatotoxic agents. The antioxidant effects and the regenerative functions of *Silymarin* cells involve protein synthesis, which has been considered as the most important actions of *Silymarin*. The hepatoprotective activity observed in the

present study may be due to the protective effect of *Sarcocephalus latifolius* on the plasma membrane of hepatocytes or cells regeneration function similar to that of *Silymarin*. These results are comparable to those [7] [20].

The histopathological results showed that *Sarcocephalus latifolius* extract exhibited good protection on the architecture of the liver. Paracetamol could have an inflammatory effect by inducing the release and action of endogenous pro-inflammatory mediators responsible for the development of inflammation. The aqueous extract of *Sarcocephalus latifolius* fruits could show an anti-inflammatory effect by preventing the release of endogenous pro-inflammatory mediators responsible for inflammation [21]. The extract of *Sarcocephalus latifolius* fruits could block the degradation of arachidonic acid by the cyclooxygenase or lipo-oxygenase pathway. It would thus oppose the production of prostaglandins, thromboxane A_2 and also leukotrienes [22]. This protection was almost to the liver of rats treated with *Silymarin*. These results validate the hepatoprotective effect of the aqueous extract of *Sarcocephalus latifolius* fruits on paracetamol-induiced hepatotoxicity.

4. Conclusion

These results validate the hepatoprotective effect of the aqueous extract of *Sarcocephalus latifolius* fruits on paracetamol-induced hepatotoxicity. By applying the appropriate dose and orally, the aqueous extract of *Sarcocephalus latifolius* fruits constitutes a good hepatoprotective drugs. But it would be important to evaluate the activity of aqueous extract of *Sarcocephalus latifolius* fruits on oxidative stress parameters *in vivo* in rats. Also it would be interesting to isolate the bioactive compounds found in the fruits of *Sarcocephalus latifolius* to confirm its use in traditional medicine.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Zhang, A., Sun, H. and Wang, X. (2013) Recent Advances in Natural Products from Plants for the Treatment of Liver Diseases. *European Journal of Medicinal Chemistry*, **63**, 570-577. https://doi.org/10.1016/j.ejmech.2012.12.062

[2] Nacoulma/Ouédraogo, O.G. (1996) Plantes médicinales et Pratiques médicales Traditionnelles au Burkina Faso: Cas du plateau central T1 & T2. Thèse de l'université Ouaga I Pr Joseph KI-ZERBO, 91-92.

[3] Plassart, L. (2015) *Sarcocephalus latifolius* (Sm.) Bruce: Études botanique, chimique et pharmacologique. Sciences Pharmaceutiques.

[4] Eze, S.O. and Obinwa, E. (2014) Phytochemical and Nutrient Evaluations of the Leaves and Fruits of *Nauclea latifolia* (Uvuru-ilu). *Communications in Applied Sciences*, **2**, 8-24.

[5] Malgras, D. (1992) Arbres et arbustes guérisseurs des savanes maliennes. Ed Karthala, Paris.

[6] Hafez, E.M., Paulis, M.G., Ahmed, M.A., *et al.* (2015) Protective and Anti-Oxidant Activity of the *Euryops arabicus* against Paracetamol Induced Hepatorenal Toxicity in Rats. *Journal of Clinical Toxicology*, **5**, 227. https://doi.org/10.4172/2161-0495.1000227

[7] Ur Rehman, J., Akhtar, N., Khan, M.Y., *et al.* (2015). Phytochemical Screening and Hepatoprotective Effect of *Alhagi maurorum* Boiss (Leguminosae) against Paracetamol-Induced Hepatotoxicity in Rabbits. *Tropical Journal of Pharmaceutical Research*, **14**, 1029-1034. https://doi.org/10.4314/tjpr.v14i6.13

[8] Parmar, S.R., Vashrambhai, P.H. and Kalia, K. (2010) Hepatoprotective Activity of Some Plants Extract against Paracetamol Induced Hepatotoxicity in Rats. *Journal of Herbal Medicine and Toxicology*, **4**, 101-106.

[9] Potter, W.Z., Thorgeirsson, S.S., Jollow D.J. and Mitchell, J.R. (1974) Acetaminophen-Induced Hepatic Necrosis V. Correlation of Hepatic Necrosis, Covalent Binding and Glutathione Depletion in Hamsters. *Pharmacology*, **12**, 129-143. https://doi.org/10.1159/000136531

[10] Aldridge, W.N. (1981) Mechanism of Toxicity: New Concepts Are Required in Toxicology. *Trends in Pharmacological Sciences*, **2**, 228-231. https://doi.org/10.1016/0165-6147(81)90321-7

[11] Tirmenstein, M.A. and Nelson, S.P. (1989) Sub Cellular Binding and Effects on Calcium Homeostasis Produced by Acetaminophen and a Non-Hepatotoxic Regioisomer 3-Hydroxyacetanilide in Mouse Liver. *Journal of Biological Chemistry*, **264**, 9814-9819. https://doi.org/10.1016/S0021-9258(18)81731-8

[12] Vermeulen, N.P.E., Bessems, J.G.M., Van, D.E. and Straat, R. (1992) Molecular Aspects of Paracetamol-Induced Hepatotoxicity and Its Mechanism Based Prevention. *Drug Metabolism Reviews*, **24**, 367-407. https://doi.org/10.3109/03602539208996298

[13] Hearse, D.J. (1979) Cellular Damage during Myocardial Ischaemia: Metabolic Changes Leading to Enzyme Leakage. In: Hearse, D.J., De Leiris, J. and Loisance, D., Eds., *Enzymes in Cardiology*, John Wiley and Sons Ltd., New York, 1-21.

[14] Plaa, G.L. and Zimmerman, H.J. (1997) Evaluation of Hepatotoxicity: Physiological and Biochemical Measures of Hepatic Function. In: McCuskey, R.S. and Earnest, D.L., Eds., *Comprehensive Toxicology*, Vol. 9, Cambridge University Press, Cambridge, 97-109.

[15] Drotman, R.B. and Lowhorn, G.T. (1978) Serum Enzymes as Indicators of Chemical Induced Liver Damage. *Drug and Chemical Toxicology*, **1**, 163-171. https://doi.org/10.3109/01480547809034433

[16] Plaa, G.L. and Hewitt, W.R. (1989) Detection and Evaluation of Chemically Induced Liver Injury. In: Wallace Hayes, A, Ed., *Principles and Methods of Toxicology*, 2nd Edition, Raven Press, New York, 399-428.

[17] Faure, M., Lissi, E., Torres, R. and Vidella, L.A. (1990) Antioxidant Activity of Liginin and Flavonoids. *Phytochem*, **29**, 3773-3775. https://doi.org/10.1016/0031-9422(90)85329-E

[18] Jin, X., Qian, J. and Lu, Y. (2011) The Role of Hepatoprotective Effect of a Flavonoid-Rich Extract of *Salvia plebeia* R.Br. on Carbon Tetrachloride Induced Acute Hepatic Injury in Mice. *Journal of Medicinal Plants Research*, **5**, 1558-1563.

[19] Badiaga, M. (2011) Etude ethnobotanique, phytochimique et activités biologiques de *Nauclea latifolia* Smith une plante medecinale recolté au Mali. Ph.D. Sciences, Université de Bamako, Bamako.

[20] Bagban, I.M., Roy, S.P., Chaudhary, A., Das, S.K., Gohil, K.J. and Bhandari, K.K.

(2012) Hepatoprotective Activity of the Methanolic Extract of *Fagonia indica* Burm in Carbon Tetra Chloride Induced Hepatotoxicity in Albino Rats. *Asian Pacific Journal of Tropical Biomedicine*, **2**, S1457-S1460. https://doi.org/10.1016/S2221-1691(12)60437-7

[21] Gobiannand, K., Vivekanandan, P., Pradeep, C.V., Mohan, R. and Karthikeyan, S. (2010) Anti-Inflammatory and Antipyretic Activities of Indian Medicinal Plant *Cassia fistula* Linn. (Golden Shower) in Albino Wistar Rats. *Journal of Pharmacology*, **6**, 719-725. https://doi.org/10.3923/ijp.2010.719.725

[22] Khalil, N.M., Sperotto, J.S. and Manfron, M.P. (2006) Anti-Inflammatory Activity and Acute Toxicity of *Dodonea viscose*. *Fitoterapia*, **77**, 478-480. https://doi.org/10.1016/j.fitote.2006.06.002