International Journal of Frontiers in
Life Science Research
Journal homepage: https://frontiersrj.com/journals/ijflsr/
ISSN: 2783-0470 (Online)

(RESEARCH ARTICLE)

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Histological and body weight effects of *Datura innoxia* seeds and leaves extracts in rats

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International Journal of Frontiers in Life Science Research, 2021, 01(01), 018–027

Publication history: Received on 04 March 2021; revised on 10 April 2021; accepted on 14 April 2021

Article DOI: https://doi.org/10.53294/ijflsr.2021.1.1.0032

Abstract

The study aimed to determine the chemical compounds in aqueous and methanolic extracts of *Datura innoxia* seeds and leaves and to evaluate their toxic effects on experimental rats. Seeds and leaves were collected from El-Obied, North Kordofan State, Sudan, in October, 2016. The aqueous and methanol extracts were carried out by using maceration method and soxhlet apparatus respectively. Sixty five male Albino Wistar rats, three months old and with an average body weight ranged 110-120 g, were randomly divided into thirteen groups, consisting of five rats in each group. Group1 served as control and fed with normal rats' food and water for thirty days. Groups 2, 6 and 10 administered aqueous seeds extract, Groups 4, 8 and 12 received methanol seeds extract, Groups 3, 7 and 11 received aqueous leaves extracts, Groups 5, 9 and 13 received methanol leaves extract, all the groups received the same type of extract were administered 40, 60 and 80 mg/kg body weight respectively. The extracts administered to the rats intra gastrically using cathodal tube daily for thirty days. The effects of oral administration of leaves and seeds extracts to60 healthy rats over 30 days were evaluated by histological studies and body weight changes. The analysis by gas chromatography-mass spectrometry (GC-MS) of aqueous and methanolic extracts revealed the presence of alkaloids (Scopolamine, atropine and Hyoscyamine), fatty acids, esters, amides, amino acids, ketones, coummarins, terpinoids, phenols, alcohols and hydrocarbons compounds. The histological results showed that administration of extracts caused pathologic changes in the organs studied. The treated Groups had lower ($p \leq 0.05$) body weight gains than control Group. The study concluded that the toxicity of seeds and leaves (methanolic and aqueous) extracts are nearly have the same toxic effects on rats due to their same active ingredients (alkaloids) and the oral administration of the extracts was found to be safe up to 40 mg/kg.

Keywords: *Datura innoxia*; Seeds and leaves; Chemical composition; Histological studies; Body weight.

1. Introduction

From the ancient time the knowledge about plants and their medicinal values were existing. All these knowledge have been transmitted from generations to generations but a little is known on their toxicity and about a suitable dose. Medicinal plants are traditionally used for the treatment of human infections and have made large contribution to human health [1]. According to World Health Organization (WHO), medicinal plants would be the best source to obtain a variety of drugs [2]. Those plants are widely used by all sections of community, whether directly as folk remedies or the medicaments of the different indigenous systems as well as in modern medicine system [3]. *D. innoxia* is native to the tropical and subtropical Americas, from south western USA and Mexico, through Central America to northern and western South America, to Peru, and east to Bolivia and Paraguay. In the USA it is native only to Texas [4], butis also recorded in the southwestern states, Arkansas and in the northeast USA as far as Ontario and Quebec, Canada [5]. *D. innoxia* has been listed as a declared weed in South Africa which is prohibited and must be controlled [6]. *Daturainnoxia* is one of the medicinal plants used by traditional healers in Sudan for the treatment of various ailments. *Datura* species,

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particularly the seeds have been used in shamanistic rituals as a path to enlightenment since ancient times [7]. All parts of the plant are anodyne, antispasmodic, hallucinogenic, hypnotic and narcotic [8]. It has been used in the past as a painkiller and also in the treatment of insanity, fevers with catarrh, diarrhoea and skin diseases. The plant contains several alkaloids, the most active of which is scopolamine [9]. This is a potent cholinergic-blocking hallucinogen, which has been used to calm schizoid patients [10].

2. Material and methods

2.1. Plant Materials (Seeds and Leaves)

D. innoxia seeds and leaves were collected from Elobied, North Kordofan state, Sudan in October, 2016. The plant was authenticated by a plant taxonomist at the Department of Botany Faculty of Science University of Kordofan to be *Daturainnoxia*. The plant leaves and seeds were cleaned, shade-dried and grinded by a mechanical grinder.

2.2. Animals (rats)

Sixty five male Wister rats, three months old and with an average body weight ranged (110-120g), were used in the present study. The rats were clinically healthy and housed within the premises of the Faculty of Science and Technology, Sudan University, Khartoum. Animal housed under standard husbandry conditions (30°C ± 2°C, 60–70% relative humidity and 12hour day-night cycle) and fed on the rat diet (flour 55.6%, meat 35%, edible oil 7.5%, sodium chloride 1.2% and vitamins and minerals 0.7%) and water provider. Animal experiments were designed and conducted in accordance with the guidelines of institutional animal ethical committee.

2.3. Methods

Extraction by Petroleum ether and methanol: The extraction was carried out according to method described by [11]: 600 g of each coarsely powdered sample (seeds and leaves) was successively extracted with 1200 ml of petroleum ether and 1200 ml of methanol using soxhlet extractor apparatus. Extraction was carried out for about four hours for petroleum ether and eight hours for methanol till the color of solvents at the last siphoning time returned colorless. Solvents were evaporated under reduced pressure using rotary evaporator apparatus. Finally the extracts allowed to air till complete dryness.

2.4. Extraction by water

For aqueous extract, 600 g of each coarsely powdered sample (seeds and leaves) was extracted with 3000ml of distilled water and heat to 70 ℃ for three hours and filtered through what man paper No. 0.1 and dried further by freeze drier.

2.5. Preparation of stock solutions

The preparation of stock solution was done by dissolving 5 g of each extract in 12.5 ml of 99.9% ethyl alcohol and completed to 250 ml with distilled water and then 2ml; 3ml and 4ml (40 mg, 60 mg and 80 mg) were taken from the stock solution and used as doses for rats orally.

2.6. Experimental Design

A total of sixty five male Wistar albino rats divided into thirteen Groups containing five each. Group 1served as control and fed with normal rat food and water for thirty days. Groups 4, 8 and 12 received methanol seeds extract with dose of 40, 60, 80mg/kg body weight/day respectively and Groups 5, 9 and 13 received methanol leaves extract with dose of 40, 60, and 80 mg/kg body weight /day respectively. Groups 2, 6 and 10 received aqueous seeds extract with dose of 40,60, 80 mg/kg body weight/day respectively and Groups 3, 7 and 11 received aqueous leaves extract with dose of 40, 60, and 80 mg/kg body weight /day respectively. The extract administered to the rats intra gastricallyusing cathodal tube for thirty days. The method was prepared according to the Standard Method of Organization for Economic Cooperation and Development [12]. The daily feed intake was monitored in the rats until termination of the experiment.

2.7. Histopathological study

Necropsy was conducted to identify gross lesion. The specimens of liver, kidney and brain were collected after slaughtering of rats and immediately fixed in 10% neutral buffered formalin, embedded in paraffin wax, sectioned at 5 cm and stained routinely with hematoxylin and eosin using Harris's heamalun [13].

2.8. GC-MS analysis conditions

The chemical composition analysis of the samples were carried out by using GC/MS technique model -TQ8040 from Japan with capillary column (RTX-5MS), column oven temperature 80 ^{0}C, injection temp. 250 ^{0}C, the sample was injected by using split mode, pressure 122 kpa, total flow 50 ml/min, column flow 1.80 ml/min, purge flow 6 ml/min, split ratio -1, helium as the carrier gas, ion source temp. 200 ^{0}C, interface temp. 250 ^{0}C, solvent cut time 2.5min, detector gain +0.30 kv, threshold 1000, start time 3min, end time 21.00 min, acquisition Mode Q3Scan, start m/z 25, end m/z 400, the oven temp. program start from 80^{0}C with rate 15^{0}C/min to 200^{0}C with 1 min hold time to 260 ^{0}C with rate 10 ^{0}C/min with 1min hold time to 280 ^{0}C as final temperature with 2 min hold time.

3. Results and discussion

3.1. Chemical compounds of methanol extract of *Datura innoxia* seeds

The study of chemical composition of methanol extract of *Datura innoxia* seeds by GC-MS analysis showed the presence of 20 compounds. The chemical compounds with their retention time (RT), chemical formula and molecular weight are presented in Table 1.

Table 1 Chemical compounds of methanol extract of *Datura innoxia* seeds

Compound name	Formula	M. wt.	Base ions	RT
Scopolamine	$C_{17}H_{21}NO_4$	303	108-138	15.48
Aziridine,1-methyl	C_3H_7N	57	42-55	6.08
Tropinone	$C_8H_{13}NO$	139	42-96	15.48
3-Tropanone	$C_8H_{13}NO$	139	96-82	4.93
Propanamide	C_3H_7NO	73	44-73	3.56
Methyl vinyl carbinol	C_4H_8O	72	43-57	3.56
Pseudoecgoninemethyl ester	$C_{10}H_{17}NO_3$	199	96-199	4.93
Atropine	$C_{17}H_{23}NO_3$	289	124-82	14.38
Apoatropin	$C_{17}H_{21}NO_2$	271	124-271	14.38
Hyoscyamine	$C_{17}H_{23}NO_3$	289	124-289	14.38
Tropacocaine	$C_{15}H1_9NO_2$	245	124-82	14.38
8-Azabicyclo{3,2,1 octane-3,6-diol,acetate (ester)	$C_{12}H_{19}NO_4$	241	94-154	15.48
Tigloidine	$C_{13}H_{12}NO_2$	223	124-82	14.37
Homatropine	$C_{16}H_{21}NO_3$	275	124-275	14.36
Benzonitril,2-amino-	$C_7H_6N_2$	118	91-118	7.73
Oleic acid	$C_{18}H_{34}O_2$	282	111-83	7.43
Azelaic acid	$C_9H_{16}O_4$	188	11-152	7.43
Acetic acid,bromo-	$C_2H_3BrO_2$	138	43-94	14.37
2-methylpyrazine carboxylic acid	$C_6H_6N_2O_2$	138	138-94	15.47
Benzoic acid, 3,5-dichloro-,8-aza-8- methylbicyclo {3,2,1} oct-3- ylester	$C_{15}H_{17}Cl_2NO_2$	313	124-82	14.38

3.2. Chemical compounds of methanol extract of *Datura innoxia* leaves

The chemical compounds identified in the methanol crude extract of *Datura innoxia* leaves are listed in Table 2. The analysis by GC-MS revealed 30 compounds.

Table 2 Chemical compounds of methanol crude extract of *Datura innoxia* leaves

Compound name	Formula	M. wt.	Base ions	RT
Alanine (Amino acid)	$C_3H_7NO_2$	89	40-44	18.15
8-Abicycl{3,2,1}octane,3- chloro-8- methyl	$C_8H_{14}C1N$	159	124-44	14.38
Atropine	$C_{17}H_{23}NO_3$	289	124-67	14.38
Tropacocaine	$C_{15}H_{19}NO_2$	245	124-82	14.38
Benzoicacid,3,5-dichloro-,8-aza-8-bicycle{3,2,1}oct-3-yl ester	$C_{15}H1C1_2NO_2$	313	124-94	14.38
Acetamide,2-cyano	$C_3H_4N_2O$	84	40-84	8.60
Phosphorodiamidous Fluoride, tetramethyl	$C_4H_{12}FN_2P$	138	94-138	15.47
d1-phenylephrine	$C_{19}H_{13}NO_2$	167	167-148	11.95
4-Hydroxy-2-methylaceto phenome	$C_9H_{10}O_2$	150	150-107	5.950
Phenol,m-tert-butyl-	$C_{10}H_{14}O$	150	135-77	5.95
4-H-pyran-4-one,2,3- 3,5-dihydroxy-6- methyl	$C_6H_8O_4$	144	144-72	4.26
4-Acetophenone,4-methoxy	$C_9H_{10}O_2$	150	135-92	5.95
2-Hydroxy-5-methylaceto phenone	$C_9H_{10}O_2$	150	150-135	5.95
Hyoscyamine	$C_{17}H_{23}NO_3$	289	124-82	13.26
Apoatropin	$C_{17}H_{21}NO_2$	271	94-124	14.38
4-Hydroxy-3-methyl, acetophenone	$C_9H_{10}O_2$	150	135-121	5.95
4-Hydroxy-2-methylaceto phenone	$C_9H_{10}O_2$	150	150-77	5.95
4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	$C_6H_8o_4$	144	140-101	4.26
Acetamide,N-(aminocarbonyl) -2-chloroacetylurea	$C_3H_5C1N_2O_2$	136	87-136	11.95
Scopolamine	$C_{17}H_{21}NO_4$	289	124-94	14.36
Pyraanone	$C_6H_8o_4$	144	73-101	4.25
Phenylephrine	$C_9H_{13}NO_2$	167	162-146	11.95
L-Glutamine	$C_5H_{10}NO_3$	146	41-84	6.22
Aminopyrazine	$C_4H_5N_3$	95	43-95	10.95
3-Methoxy Acetophenone	$C_9H_{10}O_4$	150	77-135	5.95
Hyoscyamine	$C_{17}H_{23}NO_3$	289	124-82	13.26
Phenol,3-(1,1-dimethyl)	$C_{10}H_{14}O$	150	135-150	5.95
1,2-Propanediamine	$C_3H_{10}N_2$	74	44-71	13.48
Tigloidine	$C_{13}H_{21}NO_2$	223	82-124	14.38
2-Hexanamine,4-methyl	$C_7H_{17}N$	115	44-84	8.60

3.3. Chemical compounds of aqueous crude extract of *Datura innoxia* seeds

The chemical compounds identified in aqueous crude extract of *Datura innoxia* seedsare listed in Table 3. The aqueous crude extract was analyzed by using GC-MS leading to the identification of 24 different compounds.

Table 3 Chemical compounds of aqueous crude extract of *Datura innoxia* seeds

Compound name	Formula	M. wt.	Base ions	RT
4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl	$C_6H_8O_4$	144	144-101	4.25
2,4-Dihydroxy- dimethyl- 3(2H)-furan-3-one	$C_6H_8O_4$	144	144-101	4.25
Sucrose	$C_{12}H_{22}O_{11}$	342	163-85	6.82
3-Nitrobenzl bromide	$C_7H_6BrNO_2$	215	215-90	7.08
Uric acid	$C_5H_4N_4O_3$	168	168-125	8.08
VaniLlic acid	$C_8H_8O_4$	168	168-125	8.08
Gllacetophenone	$C_8H_8O_4$	168	168-125	8.08
3-Hydroxy-4-methoxy benzoic acid	$C_8H_8O_4$	168	168-125	8.08
2-Piperidinone, 1-methyl-	$C_6H_{11}NO$	113	113-57	8.18
Limonene oxide trans	$C_{10}H_{16}O$	152	94-108	15.48
3,3-Dimethyl piperidine	$C_7H_{15}N$	113	113-84	8.17
Butanoic acid, octylester	$C_{12}H_{24}O_2$	200	112-71	8.25
n-Butyric acid,2-ethylhexylester	$C_{12}H_{24}O_2$	200	112-71	8.25
Atropine	$C_{17}H_{23}NO_3$	289	289-124	14.43
Scopolamine	$C_{17}H_{23}NO_4$	303	94-138	15.46
Pyranone	$C_6H_8O_4$	144	101-73	4.25
Hyoscyamine	$C_{17}H_{23}NO_3$	289	289-124	14.43
Tropacocaine	$C_{15}H_{19}NO_2$	245	124-82	14.43
Tigloidine	$C_{13}H_{21}NO_2$	223	124-82	14.43
(Glycine,N-(aminoimino methyl)-N-methyl	$C_4H_9N_3O_2$	131	113-84	8.18
Benzoicacid,3,5-dichloro-,8-aza-8-methyl{3,2,1} oct-3-ylester	$C_{15}H_{17}Cl_2NO_2$	313	82-128	14.39
Benzoyl ecgonine	$C_{16}H_{19}NO_4$	289	124-289	14.39
8-Azabicyclo{3,2,1 octane,3-chloro-8-methyl-	$C_8H_{14}ClN$	159	82-124	14.39
Benzoyl ecgonine	$C_{16}H_{19}NO_4$	289	124-289	14.39

3.4. Chemical compounds of aqueous crude extract of *Datura innoxia* leaves

The chemical compounds identified in aqueous crude extract of *Datura innoxia* leaves are shown in Table 4. Analysis by GC-MS revealed 31 compounds.

Table 4 Chemical compounds of aqueous crude extract of *Datura innoxia* leaves

Compound name	Formula	M. wt.	Base ions	RT
d1-beta-phenyllaticacid.(dl-alpha-Hydroxyhydrocininnamic acid)	C9H10O3	166	91-106	7.66
n-Hexadecanoic acid	C16H32O2	256	256-213	12.03
1,3-Dimethyl,-3,4,5,6-tetrahydro-2(1H)-rimidinone	C6H12N2O	128	84-128	6.88
5-Aminovaleric acid	C5H11NO2	117	30-98	3.46
Azlaic acid	C9H16O4	188	60-171	7.40
9,12-OctadecadienoicAcid (Z,Z),methylester	C19H34O2	294	81-67	13.20
3-Methyladipicacid	C7H12O4	160	114-142	7.05
Hyoscyamine	C17H23NO3	289	124-289	13.29
Atropine	C17H23NO3	289	124-289	13.92
Benzoicacid,3,5- dichloro,8-aza-8-methyl	C15H17Cl2N	313	94-124	14.54
Scopolamine	C17H21NO4	303	94-138	15.54
Scopolamine, TMSderivative	C20H29NO4	375	94-138	15.54
1H-1midazole,1-acetyl	C5H6N2O	110	68-129	6.49
5,6-dihydro-5-methyluracil	C5H8N2O2	128	56-138	6.87
9,12-Octadienoic acid(Z,Z)	C18H32O2	280	81-95	10.92
1,3-Dimethyl-3,4,5,6-tetrahyro-2(1H)-yridinone	C6H12N2O	128	128-84	6.87
Isocamphopinone	C10H16O	152	41-122	3.84
Isovaleric acid, propyl ester	C8H16O2	144	103-85	5.84
Butanoic acid,3-hydroxy-3-methyl-	C5H10O3	118	103-85	5.84
Valeric acid,3-methyl	C6H12O2	116	87-60	3.61
Aceticacid, phenyl	C8H8O2	136	91-136	5.24
Oleic acid	C18H34O2	282	282-82	7.40
Azelaic acid	C9H16O4	188	111-83	7.40
Tropacocaine	C15H19NO2	245	124-82	14.43
Benzoyl ecgonine	C16H19NO4	289	124-289	14.39
8-Azabicyclo {3,2,1}octane,3-chloro- 8-methyl-	C8H14ClN	159	82-124	14.39
Apoatropin	C17H21NO2	271	94-124	14.38
Homatropine	C16H21NO3	275	124-82	14.37
2-methylpyrazine-carboxylic acid	C6H6N2O2	138	138-94	15.48
Pyrrolidine,1-(2-methylpropenyl)-	C8H15N	125	110-124	14.39
9,12-Octadecadieneylchloride, (Z,Z)	C18H31ClO	298	81-95	10.92

Table 5 Mean weekly body weights of rats fed with methanol and aqueous extracts of *Datura innoxia* leaves and seeds for four weeks

Groups	At zero	1st week	2nd week	3rd week	4th week
G 1	±113.00	±117.42	±121.10	±124.42	±128.34
G 2	±112.60	±114.14	±116.70	±118.96	±121.36
G 3	±113.60	±115.3	±117.58	±120.54	±123.68
G 4	±113.60	±115.38	±117.04	±119.14	±121.32
G 5	±113.40	±115.80	±118.00	±120.64	±123.78
G 6	±113.80	±113.64	±91.56	±69.94	±70.10
G 7	±113.80	±113.38	±68.08	±67.74	±67.10
G8	±113.80	±113.2	±90.38	±67.22	±44.80
G 9	±115.40	±114.94	±69.56	±69.28	±46.30
G 10	±114.20	±113.08	±68.38	±45.66	±22.70
G 11	±114.00	±113.04	±90.18	±22.62	±22.50
G12	±113.80	±112.98	±67.96	±22.4	±0.00
G13	±115.40	±114.16	±68.54	±22.62	±22.50

*Values are expressed as means ±STD (Standard deviation) for five rats in each Group for four weeks.

Group 1 (control), rats fed with normal rats' food and water. Group 2, 6 and 10 rats administered 40, 60 and 80mg/kg body weight aqueous seeds extracts respectively. Groups 4, 8 and 12 rats received 40, 60 and 80mg/kg methanol seeds extracts respectively. Group 3, 7 and 11 rats received 40, 60 and 80mg/kg body weight aqueous leaves extracts respectively. Group 5, 9 and 13 rats received 40, 60 and 80mg/kg body weight methanol leaves extracts respectively.

Table 6 Comparative significant values of body weight

Groups	1st week	2nd week	3rd week	4th week
G1	0.111	0.119	0.011	0.024
G2	0.002	0.016	0.011	0.189
G3	0.001	0.019	0.050	0.075
G4	0.003	0.006	0.001	0.006
G5	0.007	0.014	0.020	0.040
G6	0.011	0.000	0.059	0.094
G7	0.000	0.071	0.074	0.162
G8	0.000	0.002	0.011	0.125
G9	0.011	0.096	0.122	0.000
G10	0.000	0.139	0.000	0.000
G11	0.000	0.001	0.000	0.000
G12	0.000	0.050	0.000	0.000
G13	0.002	0.011	0.000	0.000

*. The mean difference is significant at the 0.05 level.

3.5. Statistical analysis of Growth changes

From the results of Tables (5 and 6) the data analysis by Analysis of variance (ANOVA) is a collection of statistical models and their associated estimation procedures (such as the "variation" among and between groups) used to analyze the differences among group means in a sample. ANOVA method showed that the means of body weight gain per week, increased in group 1 (control) from first week to the fourth week as below: (113.00±, 117.42±, 121.10±, 124.42± and 128.34±) respectively.

Also the method showed that the mean weekly body weight gain against daily oral doses of *Datura innoxia* seeds and leaves aqueous extracts for four weeks, for group 2 and group 3 at 40mg/kg/body weight dose were (114.14±, 116.70±, 118.96 ±,121.36 ±, 115.30±, 117.58±, 120.54 ± and 123.68±) respectively, there was an increase of body weight, but was lower than mean weekly body weight of control group, while at 40mg/kg dose for group 4 and group 5 which received seeds and leaves methanol extracts for four weeks, their mean weekly body weight were (115.38±, 117.04±, 119.14±, 121.32±, 115.80±, 118.00±, 120.64± and 123.78±) respectively, they were similar nearly to the mean of group 2 and group 3, thus there was an increase in body weight but also less than control. Group 6 and group 7 which were fed with 60 mg\kg dose per day of aqueous seeds and leaves extracts, the mean of weekly body weight were as flow: (113.64±, 91.56±, 69.94±, 70.10 ±,113.38 ±, 68.08±, 67.74 ± and 67.10 ±) respectively, they had more lower mean of body weight than Group 1(control) and group 2 and group 3 which were fed with 40mg/kg dose of aqueous seeds and leaves extracts, at the same time the mean weekly body weight of group 7 was less than group 6. Group 8 and group 9 which were fed with 60 mg\kg dose per day of methanol seeds and leaves extracts, the mean of weekly body weight were as below: (113.20±, 90.38±, 67.22±, 44.80±, 114.94±, 69.56±, 69.28±and 46.3±) respectively, this showed that the mean weekly body weight of 60 mg/kg dose of methanol seeds and leaves extracts was more less than 60 mg/kg dose of aqueous seeds and leaves extracts, so it revealed that the methanol seeds and leaves extracts had a high toxicity than aqueous seeds and leaves extracts. Group 10 and group 11 which were fed with 80 mg\kg dose per day of aqueous seeds and leaves extracts, the mean of weekly body weight were as flow: (113.08±, 68.38±,45.66 ±, 22.70±, 113.04±, 90.18±, 22.62± and 22.50±) respectively, this declared that group 10 and group11 had most less mean of weekly body weight comparing to group (8 and 9) which received 60 mg/kg dose per day of aqueous seeds and leaves extracts and 60 mg/kg of methanol seeds and leaves extracts. Moreover, the mean weekly body weight of 80mg/kg of aqueous leaves was less than the same dose of aqueous seeds extract, this indicated that the toxicity of aqueous leaves extract was higher than the aqueous seeds extract at the same dose. Group 12 and group 13 which were fed with 80 mg\kg dose per day of methanol seeds and leaves extracts, the mean of weekly body weight were as flow: (112.98±, 67.96±, 22.40±, 0.00±, 114.16±, 68.54±, 22.62± and 22.50±) respectively, this showed that the most low mean of weekly body weight in group (12 and 13) which were fed with 80 mg/kg dose per day of methanol seeds and leaves extracts comparing to all other groups. While the mean weekly of body weight for methanol seeds extract was higher than the methanol leaves at the same dose (80 mg/kg), this was great sign for a high toxicity of methanol leaves extract. According to above mention the mean weekly body weight of groups had lower ($p \leq 0.05$) body weight gains than control (Group 1). These results agree with the results of [14]in histopathological study of aqueous and methanolic extracts of *Datura innoxia* leaves and seeds on Wistar rats and the results of[15], in evaluation of analgesic effect of *Datura stramonium* leaves in hot plate and formalin test on male rats. The observation of body weight in groups (2, 3, 4 and 5) which treated with 40 mg/kg dose is agreement to the earlier report of [16] and [17] who have noted no change in body weight of rats treated with *Datura Stramonium* seeds with the exception of an increase in the relative lung weight.

3.6. Effect of aqueous and methanolic extracts on histology of liver, brain and kidney

The effects of methanolic and aqueous (leaves and seeds) extracts on experimental animals (rats) were mainly observed in three organs (kidney, liver and brain) for different orals doses which are (40, 60and 80 mg/kg/day) for four weeks.

The histopathological changes observed in the organs were characteristic of some changes, this is in line with the observations made in the increasing or decreasing doses and the severity of the changes increased with increased of duration of the treatment of doses, suggesting a cumulative effect of the alkaloids and may due to the metabolites activities, these results agreed with [18] results in acute and chronic toxicity studies of *Datura stranomnium* stems in mice. In this study hepatocellular damage was observed especially at the doses (60 and 80) mg/kg body weight which indicates that there was a severe damage of liver, kidney and brain cells and tissues. Kidneys of rats that received 40 mg/kg/day dose of methanol and aqueous (leaves and seeds) extracts, showed that there were: congestion, hemorrhage, oedema and swelling of cells and dilatation of renal tubules in the cortex and glomerular alteration (fatty cytoplasmic change) and segmentation of cells.Livers of rats that received 40 mg/kg/day dose of methanolic and aqueous (leaves and seeds) extracts, showed that there were: congestion, oedema and hemorrhage of liver cells and centrilobular fibrosis.

Brains of rats that received (40 mg)/kg/day dose of methanol and aqueous (leaves and seeds) extracts, showed that there were: congestion, oedema and hemorrhage and hyperemic vessels in cerebellum.

Kidneys of rats that received 60 mg/kg/day dose of methanol and aqueous (leaves and seeds) extracts, showed that there were: glomerulonephritis, alteration (fatty change), hemorrahage, segmentation and degeneration of cells. Livers of rats that received 60 mg/kg/day dose of methanol and aqueous (leaves and seeds) extracts, showed there were: liver cells and tissues damage, centrilobular necrosis, hemorrhage and segmentation.Brains of rats that received 60 mg /kg/day dose of methanol and aqueous (leaves and seeds) extracts, showed that there were: cerebral neural congestion, cell degeneration, segmentation, oedema and packing in the cortex.Kidneys of rats that received 80 mg/kg/day dose of methanolic and aqueous (leaves and seeds) extracts, showed that there were: tubular necrosis, inflammatory infiltration, severe hemorrhage in kidney tissue, damage of vessels and degenerated in cells and tissue.Livers of rats that received 80 mg/kg/day dose of methanolic and aqueous (leaves and seeds) extracts, showed that there were: Centrilobular necrosis, blood vessel dilatation, mild bleeding, necrosis and high segmentation and degeneration in cells and tissue. Brains of rats that received 80 mg/kg/day dose of methanolic and aqueous (leaves and seeds) extracts, showed that there were: hemorrhage, inflammatory cell, infiltration in brain, necrosis in brain tissue and degenerated neurons, cell and tissue of brain.

4. Conclusion

GC-MS analysis of *Datura innoxia* seeds and leaves (aqueous and methanol) extracts, revealed the presence of important pharmacological bioactive compounds mainly tropane alkaloids which are toxic at high concentrations, and fatty acids, phenyl propanoids, amino acids and flavonoids. The aqueous and methanol (seeds and leaves) extracts have nearly similar effect to the experimental rats, because they are all contain main alkaloidial compounds (atropine, hyoscyamine, tropacocaine, scopolamine, apoatropin) which have toxic effect. During the experiment loss in weight was noticed in the rats in group 6 up to group 13 may be due to reduction in intake of feed and this in turn may be attributed to the effect of the extracts administered to the animals. Histological study showed that extracts at doses (40, 60 and 80 mg/kg/day) caused pathologic changes. The effects were less marked in the low dose than the high dose Group. The lethal dose (LD50)of *Datura innoxia* seeds and leaves (methanol and aqueous) extracts in rats were nearly the same and parallel, that means they have the same efficacy due to their active ingredients (tropane alkaloids) this agree with the results of [19] in acute toxicity of aqueous and petroleum ether extracts of *Daturainnoxia* leaves in mice.

Compliance with ethical standards

Acknowledgments

Authors would like to thank the members and leaders of Forensic laboratories Sudan, especially who work in Forensic Chemistry for supporting and providing us with some information and technical analysis.

Disclosure of conflict of interest

The authors declare that there are no conflicts of interest.

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