Monographycal Survey of Pharmacological Potentials of Argemone Mexicana L. (Papaveraceae), A Plant of Burkina Faso
Pharmacopeia: Determination of Antihepatotoxic and Antipyretic Activities

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Abstract: The authors present experimental results obtained from a study of pharmacological potentials of Argemone mexicana L. (Papaveraceae), a plant highly used in south western area of Burkina Faso for the treatment of several sickness: malaria fever, stomach disorder, jaundice, etc.

The aim of the present work was to determine in laboratory some pharmacological properties of Argemone mexicana as described by many traditional medical healers during several ethnobotanical enquiries. The present monographical survey has been centered on anti-hepatotoxic (hepatoprotective) and antipyretic power of the plant. Hepatoprotective activity was explored by testing the effect of sample drug against CCl4-induced liver injury in rats; liver functions were assessed by the activities of liver marker enzymes as ASAT/GOT, ALAT/GPT and ALP. Antipyretic effect of Argemone mexicana was studied by using yeast induced pyrexia method on mice.

Results of the different tests exhibited dose-dependent pharmacological activities. A similar dose-dependent profile was found with the antipyretic investigation on mice. The laboratory findings of the present study confirm the medicinal virtues advocated by traditional medical practitioners and justify the traditherapeutical use of Argemone mexicana L. (Papaveraceae).

Keywords: argemone mexicana, anti-hépatotoxic, antipyrétic; jaundice, mice, wistar rats, Burkina Faso.

1. INTRODUCTION

Ethnobotanical and ethnopharmacognostical enquiries represent an excellent mean for medicinal plants knowledge. In Burkina Faso, according to the statistics of DGPML (Health Ministry, 2006), more than 70 % of people still rely on medicinal plants for their healthcare. This demonstrates the important role played by folk medicine in the traditional health system among the rural population in the country.

For illustration, Argemone mexicana (Papaveraceae) is presented by renowned traditional healers of Beregadougou and Fabédougou villages as a medicinal plant reputed to possess several pharmacological properties. These medicinal virtues explain its multiple uses in the treatment of abdominal pains, non complicated malaria disease and particularly jaundice. Moreover, other traditional medical practitioners of the western area of Burkina Faso utilize the leaves of Argemone mexicana as anti-inflammatory, analgesic, antipyretic, antimicrobial and antispasmodic drug (Sourabié et al., 2013).

Specialized literature mentioned that Argemone mexicana (Papaveraceae) is a well-known medicinal plant used around the world: thus, in west Africa area, the leaves decoction of the plant served as...
Sourabie T.S. et al.

uncomplicated malaria remedy in Mali (Willcox et al., 2007). In Burkina Faso, studies of Sourabié et al., (2006, 2009, 2010, 2012, 2013) showed important pharmacological capacities which are at the basis of its use in the traditional medicine in Burkina Faso. Also in India, according to Indranil et al., (2006), leaves decoction are indicated for the treatment of bacterial illness in the Ayurvedic system of medicine.

On phytochemical way, many studies reported the presence of interesting secondary metabolites such tannins, glycosides, saponins and alkaloids. The alkaloids compounds met are mainly isoquinolein type: sanguinarin, dihydrosanginarin, berberin, protopin, etc. (Priya and Rao, 2012; Bose et al., 1963; Harbone and Williams, 1983; Upreti et al., 1991).

The aim of this first monographycal study consisted to determine experimentally in laboratory two (02) pharmacological properties of Argemone mexicana as described by traditional medical healers during ethnobotanical enquiries. At first, we planned to evaluate the anti-hepatotoxic (anti-icterus) and antipyretic activity suspected to be present in that plant. Other pharmacological potentials such anti-inflammatory and analgesic also described by traditional faith healers will be studied in a second survey.

For the majority of planned pharmacological tests, lyophilized extracts (water decoction) were used and this, to respect the utilization form of the traditional healers. The powdered leaves was also tested for their pharmacological potentiality.

2. MATERIAL AND METHODS

2.1 Plant Material

Argemone mexicana leaves were collected at the end of December 2004 in Bérégadougou and Fabédongou, two villages located less than 15 kilometers from Banfora (capital of Cascades region, 450 km far from Ouagadougou). A drug specimen has been brought in Ouagadougou for identification in the Pharmacognosy laboratory (UFR/SDS, University of Ouagadougou); the identification of specimen sample was also confirmed and certified later by the botanical model (specimen) preserved in the museum of Botany Department (DPF, INERA/CNRST, Ouagadougou) under the registration number HBNU 762.

2.2 Biological Material

Biological material was mainly composed by animals in function of the test planned to realize:

- determination of anti-hepatotoxic activity, male and female wistar rats (200-230g) were allotted into six groups of six animals each. They provided by the laboratory of CIRDES (360 km from Ouagadougou. Before the experiments commencement, the rats were acclimatized to laboratory conditions for one week. They were fed with standard rat feed and water ad libitum and kept in standard animal facility environment, temperature between 25 and 30°C, 12h light/12h dark (light cycle).

- determination of antipyretic property: young male and female white mice (NMRI strain) 4-6 weeks old, weighing 25-30g. They provided by CIRDES laboratory, located in Bobo-Dioulasso (360 km far from Ouagadougou). Before pharmacological experimentation, they were kept in the animal house of the Institute (Département Médecine et Pharmacopée Traditionnelles/Pharmacie) and maintained at a room temperature between 25 and 30°C, 40-70 % humidity conditions and the natural day-night cycle with an ad libitum access to food. The mice had no access to food during the hole day of experiment and the influence of circardian rythms was avoided by starting all experiments at 8.45 a.m.

2.3 Extract Preparation

Decoction: aqueous extract was obtained by decoction of 500 g leaf powder in 2 L of distilled water during 30 minutes. After this step, filtration and centrifugation (2500 rd/min for 10 min) were performed to freeze-dry the aqueous extract. Furthermore, the extract was qualitatively tested for the presence of chemical constituents. The phytochemical screening of the extract was performed using the following reagents: alkaloids with general precipitation reagents as Bouchardat, Draggendorf and Valser-Mayer tests; flavonoids with Shibata test (cyaniding test); tannins with ferric chloride solution 1% (p/v) saponins with ability to produce significant stable foam and Liebermann-Burchard reagent to highlight triterpenes and steroids.
2.4 Acute Toxicity Test

Oral acute toxicity study was performed to evaluate the acute toxic effects and to determine minimum lethal dose (LD₅₀) of the drug extract. The albino mice, male and female weighing 25-30 g were used for the experiment. The lyophilized extract was administered orally to the different groups (n= 6) of over night fasted mice at the dose of 25, 50, 100, 250, 500 and 1000 mg/kg body weight. After administration of the extract, all the animals were observed continuously for signs of toxicity and mortality during 24 h, 48 h, 72 h and beyond.

2.5 Pharmacological Tests

2.5.1 Anti-Icterus Activity

Drug and chemicals: all the drug and chemicals used were of analytical grade. Silymarin was purchased from pharmaceutical officin; carbon tetrachloride was purchased by phytochemical laboratory; biochemical reagents as SGOT, SGPT, ALP and Direct Bilirubin (DBIL) were procured from Univers Biomedical Lab, an establishment located in Ouagadougou.

Anti-hepatotoxic effect (anti-icterus power) was conducted by performing methods of Rao and Mishra (1998) combined to that of Al-Qarawi et al., (2003). These two combined protocols were appropriated to our laboratory context. For this, the animals (Wistar rats) were divided into six groups of six (06) animals each (n= 6 per group). Group I served as normal control and then received the vehicle (5mL/kg p.o.) during nine (09) days; Group II served as positive control intoxicated (CCl₄), received equally every day the vehicle (0,5mL/kg, i.p.); Group III served as standard, (silymarin is given at a dose of 100 mg/kg); groups IV, V and VI received drug treatment corresponding respectively to the doses of 125, 250 and 500 mg/kg per os.

At the seventh day, the animals of all groups, excepted those of group I received carbon tetrachloride CCl₄ (0,5 mL/kg, i.p.).

At the end of experimental period corresponding to the tenth day, the rats were sacrificed after ether anesthesia. Blood samples were collected by direct cardiac puncture and kept in EDTA containing vials for 10 minutes, centrifuged for 5-10 minutes at 2500 rpm. Blood serum was collected and used for biochemical estimations like aspartate aminotransferase (AST/GOT), alanine aminotransferase (ALT/GPT), phosphatase alkaline (ALP), total bilirubin (TBIL) and direct bilirubin (DBIL) as per standard procedures, mainly those of Mukherjee et al., (2002); Henry R.J., (1974), Enrique E. and SIlvo R., (1926). Dosage of biochemical markers was done by an automatical analyser (Konelab 20) which uses only specific reagents.

The results were expressed as percent hepatoprotective (anti-icteric) according to the formula of Al-Qarawi et al., (2003). The percentage reduction of the hepatotoxin (CCl₄) was calculated considering the enzyme level difference between the hepatotoxin-treated and the control group as 100% level of reduction.

Statistical Analysis

Results were presented as mean ± SEM for all values; One way ANOVA was used to statistically analyzed the results followed by Student “t” test. The level of significance if kept at P<0,05.

2.5.2 Antipyretic Activity

Antipyretic activity due to the lyophilized extract was measured by using Brewer’s yeast induced pyrexia in mice. For this, several groups of mice (n= 6 per group) weighting 25-35 g have been used; they were constituted as below:

*group I* (negative control): distilled water + suspended Brewer’s yeast 20%

*group II* (positive control) : paracetamol (150 mg/kg p.o.) + suspended Brewer’s yeast 20%

*group III* (test group 1) : suspended Brewer’s yeast 20% + lyophilized extract 250 mg/kg p.o.)

*group IV* (test group 2): suspended Brewer’s yeast 20% + lyophilized extract (500 mg/kg p.o.). The initial rectal temperature of each animal was noted by insertion of a clinical thermometer to a depth of 2 cm into rectum. And then after mice of control and those of tests groups received subcutaneous injection of suspended Brewer’s yeast 20% (1 mL/100 g bwt).
Sixteen (16h) hours after initial time (T_0H), the rectal temperature of all the test group (group test 1 and group test 2) received also orally two doses of the lyophilized extract (250 and 500 mg/kg bwt p.o.). Positive control group (reference) equally received Paracetamol (150 mg/kg p.o.); the measurement of temperature carried out at 1h, 2h, 3h, 4h and 5h after oral administration of vegetal drug extract. The average temperatures of test groups were compared to those of negative and positive control groups. Student test « t Test » was used for what concerning the statistical analyses (p<0,05 vs positive control group).

3. RESULTS

3.1 Phytochemical Screening

Water extract of Argemone mexicana leaves revealed the presence of interesting phytoconstituents such as alkaloids, flavonoids, sugars and glycosides, phenolic compounds as tannins, saponins (Sourabié et al., 2009). The results of phytochemical screening are resumed in Table I. Moreover, thorough chemical studies led by many authors [(Priya and Rao, (2012), Upreti et al., (1991), Bose et al., (1963)] showed the isoquinoline nature of alkaloids present in the drug. Some of these alkaloidic constituents possess bioactive properties as berberine, cheilanthifoline, coptisine, muramine, scoulerine, sanginarine and protopine (Priya and Rao, 2012).

Table I. Phytochemical compounds of Argemone mexicana leaves extract; [In study of Sourabié et al. (2009)].

<table>
<thead>
<tr>
<th>Drug yield (%)</th>
<th>AK</th>
<th>Flav</th>
<th>Cg</th>
<th>St</th>
<th>Pc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aqueous extract</td>
<td>5.13</td>
<td>++++</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

Ak = alkaloids; Flav = flavonoids; Cg = sugars and glycosides; St = steroids; Pc = phenolics compounds (tannins); +++ = abundant, ++ = present; + = slightly present

3.2 Acute Toxicity Test

No acute toxicity (LD_{50}) has been found with different types of drug extracts tested at the dose of 1000 mg/kg p.o. No mortality was recorded in any group of animals (rats and mice) after 72h of drug administration to the animals. However, at the highest dose (2500 mg/kg, p.o.) muscular weakness with slow movements was observed particularly with the mice without causing any mortality. All these signs disappeared around the end of observation period (72h).

3.3 Pharmacological Assays

3.3.1 Anti-hepatotoxic power

Table II. effect of lyophilized extract on biochemical parameters against rats CCl_{4} induced injury and treated groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Doses (mg/kg)</th>
<th>GOT (UI/L)</th>
<th>GPT (UI/L)</th>
<th>ALP (UI/L)</th>
<th>TBil (mg/dL)</th>
<th>DBil (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>--</td>
<td>65.6±2.68</td>
<td>98.7±2.56</td>
<td>131.2±3.06</td>
<td>0.36±0.04</td>
<td>0.14±0.02</td>
</tr>
<tr>
<td>II</td>
<td>--</td>
<td>148.19±2.99</td>
<td>212.26±3.45</td>
<td>219.80±2.29</td>
<td>6.57±0.81</td>
<td>11.46±3.19</td>
</tr>
<tr>
<td>III</td>
<td>100</td>
<td>80.10±0.88</td>
<td>119.37±1.06</td>
<td>149.15±1.30</td>
<td>1.30±0.10</td>
<td>1.23±0.10</td>
</tr>
<tr>
<td>IV</td>
<td>125</td>
<td>92.35±0.09</td>
<td>136.01±1.59</td>
<td>174.55±0.88</td>
<td>1.75±0.09</td>
<td>1.29±0.22</td>
</tr>
<tr>
<td>V</td>
<td>250</td>
<td>83.96±0.15</td>
<td>123.65±0.76</td>
<td>158.68±0.80</td>
<td>1.66±0.09</td>
<td>1.65±0.23</td>
</tr>
<tr>
<td>VI</td>
<td>500</td>
<td>75.56±4.08</td>
<td>111.28±0.68</td>
<td>142.81±0.72</td>
<td>1.53±0.08</td>
<td>1.51±0.07</td>
</tr>
</tbody>
</table>

Values are expressed as mean, S.E. n=6; p<0,01 vs CCl_{4}; one way analysis and Dunnnett’s test: percentage reduction between brackets. SGOT= serum glutamyl oxaloacetate transaminase; SGPT= serum glutamyl pyruvate transaminase; ALKP= alkaline phosphatase; Dbil= direct bilirubin

The effects of drug extracts (lyophilized extract, alkaloids extracts, leaf powder suspension) on biochemical markers of liver toxicity [transaminases (SGOT, SGPT), alkaline phosphatase (ALKP), total bilirubin (TBil), and direct bilirubin (DBil)] against CCl_{4}-intoxicated rats are summarized in
Monographycal Survey of Pharmacological Potentials of Argemone Mexicana L. (Papaveraceae), A Plant of Burkina Faso Pharmacopeia: Determination of Antihapatotoxic and Antipyretic Activities

tables as shown below (tables II, III, IV). A significant (p<0.01) increase of serum enzymes levels was observed with CCl₄-intoxicated group (group II) and all the tests groups comparatively to the normal control groups. This phenomenon (elevation of biochemical parameters) was also visible with TBil and DBil. Administration of drug extracts reduced significantly (p<0.05) the level of biochemical markers of CCl₄-induced injury. The reduction of tetrachloride intoxication varied according to the extract dose administered (125, 250 and 500 mg/kg b.wt) as illustrated by the leaf powder administered to the wistar rats.

Table III. effects of alkaloids extract (multi doses) on biochemical parameters of CCl₄- intoxicated groups and treated groups.

<table>
<thead>
<tr>
<th>Gropes</th>
<th>Doses (mg/kg)</th>
<th>GOT (UI/L)</th>
<th>GPT (UI/L)</th>
<th>ALP (UI/L)</th>
<th>TBIL (mg/dL)</th>
<th>DBIL (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>--</td>
<td>65.6±2.68</td>
<td>98.7±2.56</td>
<td>131.2±3.06</td>
<td>0.36±0.04</td>
<td>0.14±0.02</td>
</tr>
<tr>
<td>II</td>
<td>100</td>
<td>148.19±2.99</td>
<td>212.6±3.45</td>
<td>219.8±0.29</td>
<td>7.02±0.81</td>
<td>10.5±0.31</td>
</tr>
<tr>
<td>III</td>
<td>125</td>
<td>80.10±0.88</td>
<td>119.37±1.06</td>
<td>149.15±1.30</td>
<td>1.21±0.10</td>
<td>1.23±0.10</td>
</tr>
<tr>
<td>IV</td>
<td>250</td>
<td>84.25±0.93</td>
<td>118.6±1.05</td>
<td>148.2±0.50</td>
<td>0.72±0.09</td>
<td>1.89±0.22</td>
</tr>
<tr>
<td>V</td>
<td>500</td>
<td>76.59±0.85</td>
<td>129.92±0.82</td>
<td>163.0±1.05</td>
<td>1.67±0.09</td>
<td>1.64±0.23</td>
</tr>
<tr>
<td>VI</td>
<td>500</td>
<td>68.93±0.76</td>
<td>106.30±0.07</td>
<td>133.38±0.05</td>
<td>1.46±0.08</td>
<td>1.49±0.07</td>
</tr>
</tbody>
</table>

Values are mean ± S.E.; n = 6, values within parentheses represent percent hepatoprotection; *p<0.05; ** p<0.01 . Compared with normal control vs liver injured rats.

Table IV. effects of multi doses of crude leaf (powder) on different biochemical parameters in rats with carbon tetrachloride induced hepatotoxicity.

<table>
<thead>
<tr>
<th>Gropes</th>
<th>Doses (mg/kg)</th>
<th>GOT (UI/L)</th>
<th>GPT (UI/L)</th>
<th>ALP (UI/L)</th>
<th>TBIL (mg/dL)</th>
<th>DBIL (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>--</td>
<td>65.6±2.68</td>
<td>98.7±2.56</td>
<td>131.2±3.06</td>
<td>1.57±0.06</td>
<td>1.50±0.06</td>
</tr>
<tr>
<td>II</td>
<td>100</td>
<td>148.19±2.99</td>
<td>212.6±3.45</td>
<td>219.8±0.29</td>
<td>2.58±0.07*</td>
<td>2.46±0.07</td>
</tr>
<tr>
<td>III</td>
<td>125</td>
<td>80.10±0.88</td>
<td>119.37±1.06</td>
<td>149.15±1.30</td>
<td>1.84±0.05</td>
<td>1.76±0.05</td>
</tr>
<tr>
<td>IV</td>
<td>250</td>
<td>84.25±0.93</td>
<td>118.6±1.05</td>
<td>148.2±0.50</td>
<td>(73.26%)</td>
<td>(72.91%)</td>
</tr>
<tr>
<td>V</td>
<td>500</td>
<td>76.59±0.85</td>
<td>129.92±0.82</td>
<td>163.0±1.05</td>
<td>1.67±0.09</td>
<td>1.64±0.23</td>
</tr>
<tr>
<td>VI</td>
<td>500</td>
<td>68.93±0.76</td>
<td>106.30±0.07</td>
<td>133.38±0.05</td>
<td>1.46±0.08</td>
<td>1.49±0.07</td>
</tr>
</tbody>
</table>

Values are mean ± S.E.; n = 6, values within parentheses represent percent hepatoprotection; *p<0.05; ** p<0.01 . Compared with normal control vs liver injury rats.

3.3.2 Pharmacological profile of the anti-hepatotoxic effect

In order to know how the anti-icterus effect is manifested, we defined the “hepatoprotective power” (HP), a parameter permitting to know if the anti-icterus effect is expressed dose-dependently or not. It was calculated as below:

\[
\text{H.P. (\%)} = \frac{\text{[GOT+GPT+ALP+TBIL+DBIL]}\times 5}{\text{[GOT+GPT+ALP+TBIL+DBIL]}}
\]

H.P. = hepatoprotective power of the drug at the dose considered, expressed in mean percentage (%) of reduction. GOT: glutamic oxalacetic transaminase; GPT: glutamic pyruvic transaminase; ALP: alkaline phosphatase; TBIL: total bilirubin; DBIL: direct bilirubin;

\[
\text{[GOT+GPT+ALP+TBIL+DBIL]} = \text{the amount of reduction percentage of the 5 investigated biochemical parameters.}
\]

Hepatoprotective Power (HP) is a determinant parameter used to determine the dose-dependent profile of the anti-hepatotoxic effect concerning the different extracts of Argemone mexicana. It (Hepatoprotective Power) permitted equally to classify the different drug extracts in function of their...
anti-hepatotoxic dose-dependent potential. Results of the tests (performed) are resumed on following tables (Table V, Table VI).

Table V. dose-dependent anti-hepatotoxic profile of Argemone mexicana leaves (lyophilized extract) compared to silymarin (reference product).

<table>
<thead>
<tr>
<th>lyophilized extract (mg/kg)</th>
<th>Silymarine (100 mg/kg)</th>
<th>125 mg/kg</th>
<th>250 mg/kg</th>
<th>500 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP (%)</td>
<td>84.03%</td>
<td>69.72%</td>
<td>78.54%</td>
<td>86.73%</td>
</tr>
</tbody>
</table>

Table VI. dose-dependent profile of anti-hepatotoxic effect obtained from of Argemone mexicana leaves (alkaloid totum) compared to silymarin (reference product).

<table>
<thead>
<tr>
<th>alkaloid totum (doses en mg/kg)</th>
<th>Silymarine (100 mg/kg)</th>
<th>125 mg/kg</th>
<th>250 mg/kg</th>
<th>500 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP (%)</td>
<td>84.33%</td>
<td>80.45%</td>
<td>78.24%</td>
<td>89.32%</td>
</tr>
</tbody>
</table>

Table VII. dose-dependent profile of anti-hepatotoxic effect obtained from of Argemone mexicana crude powdered leaf compared to silymarin (reference).

<table>
<thead>
<tr>
<th>crude leaf powder (doses en mg/kg)</th>
<th>Silymarine (100 mg/kg)</th>
<th>125 mg/kg</th>
<th>250 mg/kg</th>
<th>500 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP (%)</td>
<td>77.29%</td>
<td>78.62%</td>
<td>76.82%</td>
<td>84.38%</td>
</tr>
</tbody>
</table>

Table VIII. classification of different extracts studied according to the hepatoprotective power.

<table>
<thead>
<tr>
<th>Drug parts used (extracts)</th>
<th>Standard (référence)</th>
<th>Silymarin</th>
<th>leaf powder</th>
<th>decoction*</th>
<th>maceration*</th>
<th>alk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP* (%)</td>
<td>84.08</td>
<td>79.94</td>
<td>78.33</td>
<td>78.25</td>
<td>82.67</td>
<td></td>
</tr>
</tbody>
</table>

decoction*: lyophilized extract ; maceration*: lyophilized extract ; alk*: alkaloid totum

HP*: hepatoprotective power (%).

3.3.3 Antipyretic Activity

Oral administration of Brewer’s yeast increased the rectal temperature level of mice sixteen hours after injection of the pyrexia agent. Lyophilized extract, when given to the mice at 250 and 500 mg/kg p.o., reduced significantly yeast induced fever. The reference drug (paracetamol) also suppressed fever induced by yeast in mice. The hole of results is resumed in Table IX.

Table IX. effect of lyophilized extract (250 & 500 mg/kg p.o.) and paracetamol (150 mg/kg p.o.) on brewer’s yeast induced fever in mice.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Doses (mg/kg)</th>
<th>0hr</th>
<th>1hr</th>
<th>2hrs</th>
<th>3hrs</th>
<th>4hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent (NaCl)</td>
<td>5mL/kg</td>
<td>37.26±0.28</td>
<td>37.54±0.26</td>
<td>37.66±0.31</td>
<td>37.66±0.31</td>
<td>37.60±0.33</td>
</tr>
<tr>
<td>Brewer’s yeast*</td>
<td>msp 20%</td>
<td>38.69±0.30</td>
<td>38.82±0.38</td>
<td>38.56±0.38</td>
<td>38.35±0.52</td>
<td>38.47±0.20</td>
</tr>
<tr>
<td>Paracétamol</td>
<td>50</td>
<td>38.80±0.29</td>
<td>37.95±0.25</td>
<td>37.94±0.30</td>
<td>37.66±0.30</td>
<td>37.57±0.33</td>
</tr>
<tr>
<td>Lyoph* extract</td>
<td>250</td>
<td>38.47±0.19*</td>
<td>37.50±1.08*</td>
<td>37.46±1.03</td>
<td>37.40±0.40*</td>
<td>37.36±0.66*</td>
</tr>
<tr>
<td>Lyoph* extract</td>
<td>500</td>
<td>38.57±0.22</td>
<td>37.36±0.28</td>
<td>37.34±0.26</td>
<td>7.22±0.24</td>
<td></td>
</tr>
</tbody>
</table>

Each datum represents the mean rectal temperature (°C) ± S.E.M. (n = 6), * p < 0.05, if compared with the control group (Student test); Lyoph* extract : lyophilized extract (250 & 500 mg/kg)

The elevated (hyper) pyrexia induced by brewer’s yeast was attenuated one hour (1hr) after oral administration of the two dose extract (250 & 500 mg/kg). The decrease of body temperature of mice was parallel to that exhibited by the reference drug (paracetamol, 150 mg/kg), showing thus the reality of antipyretic potential due to the lyophilized extract.
4. DISCUSSION

4.1 Anti-Icterus Potential

Protection against CCl₄-induced liver injury has been taken as a test for potential anti-hepatotoxic (hepatoprotective) agent according to several investigators such as Sha et al., (2009) and Sanmugapriya (2006). Furthermore, the changes associated with CCl₄-induced liver damage are similar to that of acute viral hepatitis (Suja et al., 2004); so CCl₄-mediated hepatotoxicity was chosen as the experimental model.

Moreover, the ability of a hepatoprotective drug (such as Argemone mexicana leaves) to reduce the injurious effects or to preserve the normal hepatic physiological mechanism, that have been disturbed by a hepatotoxin (CCl₄; 0.5 mL/kg i.p.), is the sign of its protective effect according to Yudav and Dixit (2003).

In the frame work of present survey, the increases of biochemical markers as GOT, GPT, ALP and Bilirubin (total and direct) are the signs which showed significant hepatic damage in CCl₄ intoxicated rats (group II, table 2). This hepatic injury can be attributed to the structural integrity damage of liver, because these enzymes have a cytoplasmic location and released into circulation after cellular damages, indicating development of hepatotoxicity according to Sallie et al., (1991). Carbon tetrachloride (CCl₄) is mainly the responsible of that toxicity which causes multiple liver damage. Its toxicity is due to the metabolites particularly trichloromethyl (CCl₃) and the derivative trichloromethylperoxyde. These two metabolites are generated by the intermediate of cytochrome P₄₅₀ hepatic oxidase.

Thus, these free radicals can alkylate cellular proteins and other macromolecules with a simultaneous attack on polyunsaturated fatty acids in the presence of oxygen, to provide lipids peroxides, leading to liver damage (Sarada et al., 2012; Sanmugapriya et al., 2006; Bishayee et al. 1995). Hepatocellular necrosis leads to elevation of the biochemical serum enzymes levels, which are released from the liver into blood (Ashok et al., 2002).

So, increased levels of GOT, GPT, ALP and serum bilirubin (TBil and DBil) can be considered as conventional indicators of liver injury according to Achliya et al., (2004).

Our results revealed a significant increase of the activities of GOT, GPT, ALP and serum bilirubin levels on exposure to CCl₄, indicating considerable hepatocellular damage. On the other hand, oral administration of crude powdered leaf to the intoxicated rats attenuated the increased levels of the serum enzymes, produced by CCl₄ and caused a subsequent recovery towards normalization like that of silymarin treatment.

This normalization of serum biochemical markers by crude powdered leaf of A. mexicana suggests that it is able to condition the hepatocytes so as to protect the membrane integrity against CCl₄ induced leakage of biochemical marker enzymes into the blood plasma. We can affirm with great certitude that the above changes can be considered as an expression of the functional improvement of hepatocytes.

About the mechanism of action concerning the anti-hepatotoxic effect exhibited by the crude powdered drug (leaf of Argemone mexicana), it can be attributed to the phytochemical components highlighted in the powdered suspension extracts. Effectively, according to the studies of Rathi et al. (2008), protopin, one of the alkaloidic components of A. mexicana exerts an inhibition action on lipid peroxides formation. And it has been known that lipid peroxidation is one of the important steps of CCl₄ metabolism leading to the degradation of hepatocytes cells membranes.

Inhibition of lipid peroxidation by protopin creates a good condition for liver protection against CCl₄-intoxication that is known to cause many important damages to the liver. Finally, the mechanism of action exerted by protopin is comparable to that of silymarin, considered as an inhibitor of cytochrome P₄₅₀ (Sarada K. et al., 2012). The inhibitory role of silymarin has been effectively confirmed by Letteron P. et al., (1990) about metabolism of Carbon tetrachloride (CCl₄). Silymarin inhibits the hepatic oxidase CYP₄₅₀ (Cytochrome P₄₅₀), the main enzyme responsible for the activation of carbon tetrachloride (CCl₄) transformation into its metabolites notably radical trichloromethyl which leads to trichloromethylperoxyde, free radical. This derivative free radical (trichloromethylperoxyde) plays a great role in the lipids peroxidation leading to liver damage.
4.2 Antipyretic Activity

Acting at 250 and 500 mg/kg on induced yeast pyrexia, the water aqueous decoction (lyophilized extract) showed a dose-dependent effect. This dose-dependent antipyretic effect was more accentuated with the extract tested at 500 mg/kg if compared with the one of to the reference drug (paracetamol used at 150 mg/kg) from the first to the fourth hour (1st to 4th hour) as indicated by on table IX. Figure below gives an illustration of the antipyretic effect of the two doses extracts (250 and 500 mg/kg) comparatively to the control and paracetamol used as reference drug.

Moreover, the very sensitive reduction of body temperature between the second and the fourth hour (figure above) with the two doses of drug (250 & 500 mg/kg) supposed the existence of a potential hypothermic effect due to the lyophilized extract (table IX).

4.3 Mechanism of the Antipyretic Activity

According to several authors [Sourabié et al., (2012), Owelé et al., (2005), Adeolu et al., (2008) and Sini et al., (2011)], the antipyretic potential showed by the two doses of drug extract might be attributed to the phytochemical constituents such as alkaloids, glycosides, flavonoids, phenolic compounds as tannins, saponins found in the water aqueous extract of Argemone mexicana leaves. These components exert their biological action according to a mechanism of cyclooxygenase enzymes I and II inhibition (COX-1 and COX-2) which are implicated in the production of inflammation mediating agent prostaglandin (PGE) from arachidonic acid [Parmar et al., (1978), Barar FSK (2006)].

The lyophilized extract at different doses (250 & 500 mg/kg) exerted a similar pharmacological dose-dependent effect (antipyretic action) on yeast induced pyrexia on mice when compared to the paracetamol (reference drug).

Moreover, it is known that most of the non steroidal anti-inflammatory drugs as paracetamol or lyophilized extract (in the case of this present study) possess antipyretic activity through inhibition of prostaglandins synthesis in hypothalamus [Rang et al., (2006); Santos et al., (1994)].

Both the dose extract (250 and 500 mg/kg) produced significant antipyretic activity in Brewer’s yeast induced pyrexia in mice. And this situation (both the dose extract 250 & 500 mg/kg) could inhibit the prostaglandins synthesis in hypothalamus.

5. CONCLUSION

The results of the present study showed that the different drug extracts of Argemone mexicana leaves possess both anti-hepatotoxic and antipyretic properties. These results confirm on experimental way
the medicinal virtues which explain the traditherapeutical use of this plant in the folk medicine in the western part of Burkina Faso.

Showing pharmacological potentials (anti-icterus and antipyretic effects) against jaundice (icterus) and other fever illness, Argemone mexicana Linn. (Papaveraceae) plays a great role in the traditional healthcare in folk medicine in Burkina Faso, specially in the “Cascades area”.

REFERENCES


