ASSESSMENT OF PROTECTIVE EFFECTS OF POLYPHENOL-RICH FRACTIONS FROM TRICHILIA EMETICA (MELIACEAE) ON SOME INCATORS OF LIVER AND KIDNEYS FUNCTIONS IN EXPERIMENTAL MODEL.

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ABSTRACT
The present study was conducted to evaluate the hepato and nephroprotective effects of polyphenol-rich fractions from Trichilia emetica in rodents. Animals received by gavage 75, 100 and 200 mg/kg body weight of fraction daily for a period of 28 days. Control groups received alcohol 35% and water. In vivo administration of 35% ethanol for a period of 28 days in rats showed an activity of liver marker enzymes (AST, ALT, ALP and GGT), triglycerides, total cholesterol, total bilirubin and direct bilirubin and nephrotoxicity biomarkers (total proteins, serum albumin, urea, uric acid and creatinine) in serum compared with rats which received water (control water). However, administration of 35% ethanol along with bioactive fraction decreased the activities of liver and kidneys biomarkers enzyme in serum (p<0.05 or p<0.01) comparatively to the control water groups. This study revealed that Trichilia emetica presents hepato and nephroprotective potentials and this plant could be exploited in the treatment of liver and kidneys diseases.
1. INTRODUCTION
Liver is the largest internal organ of the human body which is part of the digestive system (Karim et al., 2011). It is involved in detoxification of drugs and food substances, deamination of excess proteins, storage of iron, vitamins and glycogen, production of bile, proteins and vital enzymes in the body. Liver is sometimes damaged due to effects from medications e.g. acetaminophen (Bartlett D., 2004), alcohol abuse (Bykov et al., 2004), hepatotoxins (Appiah et al., 2009), autoimmune hepatitis viral and microbial infections (Ardanaz et al., 2006).

Moreover, liver is a vital organ that functions as metabolic centre for various nutrients such as carbohydrates, proteins and lipids (Barrett et al., 2010). Some reports say that liver takes part in metabolism of drugs, xenobiotics and excretion of their waste metabolites from the body and protects the organs against various toxicicants (Frank et al., 2006).

The kidney is known to be responsible for the maintenance of the constant extracellular environment through its involvement in the excretion of such catabolites as urea, creatinine, uric acid and regulation of water and electrolyte balance. Abnormal concentration of these catabolites and some electrolytes in the plasma or serum therefore serve as a clear indication of renal function impairment (Zanna et al., 2008). Impairment of the renal functions may be caused by several disease conditions and exposure to certain reaction or toxic metabolites, i.e., nephrotoxic substances (Crook, 2007). For instance, certain mixtures of hydrocarbon, gasoline vapours, lead, insecticides, pesticides and other chemical solvents have been reported to pose some degrees of adverse effects on the functional integrity of the renal tissues in humans and experimental animals (Uboh et al., 2011).

As herbal based therapeutic drugs has been popularized worldwide for the treatment of liver disorders by leading pharmaceutical industries and is worthwhile to search safe hepatoprotective agents (Agarwal, 2001). Most of the liver protective plants may contain various biologically active phytochemicals in it. Recently, investigators have reported about hepatoprotective activity of phytoconstituents such as alkaloids, polyphenols, glycosides, carotenoids, coumarins and flavonoids (Gong et al., 2010; Yue-Tao et al., 2011).
The roles of Reactive Oxygen Species (ROS) in diverse pathologies stimulate much interest for more effective antioxidant agents. Free radicals react with sulfhydryl groups such as glutathione and protein thiols which eventually lead to membrane lipid peroxidation and necrosis (Brautbar et al., 2002). The damaged or dead tissue usually results in the leakage of the enzymes in the affected tissues into the blood stream (Obi et al., 2001). It is however, noteworthy that a large section of the world’s population relies on herbal remedies to treat plethora of diseases due to their low costs, easy access and reduced side effects (Marino-Betlolo, 1980), but the pharmacological basis behind most herbal therapies remains widely undefined. Antioxidants are molecules of synthetic or natural origin and have ability to stabilize or deactivate free radicals. Highly reactive free radicals are major causative agents for different cellular injury liver damage (Halliwell, 1994). Many dietary constituents and phytochemicals of medicinal plants are being investigated as antioxidants for its protective effects (Gupta et al., 2011). Phytochemicals having antioxidant activity are mainly flavonoids (Zhou et al., 2011) and polyphenols (Jaggadeo et al., 2011).

Natural products are a rich source of active phytochemicals and have been extensively used for biological activity. Thus, phytochemical analyses play a vital role in search of new and novel molecules (Shu, 1998). So, further need of paradigm shift for the standardization and evaluation of herbal remedies for liver diseases is required. Plants are a major source of novel anti-oxidant and hepatoprotective agents since many industrial drugs are derived as a result of knowledge got from folklore medicine (Brander et al., 1991). Among them, there is *Trichilia emetica* L. This Meliaceae is a rare endangered terrestrial orchid plant. It can be seen only during the rainy season and is widely distributed (Nacoulma, 1996). Extracts from *Trichilia emetica* L. were repeatedly used folklorically as an analgesic, antibacterial, antifungal, anti-inflammatory, antiseptic, antispasmodic, antiparasitic, antiviral, immunostimulant, laxative, purgative sudorific and vermifuge.

Hence, aim of this study was to evaluate hepatoprotective and nephroprotective profiles of polyphenol-rich fractions from *Trichilia emetica* L.

2. MATERIALS AND METHODS

Plant materials

Leaves of *Trichilia emetica* were collected in August 2008 in Gampela, 25 Km east of Ouagadougou, capital of Burkina Faso. The plant was identified in the Laboratory of Biology and Ecology, University of Ouagadougou, where a voucher specimen was deposited.
Animals handling
Swiss NMRI mice (25–30 g) and adult albinos Wistar rats (160-165 g) of both sexes were used for this study. All animals were housed in cages under controlled conditions of 12 h light/and 12 h without light and 25°C. They received pellets of food enriched with 20% protein and water ad libitum. They were deprived of food for 15 h (but with access to drinking water) and weighed before the experiments. Experiments on the animals were performed according to the protocols already approved by the Institute of Health Sciences Research/University of Ouagadougou (Burkina Faso) and met the international standards for animal study (Konaté et al., 2012a).

Preparation of extracts for acute toxicity study
Fifty grams of powdered plant materials (dried in laboratory condition) was extracted with 500 ml of acetone 80% (400 ml acetone + 100 ml water) for 24 h under mechanic agitation (SM 25 shaker, Edmund BÜHLER, Germany) at room temperature. After filtration, acetone was removed under reduced pressure in a rotary evaporator (BÜCHI, Rotavopor R-200, Switzerland) at approximately 40°C and freeze-dried (Telstar Cryodos 50 freeze-dryer). The extract was weighed before packing in waterproof plastic flasks and stored at 4°C until use.

Polyphenols extraction
The harvested plant materials fresh (broken into leaf stems) were dried in the laboratory at room temperature (20–25°C), afterwards samples were ground to pass a sieve of 0.3 mm. Polyphenols were extracted with aqueous acetone (80%, v/v). The extract was then washed with hexane to remove chlorophyll and other low molecular weight compounds. Acetone was evaporated and the extract was lyophilized and stored at 22°C prior to biological tests. For the tests, lyophilized sample was dissolved with 10% DMSO in water at the desired concentration (Konaté et al. 2012b).

Acute toxicity study
Swiss mice (male and female) were randomly divided into 7 groups (1 control group and 6 treated groups) of 6 animals (3 males and 3 females). The control group received water containing 10% dimethylsulfoxide (DMSO) administered intraperitoneally. The aqueous acetone extract of Trichilia emetica suspended in 10% DMSO was administered intraperitoneally at doses of 1; 2; 2.5; 3; 4; 5 and 6 g/kg [24]. The general behaviour of the mice was observed for 120 min after the treatment. The animals were observed for morbidity and mortality once a day for 14 days. The number of survivors after the 14 days period was
noted. The toxicological effect was assessed on the basis of mortality for 14 days, which was expressed by the median lethal dose value (Lethal Dose 50 or LD50) estimated from the regression of log-probit mortality rate (Miller, 1944).

Hepatoprotective potential of polyphenol-rich fractions

Experimental design for hepatoprotection potential

The rats were divided randomly into five groups of six rats each. The first and second groups served as control, received water and 35% ethanol. The remaining groups (group 3; group 4; group 5) received three dose levels of polyphenol-rich fraction of *Trichilia emetica* (75, 100 and 200 mg/kg bw) suspended in 35% of ethanol, administered orally by gavage daily for a period of 28 days. Body weight was measured weekly and the animals were observed daily for signs of abnormalities throughout the study. At the end of a period of 28 days period, the animals were deprived of food for 15 h. Blood samples were collected by cardiac puncture for biochemical (Konaté *et al*., 2011).

Assessment of hepatoprotective and nephroprotective profiles

Blood samples were collected by cardiac puncture in two tubes for glucose and serum biochemistry. The blood samples with heparin and without anticoagulant were centrifuged at 3000 rpm for 5 min to obtain plasma or serum. Plasma was used to determine glucose and the serum for other biochemical parameters such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), total bilirubin and direct bilirubin, triglycerides, total cholesterol, uric acid, urea nitrogen, creatinine, total protein and serum albumin. All these biochemical parameters were measured by Selectra XL Vital Scientific (Elitech Group Company).

Statistical analyses

Data were expressed as Mean ± Standard deviation (SD) of six experiments (n = 6). Results were analyzed by one-way ANOVA followed by Dunnett’s t-test using Prism 4 software. The level of significance was considered at p ≤0.05.

3. RESULTS

Table 1: Animal weights (g) with time of treatment

<table>
<thead>
<tr>
<th>Groups</th>
<th>First day</th>
<th>First week</th>
<th>Second week</th>
<th>Third week</th>
<th>Fourth week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>162.26±1.00</td>
<td>170.30±10.60</td>
<td>200±2.40</td>
<td>221.27±3.90</td>
<td>227.61±4.18</td>
</tr>
<tr>
<td>Group 2</td>
<td>162.12±1.10</td>
<td>169.68±1.22</td>
<td>166.22±1.20</td>
<td>164.62±1.01</td>
<td>161.10±1.20</td>
</tr>
<tr>
<td>Group 3</td>
<td>162.12±2.10</td>
<td>169.48±1.60*</td>
<td>170.62±1.40**+</td>
<td>175.62±1.18**++</td>
<td>172.10±3.72**++</td>
</tr>
</tbody>
</table>
Values are mean±S.E.M. (n = 6) one-way ANOVA followed by Dunnett’s t-test: Compare all vs. control; *p<0.05; **p<0.01 compared with control water; +p<0.05; ++p<0.01 with control alcohol.

Group 1: control water, rats received water
Group 2: control alcohol, rats received 35% ethanol
Group 3: rats received 35% ethanol with polyphenol-rich fractions (75 mg/kg body weight)
Group 4: rats received 35% ethanol with polyphenol-rich fractions (100 mg/kg body weight)
Group 5: rats received 35% ethanol with polyphenol-rich fractions (200 mg/kg body weight)

Table 2: Effects of polyphenol-rich fractions (EAF) from Trichilia emetica on the weights (g) of organs of rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>Left kidney</th>
<th>Right kidney</th>
<th>Stomach</th>
<th>Lungs</th>
<th>Liver</th>
<th>Heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>0.72±0.02</td>
<td>0.72±0.04</td>
<td>2.20±1.54</td>
<td>1.50±0.20</td>
<td>5.51±0.23</td>
<td>0.60±0.10</td>
</tr>
<tr>
<td>Group 2</td>
<td>0.52±0.01</td>
<td>0.54±0.02</td>
<td>2.52±0.02</td>
<td>1.60±0.21</td>
<td>4.61±0.02</td>
<td>0.65±0.2</td>
</tr>
<tr>
<td>Group 3</td>
<td>0.60±0.01*+</td>
<td>0.61±0.04++</td>
<td>2.15±0.11</td>
<td>1.42±0.01</td>
<td>5.24±0.08+</td>
<td>0.62±0.02</td>
</tr>
<tr>
<td>Group 4</td>
<td>0.61±0.10*+</td>
<td>0.61±0.07++</td>
<td>2.18±0.22</td>
<td>1.43±0.22</td>
<td>5.30±0.54+</td>
<td>0.62±0.01</td>
</tr>
<tr>
<td>Group 5</td>
<td>0.61±0.01*+</td>
<td>0.60±0.02++</td>
<td>2.23±0.10</td>
<td>1.48±0.58</td>
<td>5.43±1.20+</td>
<td>0.63±0.03</td>
</tr>
</tbody>
</table>

Values are mean±S.E.M. (n = 6) one-way ANOVA followed by Dunnett’s t-test: Compare all vs. control; *p<0.05; **p<0.01 compared with control water; +p<0.05; ++p<0.01 with control alcohol.

Group 1: control water, rats received water
Group 2: control alcohol, rats received 35% ethanol
Group 3: rats received 35% ethanol with polyphenol-rich fractions (75 mg/kg body weight)
Group 4: rats received 35% ethanol with polyphenol-rich fractions (100 mg/kg body weight)
Group 5: rats received 35% ethanol with polyphenol-rich fractions (200 mg/kg body weight)

Table 3: Hepatoprotective effects of polyphenol-rich fractions from Trichilia emetica in alcohol intoxicated Albinos Rats

<table>
<thead>
<tr>
<th>Biochemical Parameters</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Group 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mmol/l)</td>
<td>5.53±0.16</td>
<td>8.1±0.16</td>
<td>7.51±0.19++</td>
<td>7.79±0.11*</td>
<td>7.60±0.06++</td>
</tr>
<tr>
<td>AST (UI/l)</td>
<td>52.50±2.74</td>
<td>52.50±2.74</td>
<td>88.70±2.74</td>
<td>78.60±2.25+++</td>
<td>79.00±3.23+++</td>
</tr>
<tr>
<td>ALT (UI/l)</td>
<td>46.43±13.69</td>
<td>60.10±13.69</td>
<td>58.18±10.95**+</td>
<td>60.63±13.69**</td>
<td>60.63±13.69**</td>
</tr>
<tr>
<td>ALP (UI/l)</td>
<td>29.00±2.74</td>
<td>78.23±2.74</td>
<td>61.09±2.33+++</td>
<td>63.22±1.96+++</td>
<td>62.5±2.74+++</td>
</tr>
<tr>
<td>GGT (UI/l)</td>
<td>6.68±0.52</td>
<td>14.68±0.5</td>
<td>13.20±1.71+++</td>
<td>13.93±1.02**</td>
<td>10.01±0.07+++</td>
</tr>
</tbody>
</table>
Triglycerides (mmol/l) | Group 1 | Group 2 | Group 3 | Group 4 | Group 5  
--- | --- | --- | --- | --- | ---  
0.62±0.40 | 1.20±0.40 | 0.63±0.07+ | 0.68±0.03+ | 0.65±0.05+  
Total cholesterol (mmol/l) | Group 1 | Group 2 | Group 3 | Group 4 | Group 5  
--- | --- | --- | --- | --- | ---  
1.68±0.36 | 2.11±0.36 | 1.91±0.66*+ | 1.86±0.05*+ | 1.83±0.05*+  
Total bilirubin (mmol/l) | Group 1 | Group 2 | Group 3 | Group 4 | Group 5  
--- | --- | --- | --- | --- | ---  
0.12±0.03 | 0.82±0.03 | 0.62±0.06** | 0.64±0.03***+ | 0.63±0.01***+  
Direct bilirubin (mmol/l) | Group 1 | Group 2 | Group 3 | Group 4 | Group 5  
--- | --- | --- | --- | --- | ---  
0.02±0.00 | 0.12±0.00 | 0.084±0.00**+ | 0.083±0.01**+ | 0.081±0.00**+  

AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; GGT: gamma glutamyl transferase
Values are mean±S.E.M. (n = 6) one-way ANOVA followed by Dunnett’s t-test: Compare all vs. control; *p<0.05; **p<0.01 compared with control water; +p<0.05; ++p<0.01 with control alcohol.
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Group 4: rats received 35% ethanol with polyphenol-rich fractions (100 mg/kg body weight)
Group 5: rats received 35% ethanol with polyphenol-rich fractions (200 mg/kg body weight)

Table 4: Effects of polyphenol-rich fractions from *Trichilia emetica* on nephrotoxicity biomarkers in alcohol intoxicated Albinos Rats in serum

<table>
<thead>
<tr>
<th>Biochemical Parameters</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Group 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein (mg/dl)</td>
<td>7.83±2.26</td>
<td>9.01±0.04</td>
<td>8.6±2.0*+</td>
<td>8.81±2.0*+</td>
<td>8.43±2.0*+</td>
</tr>
<tr>
<td>Serum albumin (mg/dl)</td>
<td>3.17±2.76</td>
<td>5.13±1.58</td>
<td>4.10±2.25*+</td>
<td>4.89±2.25*+</td>
<td>4.78±2.25*+</td>
</tr>
<tr>
<td>Uric acid (mmol/l)</td>
<td>0.210±0.09</td>
<td>0.42±0.10</td>
<td>0.286±0.12+</td>
<td>0.277±0.008+</td>
<td>0.272±0.017+</td>
</tr>
<tr>
<td>Urea nitrogen (mmol/l)</td>
<td>9.62±0.30</td>
<td>12.47±0.12</td>
<td>12.23±2.77*+</td>
<td>10.15±0.06*+</td>
<td>9.89±0.04*+</td>
</tr>
<tr>
<td>Creatinine (mmol/l)</td>
<td>0.041±0.06</td>
<td>0.1±0.01</td>
<td>0.07±0.07*+</td>
<td>0.07±0.04*+</td>
<td>0.062±0.01*+</td>
</tr>
</tbody>
</table>

Values are mean±S.E.M. (n = 6) one-way ANOVA followed by Dunnett’s t-test: Compare all vs. control; *p<0.05; **p<0.01 compared with control water; +p<0.05; ++p<0.01 with control alcohol.
Group 1: control water, rats received water
Group 2: control alcohol, rats received 35% ethanol
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Group 5: rats received 35% ethanol with polyphenol-rich fractions (200 mg/kg body weight)
Acute toxicity study in mice: The effect of intraperitoneal treatment of aqueous acetone extract from *Trichilia emetica* on mortality, LD$_{50}$ value. The value of LD$_{50}$ is 568.5 mg/kg for intraperitoneal administration. No significant difference in body weight gain of the treated assay groups over the period of observation. No statistical difference was observed between the organ weights in the control and the intraperitoneal route groups.

**Body weight:** We noticed no significant difference in body weight gain between control group and the test groups (p>0.05). However, there is also an increase in animal weight with time treatment (in weeks). In the first, second, third and fourth weeks, there was a significant difference in body weight gain between the test groups and the control groups (p<0.05 or p<0.01). We note a decrease in weight of animals. The results are summarised in Table 1.

**Organ weights:** Table 2 shows the effects of polyphenol-rich fractions ethyl from *Trichilia emetica* on the weights of some vital body organs in rats. The weights of kidneys and liver (75, 100 and 200 mg/kg; p<0.05) decreased significantly compared to the control groups. However there is no significant difference between the other vital body organs weights of the treated assay groups and the control groups (p>0.05).

**Biochemical analyses:** Table 3 and Table 4 show the effects of polyphenol-rich fractions from *Trichilia emetica* on the biochemical parameters. Glucose (75 mg/kg, 100 mg/kg and 200 mg/kg; p<0.01 and p<0.05), AST (75 mg/kg, 100 mg/kg and 200 mg/kg; p<0.01 and p<0.05), ALT (75 mg/kg; 100 mg/kg and 200 mg/kg; p<0.01 and p<0.01), ALP (75 mg/kg, 100 mg/kg and 200 mg/kg; p<0.01 and p<0.05), triglycerides (75, 100 and 200 mg/kg, p<0.05), cholesterol (75, 100 and 200 mg/kg; p<0.05), total bilirubin (75, 100 mg/kg and 200 mg/kg; p<0.01 and p<0.05) and direct bilirubin (75 mg/kg, 100 mg/kg and 200 mg/kg; p<0.01 and p<0.05) were significantly changed in the treated assay groups compared to the control group (10% DMSO). For the other biochemical parameters however, there is no significant difference between the control group (10% DMSO) and the other treated assay groups (p>0.05). Table 5 shows the nephroprotective effects of polyphenol-rich fractions from *Trichilia emetica* on the biochemical parameters as such uric acid (75, 100 and 200 mg/kg; p<0.05), urea nitrogen (75, 100 and 200 mg/kg; p<0.05), creatinine (75, 100 mg/kg and 200 mg/kg; p<0.05), serum albumin (75 mg/kg, 100 mg/kg and 200 mg/kg; p<0.05), total proteins (75 mg/kg, 100 mg/kg and 200 mg/kg; p<0.05).
4. DISCUSSION

Table 1 and Table 2 showed that there is a relationship between the effect of polyphenol-rich fractions from *Trichilia emetica*, the body and certain organs weights of rats and the duration of the treatment. As a result, we noted a decrease in the body and certain organs weights of rats. In addition, some studies reported that body weight is a simple and sensitive index of toxicity after exposure to toxic substance (Konaté et al., 2012a). There is a close relation between alcohol exposition and the development of oxidative stress. Alcohol not only enhances ROS generation, but also depletes antioxidants, thus, creating a state of oxidative stress (Konaté et al., 2011). In addition, much of the direct cell injury that occurs during alcohol consumption is believed to be caused by accumulation of acetaldehyde, a toxic by-product of alcohol metabolism (Konaté et al., 2011). Therefore the overall biochemical implications of the deleterious effects of the toxic acetaldehyde and ROS on the liver or kidneys are, in part, the composite signs of liver or kidneys affections. The decrease of the body or certain organs weights of rats is direct result of liver or kidneys affection signs caused by alcohol. As a result, we could say that polyphenol-rich fractions from *Trichilia emetica* (100 and 200 mg/kg bw p<0.05 and p<0.01) possess a hepatoprotective or nephroprotective potential. Our results consigned in Table 1 showed this report.

Protection against alcohol toxicity has been used as a test for potential hepatoprotective activity by many scientists. Hepatic cells contain higher concentrations of AST and ALT in the cytoplasm and AST in particular exists in the mitochondria (Tuma et al., 2003). Damage to hepatic cells induces leakage of plasma to cause an increased level of hepatospecific enzymes in serum (Tuma, 1988). The measurement of serum AST, ALT, ALP and GGT levels serve as a means for indirect assessment of liver function.

Antioxidants are among the first link between chemical reactions and biological activities (Tolman et al., 1999) and they block the process of oxidation by neutralizing free radicals. The hepatoprotective index of a drug can be evaluated by its capability to reduce the injurious effects induced by a hepatotoxin or to preserve the normal hepatic functions (Trouillas et al., 2003). For example, CCl₃O⁻ and/or CCl₂OO⁻ radicals produced as a result of metabolic conversion of CCl₄ are reported to initiate lipid peroxidation and cellular damages (Kumar et al., 2009). Polyphenol-rich fractions from *Trichilia emetica* reduced the serum levels of AST, ALT, ALP and GGT and also preserved the functional ability of the liver. This was revealed when 100 and 200 mg/kg of polyphenol-rich fractions produced significant (p<0.01 or
p<0.05) reduction in total bilirubin but increased total protein levels relative to alcohol-intoxicated, untreated rats (Table 3 and Table 4). The liver is the site for the production of various physiological proteins. On exposure to the hepatotoxin like acetaminophen, CCl₄, alcohol etc., the amount of total protein present in the serum decreases due to less activity of the hepatocytes (Gupta et al., 2006).

Results in table 3 and table 4 noticed that polyphenol-rich fractions did not show appreciable hepatoprotective or nephroprotective effects at 75 mg/kg even though there was decrease in serum ALP level and elevated total proteins value when compared with control group (alcohol 35%) (Table 3 and Table 4). The conjugating and synthesizing ability of the liver was therefore, intact.

The low hepato and nephroprotective profiles of polyphenol-rich fractions from *Trichilia emetica* at 100 and 200 mg/kg (p<0.01or p<0.05) could be explained certainly by the antioxidant capacity of the plant. In effect, many plant extracts have indicated that they could in different ways effectively protect liver from active metabolites of alcohol and free radicals produced by certain toxic products as such alcohol or CCl₄. A number of investigation have previously demonstrated that antioxidant prevent alcohol toxicity, particularly hepatotoxicity, by inhibiting lipid peroxidation (Krishna et al., 2009). The mechanism of the hepatoprotective activity of polyphenol-rich fractions from *Trichilia emetica* in alcohol intoxicated rats may be derived certainly from some antioxidant principles in the fraction and also, stabilization of cell membranes. Evidence revealed that many phytoconstituents have the ability to induce microsomal enzymes either by accelerating the excretion of hepatotoxin or by inhibiting lipid peroxidation (Teselkin et al., 2000). Flavonoids (Mehta et al., 1999; Baek et al., 1996), triterpenes (Pandit et al., 2004), saponins and alkaloids (Xiong et al., 2003) have been well established as hepatoprotective agents. In the present study we noted that the bioactive (100 and 200 mg/kg; p<0.05 and p<0.01) exhibited significant dose-dependent hepatoprotective activity against alcohol toxicity in rats. It could be explained certainly by the presence of polyphenol compounds and its free-radical scavenging capacity. In effect, flavonoids and polyphenols have already been proved as potent antioxidants of plant origin (Tran et al., 2001). This study proves that this plant has ability to ameliorate alcohol induced liver toxicity and it must have some indirect or direct effect on liver (100 and 200 mg/kg; p<0.05 and p<0.01).
This study also investigated the effect of alcohol on the kidney functions in rat model. In assessment the renal effects of alcohol, the concentration of creatinine, uric acid, urea, total proteins and albumin serum were examined. It is recorded in this study that exposure to alcohol caused a low significant increase in serum creatinine, uric acid, urea, serum albumin and serum protein in the tested groups. The results of this study therefore give a clear indication that alcohol contains some chemical substances with nephrotoxic potentials. The concentration of creatinine in the blood is known to correlate inversely with the volume of glomerular filtration. Hence, creatinine is considered to be among the useful markers of the filtration function of kidneys, particularly that creatinine is excreted only via the kidneys (Pietta, 2000). Also, increased serum urea and uric acid concentrations also explain the impaired renal function implicated in rats treated with alcohol. The high serum urea and uric acid levels may result from a decrease in the rate of urea and uric acid secretion into urine, which may results from renal insufficiency (Appelton, 1995). Therefore, increase in serum urea, uric acid and creatinine concentration is a reflection of impaired renal function. However, we noticed that the present study showed and exhibited significant dose-dependent a low nephroprotective activity against alcohol toxicity in rats (100 and 200 mg/kg; p<0.05 and p<0.01). Probably, this low protective effect could be due to the presence of the active constituents such as flavonols, flavonol oligomers and proanthrocyanidins were found in Trichilia emetica. Polyphenols could be probably responsible for the low nephroprotective potential of Trichilia emetica.

5. CONCLUSION
In conclusion, the results of our study show that polyphenol-rich fractions from Trichilia emetica has promising potent hepatoprotective and nephroprotective properties. Therefore, further investigation is required to isolate and identify other active constituents responsible for these activities.

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