Hematological and Clinical Changes in Rabbits Exposed to Cassia Senna

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Abstract:

Background and objectives: Senna alexandrina Miller. (Cassia Senna) is one of the most commonly used laxative drugs in the Eastern and Western countries for the treatment of constipation. The main objective of this study is the experimental screening of the toxicity of Cassia Sennato assure its safety and effectiveness.

Methods: In the first part a pilot study was conducted on 5 mature male albino rabbits of 1-1.5 kg. The rabbits exposed to Senna in a powder form mixed with diet in pellet form at a dose rate of 4 gm daily for 12 days. In the second part of the study healthy mature albino rabbits of 1 -1.5 kg body weight, of either sex, were divided into 4 groups of eight rabbits each, group 1 exposed to 4 gm / kg.b.wt / day ,plant with diet . 2nd group exposed to plant in decoction form at a dose 1 gm / kg / day, 3rd group as aqueous extract at a dose 100 mg / kg / day , and 4th group as alcohol extract at a dose 50 mg / kg b.wt / day for 20 days.

Results: First Part: The main clinical sings that appeared on animals of the experiments was the soft feces during the time of experiment. Body weight, body temperature, respiratory rates were none significantly changed. Heart rates significantly increased in day 2. Bleeding and cloting times were significantly increased during all time of experiment. Total leucocytes count, eosinophils%, Heterophils % Monocytes %, Lymphocytes% showed none significant changes .Basophils% significantly decreased in day 11. Hemoglobin concentration significantly decreased in day 11. PCV significantly decreased in day 4 and 11. MCV significantly decreased in day 4. MCH significantly decreased in day 4. Second part: The results revealed that body weight in the four groups did not show significant changes as it either increased or decreased none significantly, Body temperature significantly increased in 1st, 2nd groups, Heart rates in 2nd and 3rd groups significantly increased. Respiratory rates in 1st, 2nd, 3rd groups significantly increased. In 4th group significantly decreased in day 7 but increased significantly in day 12. Bleeding time increased significantly in 1st, 2nd, 3rd groups significantly increased. In 4th group decreased significantly. Cloting time in 1st and 3rd groups significantly increased. Total leucocytes count in 1st group significantly increased in day 22. Basophils% none significantly changed in all groups. Monocytes significantly increased in day 7 in 1st group, in 3rd group decreased significantly. Eosinophils in 2nd group significantly increased. Heterophils % significantly decreased in 4th group. Lymphocytes% in 2nd and 3rd group significantly increased.

Conclusion: The data suggest that administration of the aqueous extract of S. Alexandrina pods at 50 mg /kg / day is not toxic.

Keywords: Cassia Senna, Hematology, toxicity, Rabbits.

1. INTRODUCTION

Cassia italic (Mill).is considered from order Fabales, belonged to family Ceasalpiniaceae, in this family 5 trips one of which is Cassia to which belong genus Cassia , in which there are 15 species. in Iraq presents 8 species belong to the genus Cassia . One of which wild and other 7 species cultivated from which italic (Guest, 1974). In Iraq the plant founded in south east.

Senna is one of the most commonly used laxative drugs in the Eastern and Western countries for the treatment of constipation. Commercially available consists of the dried leaflets of Alexandrina Senna (Cassia acutifolia Delile) or Tinnevelly Senna (Cassia angustifoliaVahl) belonging to plant family leguminosae (United States pharmacopoeia, 2004; Wallis, 2004). Though perceived as two distinct species in several pharmacopoeias, they are now considers as a single species i.e. Cassia Senna. (WHO, 1999).
Senna is known for its purgative action. The phytoconstituents principally responsible for its characteristic action are two anthraquinone glycosides; sennoside A and sennoside B. Senna also contains small quantities of other anthraquinones such as sennosides C and D, rhein –8 – glucoside, rhein -8- diglucoside, aloe- emodin, 8- glucoside, anthrone diglucoside and rhein (Kokate et al., 2003; Kar, 2003).

Plants commonly used in traditional medicine are assumed to be safe. This safety is based on their long usage in the treatment of diseases according to knowledge accumulated over century’s. Recent evidence suggests that some of the herbs considered to be safe over the last many decades have proven to be associated with health hazards. Herbal remedies can act either as agonists or antagonists that potentiate some drug therapies (George, 2001). Adverse reactions may also result from irrational usage, such as excess dosage.

Sennaalexandrina Miller. (Syn. Cassia senna, Family CaesalpiniaACEous), cultivated in the Sudan and was formerly exported through Alexandria is mentioned in all famous herbals of the 15th and 16th century and is described in the last editions of the pharmacopies of countries all over the world (WHO, 1999). The pods and leaves are considered as one of the most used laxatives (Lemi, 1988; Migahid, 1978). The laxative quality of senna is due to the presence of sennosides A and B in its leaves and pods, which were isolated in pure form by Stoll et al (1950).

Senna can have adverse effects on the heart because regular consumption is reported deplete the body of potassium causing fatalities. Other adverse reactions include grand mal seizures, circulatory failure, hypertension and anaphylactic reaction (George, 2011) as the use of senna as a laxative drug is wide worldwide, experimental screening of the toxicity of this plant is crucial to assure the safety and effectiveness of this natural source.

(Balasankaret al 2013) referred to several scientists and researchers are of the view that the sennapossesses this property as potent cathartic or purgative owing to the apparent presence of elements and compounds such as dianthrone glycosides (1.5 – to 2 percent). Main sennosides A and B along with minor quantities of sennosides C and D and other intimately associated amalgams. Besides being a laxative, senna is used as a febrifuge, in spleenic enlargements, anemia, typhoid, cholera, biliousness, jaundice, pout, rheumatism, tumors, foul breath and bronchitis, and probably in leprosy. It is employed in the treatment of amoebic dysentery as an anthelmintic and as a mild liver stimulant. Leaves are astringent, bitter, sweet, acrid, thermogenic, cathartic, depurative, liver tonic, anthelmintic, colagogue, expectorant, febrifuge. Useful in constipation, abdominal disorders, leprosy, skin disorders, leucoderma, splenomegaly, hepatomegaly, dyspepsia, cough, and bronchitis. (Balasankaret al 2013)

Diset et al (2011). Cassia angustifolia Vahl (senna) is a plant that belongs to the Family Fabaceae

The study revealed the presence of saponins, anthraquinones, cardiac glycosides, flavonoids, reducing sugars and terpenes. The concentration of these bioactive components were slightly higher in ethanol than in aqueous leaf extract. (Timothy et al., 2012).

2. MATERIAL AND METHODS

2.1. Plant Material
The plant purchased from local market in Iraq.

2.2. Preparation of Plant Extract
Water extract was prepared by simple maceration of 150 g of powdered pods in 1500ml of distilled water, maintained at ambient temperature for 4 h. Extract was first filtered on filter paper and then freeze – dried to yield 13 g of water extract.

2.3. Animals and Experimental Design
In the first experiment a piiolet study was conducted on 5 mature male albino rabbits of 1-1.5 kg. After a period of 1 week adaptation the rabbits exposed to Senna in a powder form mixed with diet in pellet form at a dose rate of 4 gm daily for 12 days. The main parameters depended in this part were clinical including heart rates, respiratory rates, body weight, and body temperature with monitoring the animals for any abnormal behaviors or signs. In addition to hematological parameters including erythrocytes counts, Hb concentration, PCV, MCV, MCH and MCHC, total and differential leucocytes counts, according to Coles (1986). In addition to bleeding and clotting times.
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In the second part of the study healthy mature New Zealand rabbits of 1-1.5 kg body weight, of either sex, maintained under standard conditions (temperature 22±1°C, relative humidity 60%, 12 h light/dark cycle) with diet and water ad libitum. The rabbits were given 5 days adaptation period. At the end of the adaptation period, rabbits were divided into 4 groups of eight rabbits each, group 1 exposed to plant with diet at a dose rate of 4 g/kg b.wt/day, 2nd group exposed to plant in decoction form at a dose rate of 1 g/kg b.wt/day, 3rd group as aqueous extract at a dose rate 100 mg/kg b.wt/day, and 4th group as alcohol extract at a dose rate of 50 mg/kg b.wt/day for 20 days. The same parameters depended in 1st part were also depended in this part.

Statistical analysis

Data were reported as mean ± S.E.M. and statistical analysis for significance was done by ANOVA test. Data from the test groups were compared with controls.

3. RESULTS

3.1. First Part

The main clinical sings that appeared on animals of the experiments was the soft feces during the time of experiment.

The results revealed that body weight, body temperature, and respiratory rates were none significantly changed. Heart rates significantly increased in day 2. Bleeding and clotting times were significantly increased during all time of experiment (Table -1).

Table1. The changes of clinical parameters in addition to bleeding and clotting times of rabbits exposed to Senna

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Body weight kg</td>
<td>1.296±0.012a</td>
<td>1.312±0.06a</td>
<td>1.306±0.46a</td>
<td>1.06±0.052a</td>
</tr>
<tr>
<td>Heart rate/ min</td>
<td>184±4.00a</td>
<td>204±13.27b</td>
<td>173.6±4.12a</td>
<td>167.6±12.56a</td>
</tr>
<tr>
<td>Body temp °C</td>
<td>37.68±0.37a</td>
<td>38.2±0.63a</td>
<td>37.42±0.18a</td>
<td>37.76±1.1a</td>
</tr>
<tr>
<td>Respiratory rate / min</td>
<td>125.8±17.42a</td>
<td>144±22.27a</td>
<td>128.8±20.92a</td>
<td>104±21.540a</td>
</tr>
<tr>
<td>Bleed time , second</td>
<td>46±4.30a</td>
<td>85±8.7b</td>
<td>71±5.5b</td>
<td>81±7.6b</td>
</tr>
<tr>
<td>Clott. time , second</td>
<td>60±7.1a</td>
<td>213±10.8b</td>
<td>109±12.5b</td>
<td>162±14.29b</td>
</tr>
</tbody>
</table>

The values are Mean ± SE. a mean significance in comparison with 0 time of treated animals, b in comparison with 2 days, c in comparison with 4 days. significance at P < 0.05.

The results revealed that total erythrocytes none significantly decreased in day 11. Hemoglobin concentration, PCV, MCV, MCH significantly decreased. MCHC did not show significant changes (Table -2-).

Table2. Total erythrocytes count, HB concentration, PCV and erythrocyte indices of rabbits exposed to Senna.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>RBCx10³/ mm³</td>
<td>5.04±0.19a</td>
<td>5.12±0.41a</td>
<td>5.56±0.31a</td>
<td>4.65±0.51a</td>
</tr>
<tr>
<td>Hb g/dl</td>
<td>10.94±0.24a</td>
<td>10.34±0.57a</td>
<td>10.4±0.16a</td>
<td>10.2±0.33b</td>
</tr>
<tr>
<td>PCV%</td>
<td>32.2±0.73a</td>
<td>30.4±1.57a</td>
<td>30.6±0.51b</td>
<td>29.8±1.02b</td>
</tr>
<tr>
<td>MCVft</td>
<td>64.16±2.26a</td>
<td>61.20±6.97a</td>
<td>55.7±2.99b</td>
<td>66.5±6.14a</td>
</tr>
<tr>
<td>MCH pg</td>
<td>21.8±0.78a</td>
<td>20.82±2.44a</td>
<td>18.94±1.06b</td>
<td>22.73±1.96a</td>
</tr>
<tr>
<td>MCHC g/dl</td>
<td>33.98±0.81a</td>
<td>33.98±0.17a</td>
<td>33.99±0.17a</td>
<td>34.2±0.28a</td>
</tr>
</tbody>
</table>

The values are Mean ± SE. a mean significance in comparison with 0 time of treated animals, b in comparison with 2 days, c in comparison with 4 days. significance at P < 0.05.

The results revealed that total leucocytes count none significantly changed. eosinophil %, Monocytes % none significantly decreased. Heterophils % none significantly increased. Lymphocytes% none significantly decreased in day 4, but none significantly increased in day 11. Basophiles% significantly decreased in day 11 (Table -3-).
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Table 3. The total and differential leucocytes counts of rabbits exposed to Senna.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>Day</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC x 10^7</td>
<td>I</td>
<td></td>
<td>2.621±0.57a</td>
<td>3.848±0.90a</td>
<td>2.786±0.959a</td>
<td>2.728±0.405a</td>
</tr>
<tr>
<td>Eosinophils%</td>
<td>I</td>
<td></td>
<td>3±0.89a</td>
<td>2.2±0.97a</td>
<td>1.8±0.37a</td>
<td>2±0.45a</td>
</tr>
<tr>
<td>Heterophils</td>
<td>I</td>
<td></td>
<td>41.6±4.59a</td>
<td>43.6±4.95a</td>
<td>49±2.07a</td>
<td>41.2±4.44a</td>
</tr>
<tr>
<td>Monocytes</td>
<td>I</td>
<td></td>
<td>3.8±1.16a</td>
<td>2.6±0.81a</td>
<td>2±0.22a</td>
<td>2.2±0.58a</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>I</td>
<td></td>
<td>48.8±6.17a</td>
<td>48.8±5.53a</td>
<td>44.6±1.63</td>
<td>57.2±6.66</td>
</tr>
<tr>
<td>Basophiles%</td>
<td>I</td>
<td></td>
<td>2.8±0.20a</td>
<td>2.8±0.66a</td>
<td>2.6±0.68a</td>
<td>1.8±0.37b</td>
</tr>
</tbody>
</table>

The values are Mean ± SE. a mean significance in comparison with 0 time of treated animals, b in comparison with 2 days, c in comparison with 4 days. significance at P < 0.05.

3.2. Second Part

The results revealed that body weight of 1st and 4th groups did not show any significant changes in 2nd group none significantly changed. In 3rd group none significantly decreased. Body temperature significantly increased in 1st and 2nd groups. In group 3rd none significantly increased. In 4th group decreased. The results revealed that heart rates in 1st group none significantly increased. In 2nd group none significant increase in day 7, but significantly increased in day 9, 12 and 22. In 3rd group significantly increased in day 7, 9, 12 and 22. In 4th group none significantly decreased then increased significantly in day 9 and 12. The result revealed that respiratory rates in 1stand 3rd groups none significantly increased, but in day 9, 12 and 22 was significantly increased. In 2nd group none significantly decreased in day 7 then significantly increased in day 9, 12 and 22. In 4th group significantly decreased in day 7 but increased significantly in day 12. (Table 4-).

Table 4. The changes in the body weight, body temperature, Heart rates, respiratory rates of rabbits exposed to Senna

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>Day</th>
<th>0</th>
<th>7</th>
<th>9</th>
<th>12</th>
<th>22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight kg</td>
<td>I</td>
<td></td>
<td>1.323±0.111a</td>
<td>1.353±0.051a</td>
<td>1.306±0.038a</td>
<td>1.378±0.041a</td>
<td>1.349±0.048a</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td></td>
<td>1.380±0.082a</td>
<td>1.220±0.083a</td>
<td>1.273±0.114a</td>
<td>1.308±0.066a</td>
<td>1.480±0.051a</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td>1.310±0.093a</td>
<td>1.288±0.066a</td>
<td>1.438±0.103a</td>
<td>1.403±0.085a</td>
<td>1.275±0.031a</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td>1.406±0.082a</td>
<td>1.428±0.101a</td>
<td>1.335±0.053a</td>
<td>1.371±0.061a</td>
<td>1.380±0.200a</td>
</tr>
<tr>
<td>Body temperature Oc</td>
<td>I</td>
<td></td>
<td>38.95±0.26a</td>
<td>38.58±0.17a</td>
<td>38.9±0.1a</td>
<td>39.85±0.1c</td>
<td>39.18±0.25b</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td></td>
<td>38.6±0.04a</td>
<td>38.28±0.44a</td>
<td>38.67±0.29a</td>
<td>38.9±0.14b</td>
<td>39.8±0.26b</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td>39±0.49a</td>
<td>38.08±0.32a</td>
<td>38.83±0.37a</td>
<td>39.75±0.22a</td>
<td>39.4±0.18a</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td>39.32±0.17a</td>
<td>38.38±0.18b</td>
<td>38.68±0.26b</td>
<td>39.33±0.28a</td>
<td>39.9±0.20b</td>
</tr>
<tr>
<td>Heart rates /min</td>
<td>I</td>
<td></td>
<td>199.5±21.45a</td>
<td>212±4.90a</td>
<td>225±9.57a</td>
<td>220±14.14a</td>
<td>215±17.10a</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td></td>
<td>174±3.46a</td>
<td>160±23.09a</td>
<td>213.33±6.78b</td>
<td>226.67±8.33b</td>
<td>246.67±6.7b</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td>159±6.61a</td>
<td>192±10.83b</td>
<td>225±15b</td>
<td>237±15.3b</td>
<td>205±20.62a</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td>182±12.0 a</td>
<td>169±4.12a</td>
<td>223±13.5b</td>
<td>222±8.41b</td>
<td>220±9.2</td>
</tr>
<tr>
<td>Respiratory rates /min</td>
<td>I</td>
<td></td>
<td>231.5±13.12a</td>
<td>245±9.57a</td>
<td>256±5.42b</td>
<td>280±11.55b</td>
<td>270±12.91b</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td></td>
<td>212.5±8.5a</td>
<td>163±10.49b</td>
<td>246.67±6.67b</td>
<td>273.33±6.67b</td>
<td>266.67±6.5b</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td>230±5.77a</td>
<td>242±8.41a</td>
<td>245±5.0b</td>
<td>275±9.57b</td>
<td>285±9.57b</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td>234±8.72a</td>
<td>192±18.18b</td>
<td>255±15a</td>
<td>270±12.91B</td>
<td>265±11</td>
</tr>
</tbody>
</table>

Values are M ± SEM I: group 1 exposed to plant with diet; II: group exposed to plant in decoction form; III: group as aqueous extract; IV: group as alcohol extract. The level of significance was P < 0.05.

The results revealed that bleeding time increased none significantly in day 7 and 9 but become significant in day 12, in 1st group. In 2nd group none significantly increased in day 7, but become significant in day 9 and 12. In 3rd group none significantly decreased in day 7, and then increased significantly in day 9 and 12. In 4th group decreased none significantly in day 7 but become significantly decreased in day 9 the results revealed that clotting time in 1st and 3rd groups significantly increased in all time post exposure. In 2nd group none significantly decreased in day 9 in 4th group none significantly changed. The results revealed that hemoglobin concentration significantly increased in day 7 and 9 in 1st group in 2nd and 4th groups none significantly changed. In 3rd group significantly increased in day 9. The results revealed that PCV% in 1st group significantly increased in day 7 and 9. In 2nd and 4th groups no significant changes. In 3rd group significantly increased in day 9. Total erythrocytes significantly increased in 1stgroup. But in other groups none significantly changed. The results revealed that platelets count in 1st; 3rd and 4th groups
The results revealed that total leucocytes count in 1st group significantly increased in day 22. In 2nd, 3rd and 4th groups none significantly decreased. (Table 5).

Table 5. The changes in the Bleeding time, Clotting time, hemoglobin PCV, Total erythrocytes, platelets, and leucocytes of rabbits exposed to Senna

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>Day</th>
<th>7</th>
<th>9</th>
<th>22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding time, seconds</td>
<td>I</td>
<td>32.5±4.33a</td>
<td>48.75±8.75a</td>
<td>48.75±8.26a</td>
<td>62.5±9.46b</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>30±2.04a</td>
<td>40±6.77a</td>
<td>43.33±3.33b</td>
<td>46.67±6.67b</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>42.5±5.95a</td>
<td>32.5±4.33a</td>
<td>53.75±4.73b</td>
<td>52.5±6.29b</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>53±4.39a</td>
<td>45±8.66a</td>
<td>32.5±4.44b</td>
<td>35.1±2.10</td>
</tr>
<tr>
<td>Clotting time, seconds</td>
<td>I</td>
<td>80±8.42a</td>
<td>170±35.36b</td>
<td>47.5±8.29b</td>
<td>202.5±78.78b</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>153.75±28.97a</td>
<td>153.75±29.25a</td>
<td>96.67±18.56a</td>
<td>158.33±29.49a</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>62.5±8.54a</td>
<td>95±14.43b</td>
<td>47.5±8.54a</td>
<td>140±10.8b</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>77±18.28a</td>
<td>63.75±2.39a</td>
<td>73.75±16.12a</td>
<td>70.67±8.70</td>
</tr>
<tr>
<td>Hb g/ dl</td>
<td>I</td>
<td>10.88±0.59a</td>
<td>12.23±0.20b</td>
<td>12.33±0.33b</td>
<td>11.03±0.28a</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>11.48±0.31a</td>
<td>11.25±0.28a</td>
<td>11.5±0.21a</td>
<td>11.8±0.26a</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>11.23±0.27a</td>
<td>11.75±0.39a</td>
<td>12.33±0.45b</td>
<td>11.6±0.42a</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>11.16±0.38a</td>
<td>11.88±0.39a</td>
<td>11.6±0.42a</td>
<td>11.20±0.25</td>
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<tr>
<td>PCV %</td>
<td>I</td>
<td>32±1.78a</td>
<td>36±25.63b</td>
<td>36.25±0.85b</td>
<td>36.52±0.87a</td>
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<tr>
<td></td>
<td>II</td>
<td>34±0.82a</td>
<td>33.25±0.75a</td>
<td>34±0.58a</td>
<td>34.67±0.88a</td>
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<td>III</td>
<td>33.25±0.85a</td>
<td>34.5±1.19a</td>
<td>36.25±1.11b</td>
<td>34±1.22a</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>32±1.12a</td>
<td>35±1.29a</td>
<td>34±1.29a</td>
<td>33±1.19</td>
</tr>
<tr>
<td>RBC x106 / mm3</td>
<td>I</td>
<td>4.12±0.29a</td>
<td>12.23±0.20b</td>
<td>12.33±0.33b</td>
<td>11.03±0.28a</td>
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<tr>
<td></td>
<td>II</td>
<td>4.15±0.14a</td>
<td>11.25±0.28a</td>
<td>11.5±0.21a</td>
<td>11.8±0.26a</td>
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<td></td>
<td>III</td>
<td>4.36±0.48a</td>
<td>11.75±0.39a</td>
<td>12.33±0.45b</td>
<td>11.6±0.42a</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>4.75±0.20a</td>
<td>11.88±0.39a</td>
<td>11.6±0.42a</td>
<td>11.20±0.25</td>
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<tr>
<td>Platelets</td>
<td>I</td>
<td>376.13±79.74a</td>
<td>327.75±100.18a</td>
<td>303.75±52.42a</td>
<td></td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>382.5±81.17a</td>
<td>320.63±56.91a</td>
<td>315.3±173.68a</td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>368.63±106.94a</td>
<td>331.88±153.45a</td>
<td>338±120.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>455±480.77a</td>
<td>318.38±84.55a</td>
<td>328±68.65</td>
<td></td>
</tr>
<tr>
<td>WBC x103/ mm3</td>
<td>I</td>
<td>3.166±0.193</td>
<td>5.310±0.686b</td>
<td>5.04±0.97a</td>
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<tr>
<td></td>
<td>II</td>
<td>6.121±0.872a</td>
<td>5.04±0.97a</td>
<td>3.094±0.328a</td>
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<tr>
<td></td>
<td>III</td>
<td>4.521±0.849a</td>
<td>4.521±0.849a</td>
<td>4.521±0.849a</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>4.545±0.394a</td>
<td>4.545±0.394a</td>
<td>4.545±0.394a</td>
<td></td>
</tr>
</tbody>
</table>

Values are M ± SEM: I: group 1 exposed to plant with diet; II: group exposed to plant in decoction form; III: group as aqueous extract; IV: group as alcohol extract. The level of significance was P < 0.05.

Table 6. The differential leucocytes counts of rabbits exposed to Senna.

<table>
<thead>
<tr>
<th>parameters</th>
<th>Group</th>
<th>Day</th>
<th>7</th>
<th>9</th>
</tr>
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<tr>
<td>Heterophils%</td>
<td>I</td>
<td>56.5±4.09</td>
<td>41.75±4.36a</td>
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<td></td>
<td>II</td>
<td>54.75±5.57a</td>
<td>40.25±5.57b</td>
<td>45±7.22a</td>
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<tr>
<td></td>
<td>III</td>
<td>54.75±6.33a</td>
<td>44±1.87a</td>
<td>46±3.55</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>56.6±4.78a</td>
<td>43.5±3.75b</td>
<td>45±4.25</td>
</tr>
<tr>
<td>Lymphocyte%</td>
<td>I</td>
<td>36.75±3.35a</td>
<td>47.25±7.33a</td>
<td>39.75±7.06a</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>33.25±2.69a</td>
<td>44.5±4.17b</td>
<td>46±4.58b</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>39±5.64a</td>
<td>50.25±2.36b</td>
<td>47±3.0</td>
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<tr>
<td></td>
<td>IV</td>
<td>32.4±4.61a</td>
<td>47.5±4.79b</td>
<td>49±3.5</td>
</tr>
<tr>
<td>Eosinophils%</td>
<td>I</td>
<td>2.5±0.29a</td>
<td>3.25±1.25a</td>
<td>2.75±0.63a</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>3±0.71a</td>
<td>4±0.5a</td>
<td>2.33±0.33b</td>
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<td>III</td>
<td>3±0.71a</td>
<td>2.25±0.25a</td>
<td>2.65±0.32</td>
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<td>IV</td>
<td>2.8±0.49a</td>
<td>3±1a</td>
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<tr>
<td>Monocytes %</td>
<td>I</td>
<td>3.75±0.85a</td>
<td>6.25±0.75b</td>
<td>4.5±0.87a</td>
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<tr>
<td></td>
<td>II</td>
<td>8.5±2.83a</td>
<td>9.25±1.89a</td>
<td>5±3.06a</td>
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<tr>
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<td>III</td>
<td>5.25±0.25a</td>
<td>2.75±0.85b</td>
<td>3.75±0.92</td>
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<td></td>
<td>IV</td>
<td>6.4±1.91a</td>
<td>5.25±1.31a</td>
<td>5.3±5.12</td>
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<tr>
<td>Basophiles%</td>
<td>I</td>
<td>1.5±0.29a</td>
<td>1.5±0.5a</td>
<td>1.25±0.63</td>
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<td></td>
<td>II</td>
<td>0.5±0.5a</td>
<td>1.25±0.25a</td>
<td>1.5±0.9a</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>0.5±0.29a</td>
<td>0.5±0.29a</td>
<td>0.75±0.32</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>2±0.91a</td>
<td>0.75±0.25a</td>
<td>1.25±0.35</td>
</tr>
</tbody>
</table>

Values are M ± SEM: I: group 1 exposed to plant with diet; II: group exposed to plant in decoction form; III: group as aqueous extract; IV: group as alcohol extract. The level of significance was P < 0.05.
The results revealed that Heterophils in 1st and 3rd groups none significantly decreased in day 7. In 2nd and 4th groups significantly decreased in day 7. Lymphocytes In 1st group none significantly increased in 7 and 9 day. 2nd group significantly increased in day 7 and 9. In 3rd and 4th groups significantly increased in day 7. Esinophils in 1st group none significantly increased in day 7. In 2nd group significantly increased in day 7. In 3rd and 4th group none significantly changed. Monocytes significantly increased in day 7 in 1st group. In 2nd group none significantly increased in day 7, but decreased none significantly in day 9. In 3rd group decreased significantly in day 7. In 4th group decreased none significantly. Basophiles none significantly changed in all groups. (Table -6).

The histopathological changes in rabbits exposed to Cassia Senna showed: Aqueous extract (Figure 1-A, B, C): section in kidney (Figure 1-A) shows marked inflammatory cells particularly mononuclear cells infiltration in the interstitial tissues. Section in liver (Figure 1-B) shows inflammatory cells in dilated sinusoids. Section in spleen (Figure 1-C) shows depletion of white pulp with hemosiderin in red pulp. While in those exposed to alcohol extract (Figure 1- D, E) showed: section in liver (Figure 1- D). Shows inflammatory cells in fibrosis portal area. Section in liver (Figure 1-E).shows fibrosis in portal area around hyperplasia of bile ducts.

![Histopathological section in kidney](image1)

**Fig1-A.** (Aqueous extract): Histopathological section in kidney shows marked inflammatory cells particularly mononuclear cells infiltration in the interstitial tissue (H&E stain 400X).

**Fig1-B.** (Aqueous extract): Histopathological section in liver shows inflammatory cells in dilated sinusoids (H&E stain 400X).

**Fig1-C.** (Aqueous extract): Histopathological section in spleen shows depletion of white pulp with hemosiderin in red pulp (H&E stain 400X).

**Fig1-D.** (Alcoholic extract): Histopathological section in liver shows inflammatory cells in fibrosis portal area (H&E stain 400X).

**Fig1-E.** (Alcoholic extract): Histopathological section in liver of animal of twenty five group shows fibrosis in portal area around hyperplasia of bile ducts (H&E stain 400X).

4. DISCUSSION

The results of present study revealed that the main signs showed by exposed rabbits in both 1st and 2nd parts were soft feces. Ibrahim et al., (2012) referred that rabbits received S. Alexandria at 50 mg / kg / day showed diarrhea, while those were given the dose at 100 mg / kg / day showed no clinical signs. One rabbits that were given the plant at 300 mg/kg/day died at day 10. Diarrhea appeared might be due to enteritis and erosion on the intestinal mucosa. Death in rabbits given higher doses indicates toxicity of the active ingredient in the plant and mostly due to the severe damage of the vital organs seen in the histopathology.

Sennosides, relieve severe constipation. Normally. The senno sides do not alter the routine defecation time pastern and soft the stool. (WHO, 1999; Qadry et al., 2005).
Hematological and Clinical Changes in Rabbits Exposed to Cassia Senna

The present study results in the 1st part revealed that body weight, body temperature, and respiratory rates were none significantly changed. Heart rates significantly increased. While in 2nd part of the study the body weight of 1st, 2nd and 4th groups did not show any significant changes. In 3rd group none significantly decreased. Body temperature significantly increased in 1st and 2nd groups. In group 3rd none significantly increased. In 4th group decreased. Heart rates in 1st group none significantly increased. In 2nd group none significant increase in day 7, but significantly increased in day 9, 12 and 22. In 3rd group significantly increased in day 7, 9, 12 and 22. In 4th group none significantly decreased then increased significantly in day 9 and 12. Respiratory rates in 1st and 3rd groups none significantly increased, but in day 9, 12 and 22 was significantly increased. In 2nd group none significantly decreased in day 7 then significantly increased in day 9, 12 and 22. In 4th group significantly decreased in day 7 but increased significantly in day 12.

(Ibrahim et al., 2012), no significant differences in body weight in rabbits received plant at dose rate of 50 and 100 mg / kg / day during the whole period of the experiment, while body weight of rabbits that given the extract at 300 mg / kg / day significantly decreased at weeks 2 and 4 of the experiment. This growth depression was probably due to reduced feed intake and / or inefficiency of feed utilization. Rats treated with various doses of hydro ethanolic extract of S. alata had progressive weight gained. This increase in weight is significantly different from that of the control group. The progressive increase in body weight at doses 500 and 1000 mg / kg of female and male rats during 26 days of administration of aqueous ethanol extract of S. alata may indicate the improvement of the nutritional state of the animal. (Pimeet et al., 2006). Oral administration of S. siamae for 28 days produced neither mortality nor changes in behavior or any physiological activities. Results obtained showed that the extract insignificantly affected the mean body and organs weight of Wistar rats. (Otimenyinet al., 2010). The increase in body weight observed were due to normal growth resulting from nutritious feeding. This increases cuts across the groups, and there was no significant difference when treated groups were compared with the control group at different stages of this experiment (Otimenyinet al., 2010).

The results of 1st part of this study showed Bleeding and clotting times were significantly increased. The results revealed that bleeding time increased none significantly in day 7 and 9 but become significant in day 12, in 1st group. In 2nd group none significantly increased in day 7, but become significant in day 9 and 12. In 3rd group none significantly decreased in day 7, and then increased significantly in day 9 and 12. In 4th group decreased none significantly in day 7 but become significantly decreased in day 9. The results revealed that clotting time in 1st and 3rd groups significantly increased in all time post exposure. In 2nd group none significantly decreased in day 9 in 4th group none significantly changed.

The results of 1st part of our study revealed that total erythrocytes none significantly decreased. Hemoglobin concentration, PCV, MCV, MCH significantly decreased. MCHC did not show significant changes. The results revealed that haemoglobin concentration significantly increased in day 7 and 9 in 1st group. In 2nd and 4th groups none significantly changed. In 3rd group significantly increased in day 9. The results revealed that PCV% in 1st group significantly increased in day 7 and 9. In 2nd and 4th groups no significant changes. In 3rd group significantly increased in day 9. The crude aqueous extract of the root of S. siamae showed no significant effect on hematological, histological and biochemical parameters evaluated.

(Ibrahim et al., 2012) haematologically, Hb concentration decreased in all groups at week 2 through week 4, but this decrease was not significant in group given the dose at 50 and 100 mg / kg / day. Hb decrease was significant at 300 mg / kg / day. This decrease might have been due to disorder in the activity of ferritin which is important in iron metabolism or due to iron deficiency. Red blood cells decreased significantly in all groups throughout the experiment this might have been due either to haemolysis or disorder in the bone marrow function as well as bleeding leading to anemia (Eichner, 1973.1984) PCV were decreased in all groups, The MCV differed significantly in the group given a doses of 100 mg / kg / day and group received 300 mg / kg / day. No significant difference in all groups in MCH (Ibrahim et al., 2012).

Hematological parameters (PCV, Hb, WBC, and RBC) and biochemical parameters were not affected by the extract of S. siamae. The rats that received the extract had dose dependent changes in the WBC, PCV, and Hb. (Otimenyinet al., 2010).
The hematological status after 26 days of oral administration of hydro alcoholic extract of S. alata no significant variation for RBC, and WBC were observed. However, the variation was significantly different for platelets. In general the results showed that the values for the RBC and WBC were slightly increased in female and male groups compared to the control. The small transient of values observed in blood hematology did not show any dose responsiveness. (Piemet et al., 2006).

The results revealed that total leucocytes count in 1st group significantly increased in day 22. In 2nd, 3rd and 4th groups none significantly decreased. None significantly changed in all groups. Monocytes significantly increased in day 7 in 1st group. In 2nd group none significantly increased in day 7, but decreased none significantly in day 9. In 3rd group decreased significantly in day 7. In 4th group decreased none significantly. Eosinophils in 1st group none significantly increased in day 7. In 2nd group significantly increased in day 7. In 3rd and 4th group none significantly changed. Heterophils in 1st and 3rd groups none significantly decreased in day 7. In 2nd and 4th groups significantly decreased in day 7. Lymphocytes %in 1st group none significantly increased in 7 and 9 days. 2nd group significantly increased in day 7 and 9. In 3rd and 4th groups significantly increased in day 7. In 2nd part of the present study

The results revealed that platelets count in 1st, 3rd and 4th groups none significantly decreased. In 2nd group none significantly decreased in day 7 but increased none significantly in day 9.

Ibrahim et al (2012) found no significant pathological changes were observed in rabbits given a dose of 50 mg / kg / day. However, at higher doses alterations in the levels of blood hematological parameters, transaminase, Creatinine, albumin, and globulin were observed, such changes are likely to occur due to spleen, hepatic and renal injury, which was confirmed by histopathological analysis. Senna alata and S. podocarpa significantly elevated the hematocrit of albino rats, with no significant changes in the white blood cells, platelets and leucocytes population. S. podocarpa did not significantly affect the population affect the population of monophils, whereas S. alata on the other hand significantly increased the monophils population. The population of eosinophils was significantly increased.

The intake of hydromethanolic leaf extract of S. alata and S. Podocarpa did not affect the functions of the bone marrow as reflected by the values of WBC (total and differential) and platelets, neither was they quantitatively nor qualitatively destroyed, consequently leucopoiesis was not affected. It is likely that the extract may have affected the circulating erythrocytes and possibly hematopoiesis as reflected by changes in PCV and eosinophils. The increase in PCV values may be taken to be a reflection of the hydration states of RBCs. (Adebsen, 2013).

S. siamea root is rich in alkaloids, saponin, phylobatannins, flavonoids, tannin, steroid, carbohydrate, glycoside and anthraquinone. Its leaves have been reported to be toxic. (Otimenyin et al., 2010). the leaves of S. siamea have been reported to be toxic. The toxic effect of the leaves of Si. Simea was linked to the presence of tannin, oxalate, phytate (Ali Smith, 2009.) andbarakol (Padumanonda and Gritsanapan, 2006). Tanit (Padumanonda and Gritsanapan, 2006).

5. CONCLUSION

The data suggest that administration of the aqueous extract of S. Alexandrina pods at 50 mg /kg / day is not toxic. The observed toxic effect might be due to higher doses and / or frequency of administration. Although in traditional medicine the extract is administrated at a low dose, the results suggest the necessity of standardization of the drug.

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REFERENCES


Hematological and Clinical Changes in Rabbits Exposed to Cassia Senna


