

## 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 piolet 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 , 2<sup>nd</sup> group exposed to plant in decoction form at a dose 1 gm / kg / day, 3<sup>rd</sup> group as aqueous extract at a doe 100 mg / kg / day , and 4<sup>th</sup> group as alcohol extract at a dose 50 mg / kg b.wt / day for 20 says .

**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 clotting times were significantly increased during all time of experiment. Total leucocytes count, eosinophils%, Heterophils % Monocytes %, Lymphocytes% showed none significant changes .Basophiles% 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 1<sup>st</sup>, 2<sup>nd</sup> groups. Heart rates in 2<sup>nd</sup> and 3<sup>rd</sup> groups significantly increased. Respiratory rates in 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> groups significantly increased. In 4<sup>th</sup> group significantly decreased in day 7 but increased significantly in day 12. Bleeding time increased significantly in 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> groups significantly increased. In 4<sup>th</sup> group decreased significantly. Clotting time in 1<sup>st</sup> and 3<sup>rd</sup> groups significantly increased. Total leucocytes count in 1<sup>st</sup> group significantly increased in day 22. Basophils% none significantly changed in all groups .Monocytes significantly increased in day 7 in 1<sup>st</sup> group, in 3<sup>rd</sup> group decreased significantly. Esinophils 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.

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### **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 *italica* (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 angustifolia* Vahl) 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, aloë- 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 Caesalpinaceae), cultivated in the Sudan and was formerly exported through Alexandria is mentioned in all famous herbals of the 15<sup>th</sup> and 16<sup>th</sup> 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 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). Mainsennosides 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 splenic enlargements, anemia, typhoid, cholera, biliousness, jaundice , pout , rheumatism, , tumors , foul breath and bronchitis , and probably in leprosy . Itis employed in the treatment of amoebic dysentery as an anthelmintic and as a mild liver stimulant. Leaves are astringent, bitter, sweet, acrid, thermogenic, catharitic, depurative, liver tonic, anthelmintic, colagogue, expectorant, febrifuge. Useful in constipation, abdominal disorders, leprosy, skin disorders, leucoderma, splenomegaly, hepatomegaly, dyspepsia, cough, and bronchitis. (Balasankaret al2013)

Diseet al (2011).Cassia angustifoliaVahl (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 piolet 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.

## Hematological and Clinical Changes in Rabbits Exposed to Cassia Senna

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  $22 \pm 1^\circ\text{C}$ , 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, 2<sup>nd</sup> group exposed to plant in decoction form at a dose rate of 1 g/kg b.wt/day, 3<sup>rd</sup> group as aqueous extract at a dose rate 100 mg/kg b.wt/day, and 4<sup>th</sup> group as alcohol extract at a dose rate of 50 mg/kg b.wt/day for 20 days. The same parameters depended in 1<sup>st</sup> 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 signs 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

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

The values are Mean  $\pm$  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.

Parameter.	Day			
	0	2	4	11
RBCx10 <sup>6</sup> / mm <sup>3</sup>	5.04 $\pm$ 0.19a	5.12 $\pm$ 0.41 a	5.56 $\pm$ 0.31a	4.65 $\pm$ 0.51a
Hb g/ dl	10.94 $\pm$ 0.24a	10.34 $\pm$ 0.57a	10.4 $\pm$ 0.16a	10.20 $\pm$ 0.33b
PCV%	32.2 $\pm$ 0.73a	30.4 $\pm$ 1.57a	30.6 $\pm$ 0.51b	29.8 $\pm$ 1.02b
MCVft	64.16 $\pm$ 2.26a	61.20 $\pm$ 6.97a	55.71 $\pm$ 2.99b	66.52 $\pm$ 6.14a
MCH pg	21.8 $\pm$ 0.78a	20.82 $\pm$ 2.44a	18.94 $\pm$ 1.06b	22.73 $\pm$ 1.96a
MCHC g/ dl	33.98 $\pm$ 0.81a	33.98 $\pm$ 0.17a	33.99 $\pm$ 0.17a	34.24 $\pm$ 0.28a

The values are Mean  $\pm$  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-).

**Table3.** The total and differential leucocytes counts of rabbits exposed to Senna.

Parameter.	Day			
	0	2	4	11
WBCx10 <sup>3</sup> / mm <sup>3</sup>	2.621±0.57a	3.848±0.90a	2.786±0.959a	2.728±0.405a
Eosinophils%	3±0.89a	2.2±0.97a	1.8±0.37a	2±0.45a
Heterophils	41.6±6.59a	43.6±4.95a	49±2.07a	41.2±4.44a
Monocytes	3.8±1.16a	2.6±0.81a	2±0.22a	2.2±0.58a
Lymphocyte	48.8±6.17a	48.8±5.53a	44.6±1.63	57.2±6.66
Basophiles%	2.8±0.20a	2.8±0.66a	2.6±0.68a	1.8±0.37b

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 1<sup>st</sup> and 4<sup>th</sup> groups did not show any significant changes. In 2<sup>nd</sup> group none significantly changed. In 3<sup>rd</sup> 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 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. (Table -4-).

**Table4.** The changes in the body weight, body temperature, Heart rates, respiratory rates of rabbits exposed to Senna

Parameter.	Group	Day				
		0	7	9	12	22
Body weight kg	I	1.323±0.111a	1.353±0.051a	1.306±0.038a	1.378±0.041a	1.349±0.048a
	II	1.380±0.082a	1.220±0.083a	1.273±0.114a	1.308±0.066a	1.480±0.051a
	III	1.310±0.093a	1.288±0.066a	1.438±0.103a	1.403±0.085a	1.275±0.031a
	IV	1.406±0.082a	1.428±0.101a	1.335±0.053a	1.371±0.061a	1.380±0.200
Body temperature Oc	I	38.95±0.26a	38.58±0.17a	38.9±0.1a	39.85±0.1c	39.18±0.25b
	II	38.6±0.04a	38.28±0.44a	38.67±0.29a	38.9±0.14b	39.8±0.26b
	III	39.0±0.49a	38.08±0.32a	38.83±0.37a	39.75±0.22a	39.4±0.18a
	IV	39.32±0.17a	38.38±0.18b	38.68±0.26b	39.33±0.28 a	38.9±0.20
Heart rates / min	I	199.5±21.45a	212±4.90a	225±9.57a	220±14.14a	215±17.10a
	II	174±3.46a	160±23.09a	213.33±6.67b	226.67±8.33b	246.67±6.67b
	III	159±6.61a	192±10.83b	225±15b	237±13.5b	205±20.62a
	IV	182±12.0 a	169±4.12a	223±13.5b	222±8.41b	220±9.2
Respiratory rates/ min	I	231.5±13.12a	245±9.57a	256±5.42b	280±11.55b	270±12.91b
	II	212.5±8.5a	163±10.49b	246.67±6.67b	273.33±6.67b	266.67±6.5b
	III	230±5.77a	242±8.41a	245±5.0b	275±9.57b	285±9.57b
	IV	234±8.72a	192±18.18b	255±15a	270±12.91B	265±11

Values are  $M \pm SEM$  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 1<sup>st</sup> group. In 2<sup>nd</sup> group none significantly increased in day 7, but become significant in day 9 and 12. In 3<sup>rd</sup> group none significantly decreased in day 7, and then increased significantly in day 9 and 12. In 4<sup>th</sup> 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 1st group. But in other groups none significantly changed. The results revealed that platelets count in 1st; 3rd and 4th groups

## Hematological and Clinical Changes in Rabbits Exposed to Cassia Senna

none significantly decreased. In 2nd group none significantly decreased in day 7 but increased none significantly in day 9. 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- ).

**Table5.** The changes in the Bleeding time, Clotting time, hemoglobin PCV, Total erythrocytes, platelets, and leucocytes of rabbits exposed to Senna

Parameter.	Group	Day			
		0	7	9	22
Bleeding time, seconds	I	32.5±4.33a	48.75±8.75a	48.75±8.26a	62.5±9.46b
	II	30±2.04a	40±6.77a	43.33±3.33b	46.67±6.67b
	III	42.5±5.95a	32.5±4.33a	53.75±4.73b	52.5±6.29b
	IV	53±9.3a	45±8.66a	32.5±1.44b	35.1±2.10
Clotting time, seconds	I	80±8.42a	170±35.36b	47.5±8.29b	202.5±78.78b
	II	153.75±28.97a	153.75±29.25a	96.67±18.56a	158.33±29.49a
	III	62.5±8.54a	95±14.43b	47.5±8.54a	140±10.8b
	IV	77±18.28a	63.75±2.39a	73.75±16.12a	70.67±8.70
Hb g/ dl	I	10.88±0.59a	12.23±0.20b	12.33±0.33b	11.03±0.28a
	II	11.48±0.31a	11.25±0.28a	11.5±0.21a	11.8±0.26a
	III	11.23±0.27a	11.75±0.39a	12.33±0.45b	11.63±0.42a
	IV	11.16±0.38a	11.88±0.39a	11.63±0.42a	11.20±0.25
PCV %	I	32±1.78a	36.25±0.63b	36.25±0.85b	32.5±0.87a
	II	34±0.82a	33.25±0.75a	34±0.58a	34.67±0.88a
	III	33.25±0.85a	34.5±1.19a	36.25±1.11b	34±1.22a
	IV	32.6±1.12a	35±1.29a	34±1.29a	33±1.19
RBC x106 / mm3	I	4.12±0.29a			5.42±0.33b
	II	4.15±0.14a			4.1±0.33a
	III	4.36±0.48a			3.36±0.12
	IV	4.75±0.20a			5.0±0.15
Platelets	I	376.13±79.74a	327.75±100.18a	303.75±52.42a	
	II	382.5±81.17a	320.63±56.91a	513.5±173.68a	
	III	368.63±106.94a	331.88±153.45a	338±120.5	
	IV	455.4±80.77a	318.38±84.55a	328±68.65	
WBC x103/ mm3	I	3.166±0.193			5.310±0.686b
	II	6.121±0.872a			5.504±0.907a
	III	4.521±0.849a			3.094±0.328a
	IV	4.545±0.394a			4.210±0.287a

Values are  $M \pm SEM$  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  $P < 0.05$ .

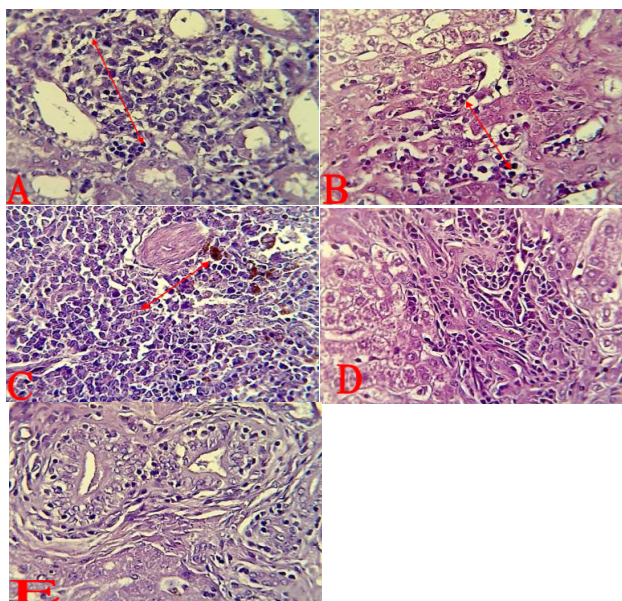
**Table6.** The differential leucocytes counts of rabbits exposed to Senna.

parameters	Group	Day		
		0	7	9
Heterophils%	I	56.5±4.09	41.75±6.36a	53.75±6.43a
	II	54.75±3.57a	40.25±5.57b	45±7.72a
	III	54.75±6.33a	44±1.87a	46±3.55
	IV	56.6±4.78a	43.5±3.75b	45±4.25
Lymphocyte%	I	36.75±3.35a	47.25±7.33a	39.75±7.06a
	II	33.25±2.69a	44.5±4.17b	46±4.58b
	III	39±5.64a	50.25±2.36b	47±3.0
	IV	32.2±4.61a	47.5±4.79b	49±3.5
Eosinophils%	I	2.5±0.29a	3.25±1.25a	2.75±0.63a
	II	3±0.71a	4±0.5a	2.33±0.33b
	III	3±0.71a	2.25±0.25a	2.65±0.32
	IV	2.8±0.49a	3±1 a	2.98±0.50
Monocytes %	I	3.75±0.85a	6.25±0.75b	4.5±0.87a
	II	8.5±2.83a	9.25±1.89a	5±3.06a
	III	5.25±0.25a	2.75±0.85b	3.75±0.92
	IV	6.4±1.91a	5.25±1.31a	5.35±1.26
Basophiles%	I	1.5±0.29a	1.5±0.5a	1.25±0.63
	II	0.5±0.5a	1.25±0.25a	1.5±0.9a
	III	0.5±0.29a	0.5±0.29a	0.75±0.32
	IV	2±0.91a	0.75±0.25a	1.25±0.35

Values are  $M \pm SEM$  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. 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. 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.



**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 r shows depletion of white pulp with hemosidren in red pulp ↔ (H&E stain 400X).

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

**FigE.** (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 1<sup>st</sup> and 2<sup>nd</sup> 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; Qadryet *al.*, 2005).

The present study results in the 1<sup>st</sup> part revealed that body weight, body temperature, and respiratory rates were none significantly changed. Heart rates significantly increased. While in 2<sup>nd</sup> part of the study the body weight of 1<sup>st</sup>, 2<sup>nd</sup> and 4<sup>th</sup> groups did not show any significant changes. In 3<sup>rd</sup> group none significantly decreased. Body temperature significantly increased in 1<sup>st</sup> and 2<sup>nd</sup> groups. In group 3<sup>rd</sup> none significantly increased. In 4<sup>th</sup> group decreased. Heart rates in 1<sup>st</sup> group none significantly increased. In 2<sup>nd</sup> group none significant increase in day 7, but significantly increased in day 9, 12 and 22. In 3<sup>rd</sup> group significantly increased in day 7, 9, 12 and 22. In 4<sup>th</sup> group none significantly decreased then increased significantly in day 9 and 12. Respiratory rates in 1<sup>st</sup> and 3<sup>rd</sup> groups none significantly increased, but in day 9, 12 and 22 was significantly increased. In 2<sup>nd</sup> group none significantly decreased in day 7 then significantly increased in day 9, 12 and 22. In 4<sup>th</sup> 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. (Piemeet *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 *et 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 *et al.*, 2010).

The results of 1<sup>st</sup> 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 1<sup>st</sup> group. In 2<sup>nd</sup> group none significantly increased in day 7, but become significant in day 9 and 12. In 3<sup>rd</sup> group none significantly decreased in day 7, and then increased significantly in day 9 and 12. In 4<sup>th</sup> group decreased none significantly in day 7 but become significantly decreased in day 9. The results revealed that clotting time in 1<sup>st</sup> and 3<sup>rd</sup> groups significantly increased in all time post exposure. In 2<sup>nd</sup> group none significantly decreased in day 9. In 4<sup>th</sup> group none significantly changed.

The results of 1<sup>st</sup> 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 hemoglobin concentration significantly increased in day 7 and 9 in 1<sup>st</sup> group. In 2<sup>nd</sup> and 4<sup>th</sup> groups none significantly changed. In 3<sup>rd</sup> group significantly increased in day 9.

The results revealed that PCV% in 1<sup>st</sup> group significantly increased in day 7 and 9. In 2<sup>nd</sup> and 4<sup>th</sup> groups no significant changes. In 3<sup>rd</sup> group significantly increased in day 9. The crude aqueous extract of the root of *S. siamea* 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 (Eichiner, 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 *et 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. (Piemeet *et al.*, 2006).

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

The results revealed that platelets count in 1<sup>st</sup>; 3<sup>rd</sup> and 4<sup>th</sup> groups none significantly decreased. In 2<sup>nd</sup> 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 albinorats, with no significant changes in the white blood cells, platelets and leucocytes population. *S. podocarpa* did not significantly 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 *S. siamea* was linked to the presence of tannin, oxalate, phytate (Ali Smith, 2009). and barakol (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 administered at a low dose, the results suggest the necessity of standardization of the drug.

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