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Research Article

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Turmeric (Curcuma Longa) protection against the Liver Toxicity Caused by Aluminum Chloride (AlCl3) in Adult Male Rats

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ABSTRACT

Recently increased attention is being paid to most aluminum compound due to their serious effects on the energy metabolism and hematology, fertility and reproduction. Natural products are good options when treating heavy metals toxicity because of their effectiveness, fewer side effects and relatively low cost. The study was made on 336(8 weeks old) male albino Wistar rats (weighing between 150-200 g). The animals were given a dose of Aluminum Chloride (AlCl3) (30mg/kg) every other day intraperitoneally for eight weeks, and a dose of Turmeric (Curcuma Longa) (4mg/kg) daily intraperitoneally for eight weeks. The following parameters were measured in blood serum: glucose, total protein, albumin, total cholesterol, triglycerides, bilirubin, alkaline phosphatase (ALP), aspartate amino transferase (AST), alanine amino transferase (ALT), gamma glutamyl transferase (GGT). Aluminum Chloride caused an increase in serum glucose levels, total cholesterol and triglycerides, bilirubin, ALP, AST, ALT and GGT. Aluminum Chloride caused a decrease of total protein and albumin level, and caused hepatocytic degenerations and necrosis in addition to severe vascular congestion, especially in the portal blood vessel in the liver, while Curcuma Longa ameliorates these effects near to their normal values.

Key words: *Aluminum chloride (AlCl3), turmeric (Curcuma Longa), glucose, total protein, albumin, total cholesterol, triglycerides, bilirubin, alkaline phosphatase (ALP), aspartate amino transferase (AST), alanine amino transferase (ALT), gamma glutamyl transferase (GGT), liver, histology.*

INTRODUCTION

Aluminum is the third most common element found on earth. It constitutes of approximately 8% of total mineral components in the earth's crust. It is found in combination with oxygen, silicon, fluorine and other elements in soil, rocks, clays and gems. Aluminum has significant toxic potential for humans [1]. Aluminum is widely distributed in the environment and extensively used in daily life, therefore, humans are easily exposed to it in its different forms. It gets access to the human and animal's body via the gastrointestinal and the respiratory tracts. Aluminum accumulates in all tissues of the body, including kidney, liver, heart, blood, bone and brain [2&3]. Chronic exposition to this trace element can cause alterations in skeletal, nervous, hematopoietic and respiratory systems [4&5]. Several cosmetics including antiperspirant and deodorant contain significant amount of aluminum chloride (AlCl3) [6].

Herbs and herbal products are incorporate in livestock feeds instead of chemical products and antibiotics in order to stimulate the effectiveness of feed nutrients which result in more rapid gain, higher production and better feed efficiency. Herbs contain active substances which stimulate body metabolism, improve digestion, and have bactericidal and immunostimulant action improved productivity of poultry [7].

The Curcuma Longa L. (Family: Zingiberaceae) named turmeric is perennial herb. Curcuma Longa L. has received attention as a component of designer foods for its cancer- preventing ability [8]. Curcumin a major component in turmeric has a potent antioxidant activity [9]. Turmeric has also been used as a traditional remedy for treatment of inflammation and other disease [10]. Dietary Curcuminoids have been associated with anti-oxidative [11] and anti-carcinogenic [12] activities. In recent years, much attention has been focused on the apoptotic action of curcumin [13].

MATERIALS AND METHODS:

1) Aluminum chloride (AlCl3):

The animals will be given a dose of 30mg/kg every other day intraperitoneally for eight weeks [14].

2) Turmeric (Curcuma Longa):

The animals will be given a dose of 4mg/kg intraperitoneally daily for eight weeks [15].

The animals to be sampled were weighed and they are 36 animals as of 6 animals from each group. Blood sampling was immediately after slaughter the testes was preserved in neutral formalin solution until histological section were made.

The serum was collected in small glass bottles for each animal and were kept in the freezer at -18°C to be used for biochemical measurements.

Glucose, total protein, albumin, total cholesterol, triglycerides, bilirubin, alkaline phosphatase (ALP), aspartate amino transferase (AST), alanine amino transferase (ALT), gamma-glutamyl transferase (GGT) were measured.

Statistical study:

Mean will be calculated for control group and treated groups, also the standard deviation S.E. for means and T-Test at a 5% significant level [16].

RESULTS

1) Glucose:

There was a significant increase in glucose of the AlCl3 group in all 8 weeks compared to control. A significant decrease was noticed in glucose in curcumin group in the first week compared to control, and a significant decrease in all 8 weeks except for the fourth week compared to AlCl3 group. There was a significant decrease in AlCl3+curcumin group in all 8 weeks compared to AlCl3 group (Table 1).

2) Total protein:

Aluminum chloride group showed a significant decrease in total protein in all 8 weeks of experiment except for the first week compared to control. There was a significant increase in total protein of the curcumin group from week 2, 4, 5, 6 and 8 compared to AlCl3 group, but no significant difference in week 1, 3 and 7 compared to control and AlCl3 group. A significant decrease in total protein was seen in the AlCl3+curcumin group in the second week compared to control, and a significant increase in week 7 compared to control, and a significant increase from week 3 to 8 compared to AlCl3 group, but no significant difference in the first week compared to control and AlCl3 group (Table 2).

Table (1): Effect of daily administration of Curcuma longa (4 mg/kg), Aluminum chloride (30 mg/kg) and combination of Curcuma longa and Aluminum chloride on glucose (mg/dl) of adult albino rats.

	Control Mean ± S.E	AlCl3 Mean ± S.E	Curcuma longa Mean ± S.E	AlCl3+ Curcuma longa Mean ± S.E
Week1	84.97 ± 4.76	116.02 ± 5.85 a 36.55 %	63.00 ± 3.55a,b -25.85 %	84.03 ± 5.56 b -1.11 %
Week2	80.95 ± 5.80	101.03 ± 6.63 a 24.81 %	73.79 ± 5.53 b -8.84 %	72.73 ± 4.04 b -10.15 %
Week3	101.64 ± 4.37	138.32 ± 7.73 a 36.09 %	77.00 ± 6.97a,b -24.25 %	115.08 ± 7.15 b 13.22 %
Week4	99.76 ± 1.90	133.17 ± 12.19 a 33.49 %	95.09 ± 6.54 b -4.68 %	96.40 ± 7.98 b -3.37 %
Week5	108.78 ± 3.33	139.60 ± 8.77 a 28.33 %	104.24 ± 8.71 b -4.17 %	108.18 ± 5.41 b -0.55 %
Week6	113.82 ± 6.53	144.47 ± 4.14 a 26.93 %	116.57 ± 3.46 b 2.42 %	125.12 ± 2.82 b 9.93 %
Week7	97.48 ± 3.37	136.18 ± 2.90 a 39.71 %	82.52 ± 8.19 b -15.34 %	94.19 ± 2.82 b -3.37 %
Week8	111.27 ± 5.47	158.27 ± 3.13 a 42.25 %	109.48 ± 6.52 b -1.61 %	119.84 ± 4.11 b 7.70 %

a Significant difference from the control group at $p < 0.05$.b Significant difference from the AlCl3-intoxicated group at $p < 0.05$.

statistical analysis was performed between control (C=6) and treated (T=6) using T-Test

Table (2): Effect of daily administration of Curcuma longa (4 mg/kg), Aluminum chloride (30 mg/kg) and combination of Curcuma longa and Aluminum chloride on total protein (g/dl) of adult albino rats.

	Control Mean ± S.E	AlCl3 Mean ± S.E	Curcuma longa Mean ± S.E	AlCl3+ Curcuma longa Mean ± S.E
Week1	6.56 ± 0.43	6.97 ± 0.31 6.38 %	6.59 ± 0.56 0.49 %	6.21 ± 0.44 -5.23 %
Week2	6.75 ± 0.31	5.29 ± 0.22 a -21.57 %	6.47 ± 0.39 b -4.14 %	5.66 ± 0.26 a -16.11 %
Week3	6.47 ± 0.36	5.25 ± 0.34 a -18.90 %	6.03 ± 0.28 -6.85 %	6.22 ± 0.22 b -3.92 %
Week4	5.79 ± 0.27	4.16 ± 0.24 a -28.14 %	5.34 ± 0.26 b -7.71 %	5.09 ± 0.23 b -12.08 %
Week5	7.00 ± 0.35	5.84 ± 0.20 a -16.50 %	6.50 ± 0.38 b -7.05 %	6.49 ± 0.21 b -7.20 %
Week6	6.16 ± 0.18	5.27 ± 0.18 a -14.44 %	6.46 ± 0.46 b 4.81 %	6.81 ± 0.45 b 10.44 %
Week7	6.18 ± 0.30	4.98 ± 0.39 a -19.40 %	5.90 ± 0.19 -4.48 %	7.33 ± 0.34a,b 18.69 %
Week8	7.37 ± 0.11	5.64 ± 0.25 a -23.43 %	7.41 ± 0.55 b 0.57 %	7.64 ± 0.44 b 3.63 %

a Significant difference from the control group at $p < 0.05$.b Significant difference from the AlCl3-intoxicated group at $p < 0.05$.

statistical analysis was performed between control (C=6) and treated (T=6) using T-Test

3) Albumin

A significant decrease in albumin was noticed in the AlCl3 group in all 8 weeks compared to control. The curcumin group had a significant increase in albumin in all 8 weeks except for week 4 and 6 compared to AlCl3 group, and had no significant change in week 4 as compared to control and AlCl3 group. Aluminum chloride + curcumin had a significant increase in albumin in week 1 and 3 to 8 compared to AlCl3 group (Table 3).

Table (3): Effect of daily administration of Curcuma longa (4 mg/kg), Aluminum chloride (30 mg/kg) and combination of Curcuma longa and Aluminum chloride on albumin (g/dl) of adult albino rats.

	Control Mean ± S.E	AlCl3 Mean ± S.E	Curcuma longa Mean ± S.E	AlCl3+ Curcuma longa Mean ± S.E
Week1	4.44 ± 0.21	3.76 ± 0.17 a -15.44 %	4.82 ± 0.34 b 8.49 %	4.48 ± 0.22 b 0.72 %
Week2	3.23 ± 0.25	2.38 ± 0.16 a -26.45 %	3.59 ± 0.32 b 11.08 %	2.86 ± 0.13 -11.48 %
Week3	3.37 ± 0.14	2.50 ± 0.15 a -25.67 %	3.13 ± 0.16 b -7.00 %	3.07 ± 0.18 b -8.93 %
Week4	4.18 ± 0.31	2.77 ± 0.15 a -33.70 %	3.39 ± 0.34 -18.97 %	3.73 ± 0.20 b -10.87 %
Week5	4.40 ± 0.20	3.32 ± 0.09 a -24.68 %	4.34 ± 0.30 b -1.43 %	4.27 ± 0.32 b -3.04 %
Week6	3.38 ± 0.28	2.25 ± 0.12 a -33.33 %	3.84 ± 0.23 b 13.79 %	3.74 ± 0.27 b 10.76 %
Week7	3.17 ± 0.10	2.15 ± 0.10 a -32.10 %	3.16 ± 0.20 b -0.37 %	3.24 ± 0.22 b 2.35 %
Week8	3.73 ± 0.29	2.31 ± 0.17 a -37.95 %	3.75 ± 0.19 b 0.62 %	3.13 ± 0.27 b -15.93 %

a Significant difference from the control group at $p < 0.05$.b Significant difference from the AlCl3-intoxicated group at $p < 0.05$.
statistical analysis was performed between control (C=6) and treated (T=6) using T-Test

4) Total cholesterol:

There was a significant increase in cholesterol in the AlCl3 group in all 8 weeks compared to control. A significant decrease in cholesterol of the curcumin and AlCl3+curcumin in all 8 weeks compared to AlCl3 group, and a significant decrease in cholesterol of the curcumin treated group in week 1, 3, 7 and 8 compared to control, a significant decrease can be seen in cholesterol of the AlCl3+curcumin group in week 1, 3 and 8 compared to control group (Table 4).

5) Triglycerides:

Aluminum chloride group showed a significant increase in triglycerides in all 8 weeks compared to control. There was a significant decrease in the triglycerides of curcumin group in week 4 and 6 compared to control, and there was a significant decrease in triglycerides in all 8 weeks compared to AlCl3 group. There was a significant decrease in triglycerides of AlCl3+curcumin group in all 8 weeks except for the first week compared to AlCl3 group, and a significant increase in week 2 and 5 of AlCl3+curcumin group, and a significant decrease in week 8 of AlCl3+curcumin group compared to control (Table 5).

Table (4): Effect of daily administration of *Curcuma longa* (4 mg/kg), Aluminumchloride (30 mg/kg) and combination of *Curcuma longa* and Aluminumchloride on total cholesterol (mg/dl) of adultalbino rats.

	Control Mean ± S.E	$AlCl_3$ Mean ± S.E	Curcuma longa Mean ± S.E	$AlCl_3$+ Curcuma longa Mean ± S.E
Week1	71.73 ± 2.93	95.83 ± 6.77 [a] 33.61 %	34.42 ± 0.81[a,b] -52.01 %	56.99 ± 4.62[a,b] -20.54 %
Week2	83.39 ± 3.65	110.71 ± 2.76 [a] 32.76 %	79.02 ± 8.52 [b] -5.25 %	85.63 ± 6.67 [b] 2.68 %
Week3	95.74 ± 4.91	115.38 ± 6.27 [a] 20.52 %	78.11 ± 4.00[a,b] -18.41 %	75.08 ± 3.26[a,b] -21.57 %
Week4	46.38 ± 1.55	74.59 ± 5.24 [a] 60.81 %	44.04 ± 2.40 [b] -5.04 %	52.92 ± 4.66 [b] 14.10 %
Week5	86.99 ± 2.87	98.84 ± 2.78 [a] 13.62 %	82.69 ± 4.49 [b] -4.94 %	80.84 ± 4.86 [b] -7.08 %
Week6	70.77 ± 4.83	86.82 ± 3.71 [a] 22.67 %	64.47 ± 5.63 [b] -8.91 %	73.16 ± 1.21 [b] 3.37 %
Week7	87.80 ± 6.75	121.52 ± 4.38 [a] 38.40 %	68.79 ± 4.51[a,b] -21.66 %	68.48 ± 6.69 [b] -22.00 %
Week8	99.80 ± 7.63	130.92 ± 4.17 [a] 31.18 %	79.84 ± 1.73[a,b] -19.99 %	80.16 ± 1.30[a,b] -19.68 %

[a]Significantdifferencefrom the control group at $p < 0.05$.[b]Significantdifferencefrom the $AlCl_3$-intoxicated group at $p < 0.05$.

statisticalanalysiswasperformedbetween control (C=6) and treated (T=6) using T-Test

Table (5): Effect of daily administration of *Curcuma longa* (4 mg/kg), Aluminum chloride (30 mg/kg) and combination of *Curcuma longa* and Aluminum chloride on triglycerides (mg/dl) of adult albino rats.

	Control Mean ± S.E	$AlCl_3$ Mean ± S.E	Curcuma longa Mean ± S.E	$AlCl_3$+ Curcuma longa Mean ± S.E
Week1	71.45 ± 3.61	84.96 ± 6.64 [a] 18.92 %	64.28 ± 4.40 [b] -10.04 %	82.42 ± 7.75 15.35 %
Week2	82.22 ± 4.25	107.63 ± 5.05 [a] 30.90 %	91.98 ± 5.05 [b] 11.87 %	94.88 ± 2.19[a,b] 15.39 %
Week3	91.64 ± 4.27	113.60 ± 3.89 [a] 23.97 %	94.20 ± 6.19 [b] 2.80 %	101.56 ± 3.14 [b] 10.83 %
Week4	83.28 ± 3.88	120.36 ± 9.20 [a] 44.53 %	57.95 ± 2.28[a,b] -30.41 %	91.49 ± 3.35 [b] 9.85 %
Week5	63.37 ± 3.21	151.12 ± 4.12 [a] 138.48 %	57.60 ± 5.25 [b] -9.11 %	106.83 ± 10.15[a,b] 68.59 %
Week6	104.96 ± 7.52	172.66 ± 7.57 [a] 64.51 %	81.66 ± 3.97[a,b] -22.20 %	109.69 ± 7.37 [b] 4.51 %
Week7	154.33 ± 4.03	293.97 ± 1.96 [a] 90.48 %	154.74 ± 11.88 [b] 0.27 %	167.97 ± 11.59 [b] 8.84 %
Week8	118.91 ± 10.84	308.24 ± 8.67 [a] 159.23 %	98.91 ± 4.64 [b] -16.82 %	89.58 ± 2.92[a,b] -24.67 %

[a] Significant difference from the control group at $p < 0.05$.[b] Significant difference from the $AlCl_3$-intoxicated group at $p < 0.05$.

statistical analysis was performed between control (C=6) and treated (T=6) using T-Test

6) Bilirubin:

A significant increase in AlCl3 group in bilirubin can be noticed in all 8 weeks compared to control. A significant decrease in bilirubin was seen in curcumin and AlCl3+curucmin in all 8 weeks compared to AlCl3 group. There was a significant decrease in bilirubin in week 1 and 2 of curcumin group, and in week 2, 3, 7 and 8 of AlCl3+curucmin group compared to control group (Table 6).

Table (6): Effect of daily administration of Curcuma longa (4 mg/kg), Aluminumchloride (30 mg/kg) and combination of Curcuma longa and Aluminumchloride on bilirubin (mg/dl) of adultalbino rats.

	Control Mean ± S.E	AlCl3 Mean ± S.E	Curcuma longa Mean ± S.E	AlCl3+ Curcuma longa Mean ± S.E
Week1	1.73 ± 0.08	1.99 ± 0.02 a 15.00 %	1.40 ± 0.11a,b -19.50 %	1.72 ± 0.05 b -0.87 %
Week2	1.21 ± 0.02	1.79 ± 0.16 a 47.50 %	0.90 ± 0.03a,b -25.89 %	0.89 ± 0.05a,b -26.61 %
Week3	1.36 ± 0.06	1.71 ± 0.09 a 25.88 %	1.33 ± 0.09 b -2.24 %	0.75 ± 0.04a,b -44.89 %
Week4	0.87 ± 0.07	1.19 ± 0.02 a 37.06 %	0.95 ± 0.07 b 9.45 %	1.00 ± 0.05 b 15.17 %
Week5	0.93 ± 0.07	1.43 ± 0.11 a 53.15 %	0.97 ± 0.06 b 3.95 %	1.19 ± 0.07 b 27.67 %
Week6	1.23 ± 0.02	1.47 ± 0.05 a 19.83 %	1.22 ± 0.07 b -0.67 %	1.17 ± 0.06 b -4.56 %
Week7	1.27 ± 0.03	1.52 ± 0.04 a 19.56 %	1.19 ± 0.06 b -6.89 %	1.14 ± 0.05a,b -10.32 %
Week8	0.38 ± 0.02	1.45 ± 0.06 a 283.91 %	0.37 ± 0.02 b -0.86 %	0.51 ± 0.04a,b 36.21 %

aSignificantdifferencefrom the control group at $p < 0.05$.bSignificantdifferencefrom the AlCl3-intoxicated group at $p < 0.05$.
statisticalanalysiswasperformedbetween control (C=6) and treated (T=6) using T-Test

7) Alkaline phosphatase (ALP):

A significant increase was seen in AlCl3 group in ALP in all 8 weeks compared to control. A significant decrease in ALP was found in curcumin group in week 1, 5, 7 and 8 compared to control group, and a significant decrease in ALP in all 8 weeks except for the fourth week compared to AlCl3 group, no significant difference in ALP in week 4 compared to control and AlCl3 group. Aluminum chloride+curucmin had a significant decrease in ALP during 8 weeks of administration compared to AlCl3 group, and a significant decrease in week 5, 7 and 8 compared to control for AlCl3+curucmin group (Table 7).

8) Aspartate aminotransferase (AST):

A significant increase was seen in AlCl3 group in AST in all 8 weeks except for the first week compared to control, and there was no significant difference in the first week compared to control. Curcumin group showed a significant decrease in AST in all 8 weeks except for the first week compared to AlCl3 group, there was a significant increase in curcumin group in AST in the second week and a significant decrease in AST in week 5, 6, 7 and 8 compared to control group. A significant decrease in AST was seen in AlCl3+curcumin group in all 8 weeks compared to AlCl3 group, and a significant decrease in week 1, 3 and 5 to 8 compared to control (Table 8).

Table (7): Effect of daily administration of Curcuma longa (4 mg/kg) Aluminumchloride (30 mg/kg) and combination of Curcuma longa and Aluminumchloride on alkaline phosphatase (ALP) (U/l) of adultalbino rats.

	Control Mean ± S.E	AlCl3 Mean ± S.E	Curcuma longa Mean ± S.E	AlCl3+ Curcuma longa Mean ± S.E
Week1	30.68 ± 2.04	43.65 ± 3.22 a 42.28 %	24.35 ± 1.42a,b -20.64 %	35.99 ± 2.31 b 17.31 %
Week2	46.57 ± 4.22	64.78 ± 5.51 a 39.09 %	43.36 ± 2.47 b -6.91 %	43.26 ± 2.67 b -7.12 %
Week3	46.71 ± 3.22	75.62 ± 4.37 a 61.91 %	48.24 ± 3.32 b 3.28 %	47.02 ± 3.76 b 0.66 %
Week4	67.53 ± 3.19	82.55 ± 3.64 a 22.24 %	68.15 ± 5.49 0.92 %	67.39 ± 4.69 b -0.21 %
Week5	79.75 ± 3.44	93.26 ± 4.75 a 16.95 %	62.64 ± 4.55a,b -21.46 %	58.04 ± 4.09a,b -27.22 %
Week6	82.68 ± 4.84	116.55 ± 5.82 a 40.97 %	75.17 ± 4.63 b -9.09 %	78.64 ± 6.81 b -4.89 %
Week7	95.85 ± 2.41	118.72 ± 2.59 a 23.86 %	35.52 ± 3.37a,b -62.94 %	49.81 ± 3.93a,b -48.03 %
Week8	73.18 ± 1.19	118.00 ± 5.74 a 61.26 %	40.57 ± 3.03a,b -44.55 %	33.04 ± 0.72a,b -54.85 %

aSignificantdifferencefrom the control group at $p < 0.05$.bSignificantdifferencefrom the AlCl3-intoxicated group at $p < 0.05$.
statisticalanalysiswasperformedbetween control (C=6) and treated (T=6) using T-Test

Table (8): Effect of daily administration of Curcuma longa (4 mg/kg), Aluminumchloride (30 mg/kg) and combination of Curcuma longa and Aluminumchloride on aspartate aminotransferase (AST) (U/l) of adultalbino rats.

	Control Mean ± S.E	AlCl3 Mean ± S.E	Curcuma longa Mean ± S.E	AlCl3+ Curcuma longa Mean ± S.E
Week1	28.18 ± 1.66	28.50 ± 2.20 1.14 %	29.04 ± 1.96 3.07 %	22.18 ± 1.89a,b -21.29 %
Week2	33.63 ± 1.93	51.53 ± 2.61 a 53.19 %	39.99 ± 1.84a,b 18.89 %	38.97 ± 3.23 b 15.86 %
Week3	31.21 ± 1.00	53.14 ± 4.10 a 70.24 %	32.18 ± 1.66 b 3.10 %	25.79 ± 1.79a,b -17.39 %
Week4	36.83 ± 2.07	63.24 ± 3.95 a 71.71 %	34.80 ± 3.06 b -5.52 %	32.76 ± 2.43 b -11.05 %
Week5	39.36 ± 3.00	65.18 ± 3.51 a 65.62 %	30.82 ± 1.85a,b -21.68 %	25.20 ± 2.34a,b -35.96 %
Week6	39.74 ± 2.71	75.15 ± 1.43 a 89.12 %	31.28 ± 1.62a,b -21.28 %	28.40 ± 1.32a,b -28.53 %
Week7	39.67 ± 0.73	76.40 ± 0.72 a 92.60 %	31.86 ± 2.13a,b -19.68 %	30.51 ± 2.38a,b -23.09 %
Week8	43.80 ± 2.37	88.73 ± 3.13 a 102.59 %	30.86 ± 2.49a,b -29.55 %	31.50 ± 0.84a,b -28.09 %

aSignificantdifferencefrom the control group at $p < 0.05$.bSignificantdifferencefrom the AlCl3-intoxicated group at $p < 0.05$.
statisticalanalysiswasperformedbetween control (C=6) and treated (T=6) using T-Test

9) Alanine aminotransferase (ALT):

A significant increase was seen in AlCl3 group in ALT in all 8 weeks compared to control. A significant decrease was found in curcumin group in ALT in all 8 weeks compared to control and AlCl3 group. A significant decrease in ALT was seen in AlCl3+ curcumin group in all 8 weeks compared to AlCl3 group, and a significant decrease in all 8 weeks except for the seventh week compared to control (Table 9).

Table (9): Effect of daily administration of *Curcuma longa* (4 mg/kg), Aluminum chloride (30 mg/kg), combination of *Curcuma longa* and Aluminum chloride on alanine aminotransferase (ALT) (U/l) of adult albino rats.

	Control Mean ± S.E	$AlCl_3$ Mean ± S.E	Curcuma longa Mean ± S.E	$AlCl_3$+ Curcuma longa Mean ± S.E
Week1	14.93 ± 0.34	24.29 ± 0.47 [a] 62.72 %	6.88 ± 0.35[a,b] -53.90 %	5.04 ± 0.38[a,b] -66.25 %
Week2	11.52 ± 0.63	18.42 ± 1.01 [a] 59.95 %	8.24 ± 0.32[a,b] -28.46 %	5.62 ± 0.45[a,b] -51.19 %
Week3	13.47 ± 0.49	25.90 ± 1.00 [a] 92.31 %	10.72 ± 0.95[a,b] -20.41 %	8.43 ± 0.75[a,b] -37.43 %
Week4	16.77 ± 0.69	25.10 ± 2.10 [a] 49.71 %	11.63 ± 0.67[a,b] -30.63 %	8.72 ± 0.81[a,b] -48.00 %
Week5	12.99 ± 0.81	28.97 ± 0.80 [a] 123.04 %	10.85 ± 0.32[a,b] -16.48 %	3.78 ± 0.23[a,b] -70.91 %
Week6	13.57 ± 0.68	28.27 ± 1.16 [a] 108.35 %	9.64 ± 0.79[a,b] -28.95 %	8.28 ± 0.33[a,b] -38.96 %
Week7	21.04 ± 1.18	31.90 ± 1.37 [a] 51.60 %	17.09 ± 1.20[a,b] -18.77 %	19.17 ± 1.03 [b] -8.93 %
Week8	26.44 ± 1.29	32.54 ± 0.51 [a] 23.10 %	22.27 ± 0.71[a,b] -15.75 %	14.92 ± 0.73[a,b] -43.56 %

[a] Significant difference from the control group at $p < 0.05$.[b] Significant difference from the $AlCl_3$-intoxicated group at $p < 0.05$.

statistical analysis was performed between control (C=6) and treated (T=6) using T-Test

10) Gamma-glutamyl transferase (GGT)

A significant increase was seen in AlCl3 group in GGT in all 8 weeks compared to control. A significant decrease in GGT was seen in curcumin group and AlCl3+ curcumin group in all 8 weeks compared to AlCl3 group, there was a significant decrease in in GGT in all 8 weeks except for the fourth week of curcumin group, and in week 3, 4, 6, 7 and 8 for AlCl3+ curcumin group, but there was a significant increase in the first week for AlCl3+ curcumin group compared to control (Table 10).

Effect of Aluminum chloride (AlCl3) on histological structures of liver:

Results in (Fig. 1) shows normal liver structure of the control group. The study of histological structures of liver of the Aluminum chloride intoxicated rats showed that after two weeks of administration, (Fig. 2) there was distortion and inflammation of portal area, deposition of red blood cells in the portal vein and lipid droplets. After four weeks of administration (Fig. 3) there was bleeding in sinusoids and distorted portal area. After six weeks of administration (Fig. 4) showed distorted portal area, bleeding in the portal vein, bleeding in sinusoids and lipid droplets. After eight weeks of administration (Fig. 5, 6) showed distorted portal area and oedema, bleeding in the portal vein, fibrosis around portal area and vacuolar degeneration of hepatocytes.

Table (10): Effect of daily administration of *Curcuma longa* (4 mg/kg), Aluminumchloride (30 mg/kg) and combination of *Curcuma longa* and Aluminumchloride on gamma glutamyltransferase (GGT) (U/l) of adultalbino rats.

	Control	$AlCl_3$	Curcuma longa	$AlCl_3$+ Curcuma longa
	Mean ± S.E	Mean ± S.E	Mean ± S.E	Mean ± S.E
Week1	3.26 ± 0.21	5.45 ± 0.40 [a] 67.04 %	4.22 ± 0.35[a,b] 29.19 %	4.36 ± 0.08[a,b] 33.62 %
Week2	4.70 ± 0.08	6.10 ± 0.37 [a] 29.81 %	3.24 ± 0.26[a,b] -31.05 %	4.58 ± 0.37 [b] -2.60 %
Week3	6.03 ± 0.21	8.17 ± 0.75 [a] 35.53 %	4.98 ± 0.24[a,b] -17.43 %	4.12 ± 0.17[a,b] -31.62 %
Week4	6.45 ± 0.44	8.87 ± 0.18 [a] 37.51 %	5.38 ± 0.35 [b] -16.63 %	3.78 ± 0.24[a,b] -41.41 %
Week5	4.38 ± 0.21	8.25 ± 0.09 [a] 88.58 %	2.56 ± 0.09[a,b] -41.52 %	3.90 ± 0.22 [b] -10.82 %
Week6	6.18 ± 0.57	9.90 ± 0.68 [a] 60.29 %	3.49 ± 0.16[a,b] -43.57 %	4.45 ± 0.41[a,b] -27.98 %
Week7	6.61 ± 0.03	9.21 ± 0.22 [a] 39.25 %	1.48 ± 0.06[a,b] -77.57 %	1.54 ± 0.05[a,b] -76.77 %
Week8	6.00 ± 0.17	9.52 ± 0.19 [a] 58.62 %	2.31 ± 0.22[a,b] -61.45 %	2.62 ± 0.12[a,b] -56.36 %

[a]Significantdifferencefrom the control group at $p < 0.05$.[b]Significantdifferencefrom the $AlCl_3$-intoxicated group at $p < 0.05$.
statisticalanalysiswasperformedbetween control (C=6) and treated (T=6) using T-Test

Effect of Curcuma longa on histological structures of liver:

Histological structures of liver in the animals treated with Curcuma longa (Fig. 7, 8, 9 and 10) showed a normal tissue structure of liver which is the same as the control group tissue.

Effect of combination of Curcuma longa and Aluminum chloride on histological structures of liver:

Studying the histological structure of liver in the AlCl3+Curcuma group after two weeks (Fig. 11) showed normal hepatocytes nucleus, atrophy of hepatocytes nucleus and slight bleeding in sinusoids. After 4 weeks (Fig. 12) there was an improvement of liver structure as seen in the normal portal area, no bleeding in the portal vein, normal bile duct, normal hepatocytes nucleus and atrophy of hepatocytes nucleus. After six weeks (Fig. 13) there was a slight bleeding in the central vein, normal hepatocytes nucleus, atrophy of hepatocytes nucleus and lipid droplets. After 8 weeks of administration (Fig. 14) there was no bleeding in the central vein, expansion of sinusoids around the central vein, normal hepatocytes nucleus and atrophy of hepatocytes nucleus.

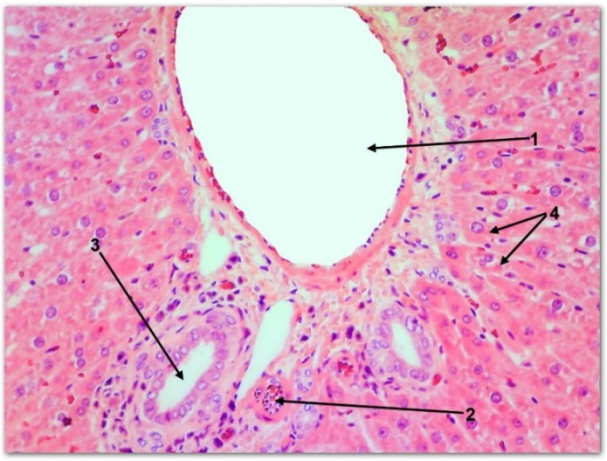

Fig. 1: A transverse section in rat liver from the control group that shows normal liver structure: 1- Branch of portal vein. 2- Branch of hepatic artery. 3- Branch of bile duct. Portal area. 4- Hepatocytes arranged in sheets.X400, H&E.

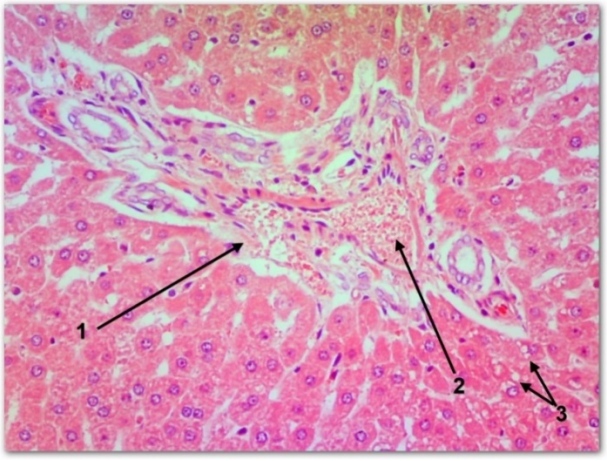

Fig. 2: A transverse section in rat liver from the two weeks AlCl3 intoxicated group shows distortion and inflammation of portal area (1), deposition of red blood cells in the portal vein (2) and lipid droplets (3).X400, H&E.

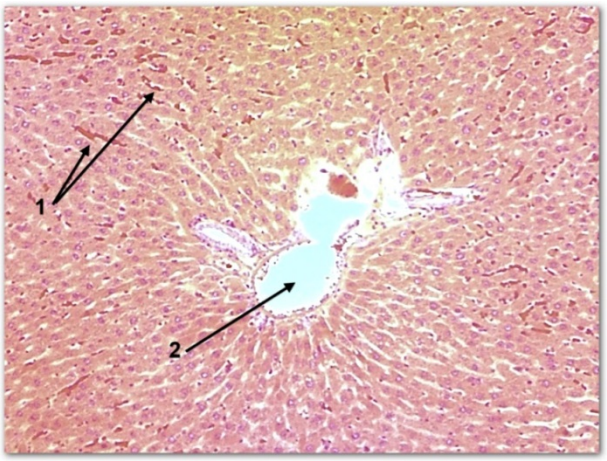

Fig. 3: A transverse section in rat liver from the four weeks AlCl3 intoxicated group shows bleeding in sinusoids (1) and distorted portal area (2). X400, H&E.

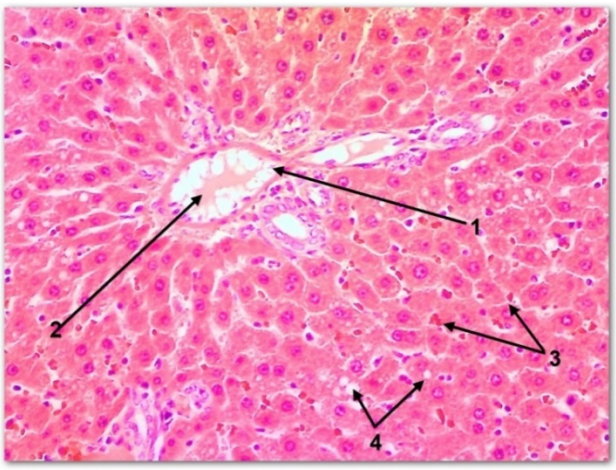

Fig. 4: A transverse section in rat liver from the six weeks AlCl3 intoxicated group shows distorted portal area (1), bleeding in the portal vein (2), bleeding in sinusoids (3) and lipid droplets (4). X400, H&E.

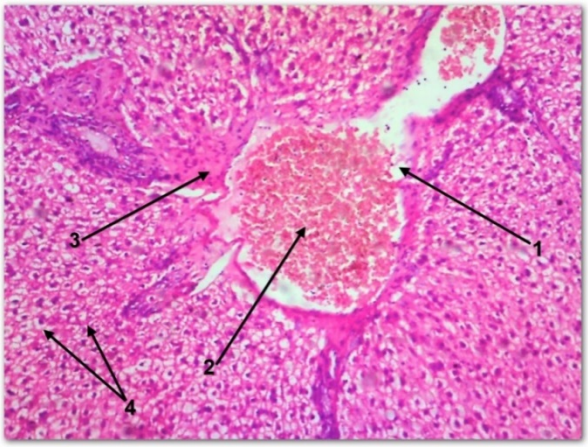

Fig. 5: A transverse section in rat liver from the eight weeks AlCl3 intoxicated group shows distorted portal area and oedema (1), bleeding in the portal vein (2), fibrosis around portal area (3) and vacuolar degeneration of hepatocytes (4). X400, H&E.

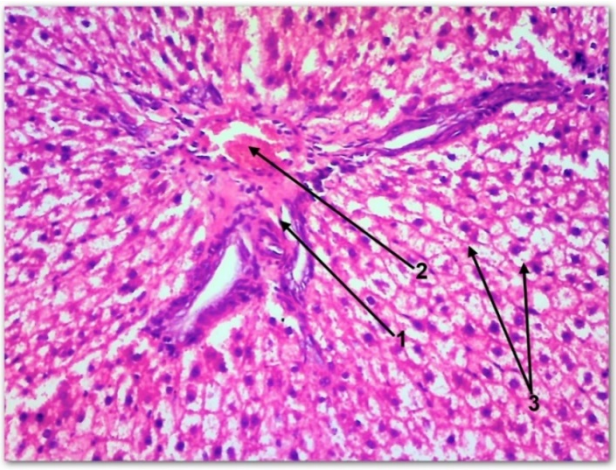

Fig. 6: A transverse section in rat liver from the eight weeks AlCl3 intoxicated group shows distorted portal area (1), bleeding in the portal vein (2) and vacuolar degeneration of hepatocytes and necrosis (3). X400, H&E.

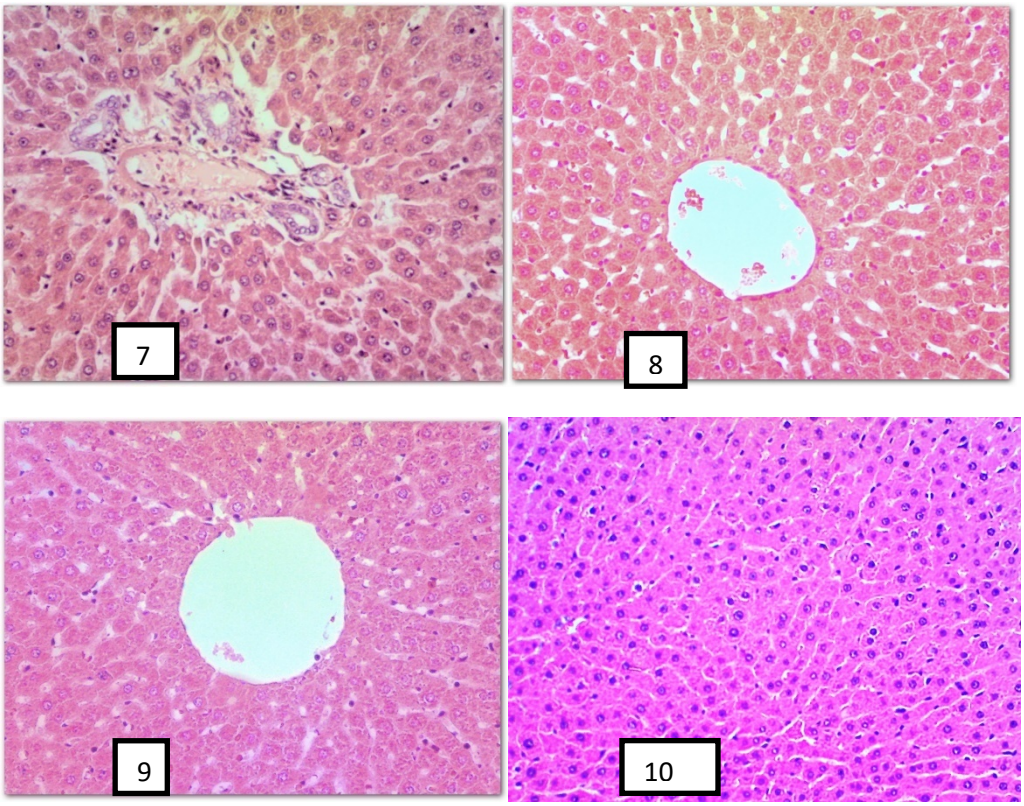

Fig. 7, 8, 9, and 10: A transverse section in rat liver from the Curcuma longa group from one to eight weeks shows normal tissue structure of liver.X400, H&E.

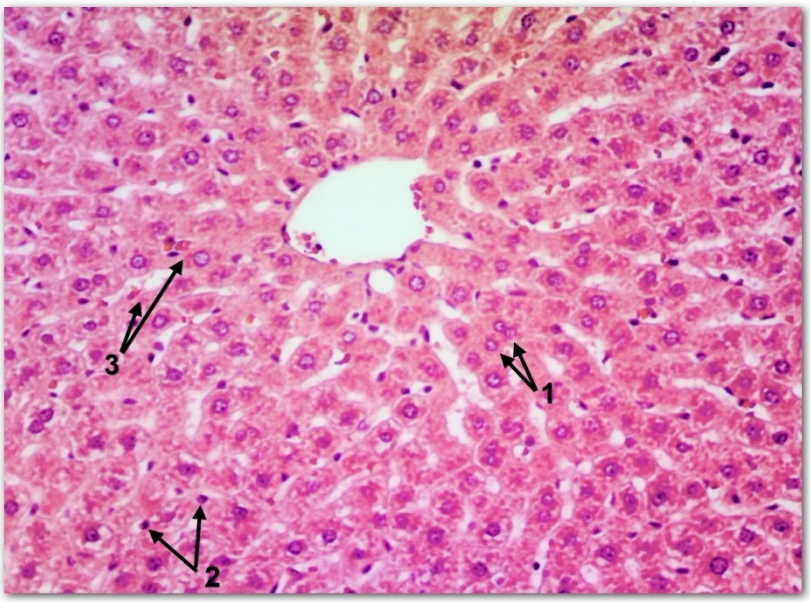

Fig. 11: A transverse section in rat liver from the two weeks AlCl3+Curcuma group shows normal hepatocytes nucleus (1), atrophy of hepatocytes nucleus (2) and slight bleeding in sinusoids (3).X400, H&E.

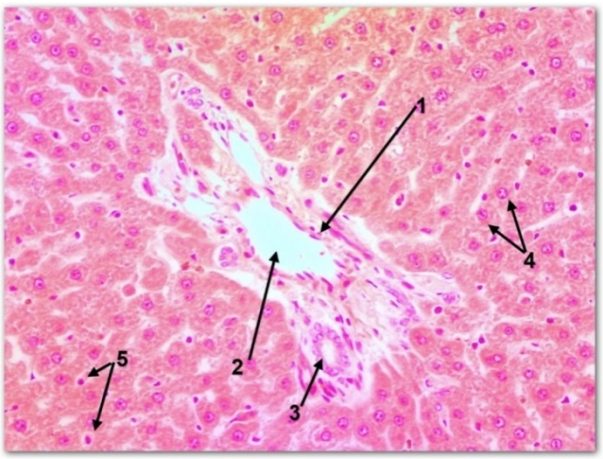

Fig. 12: A transverse section in rat liver from the four weeks AlCl3+Curcuma group shows improvement of liver structure: normal portal area (1), no bleeding in the portal vein (2), normal bile duct (3), normal hepatocytes nucleus (4) and atrophy of hepatocytes nucleus (5). X400, H&E.

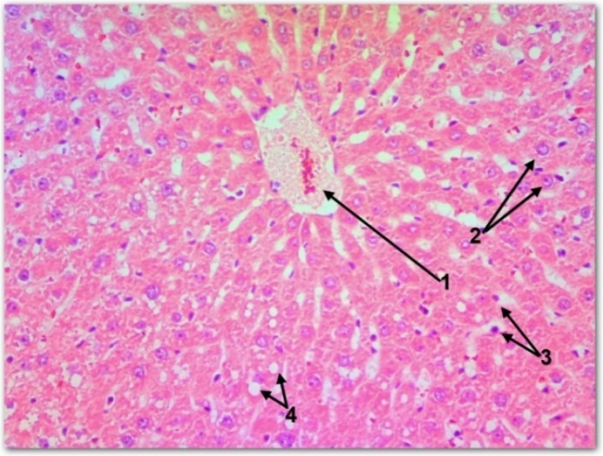

Fig. 13: A transverse section in rat liver from the six weeks AlCl3+Curcuma group shows slight bleeding in the central vein (1) normal hepatocytes nucleus (2), atrophy of hepatocytes nucleus (3) and lipid droplets (4). X400, H&E.

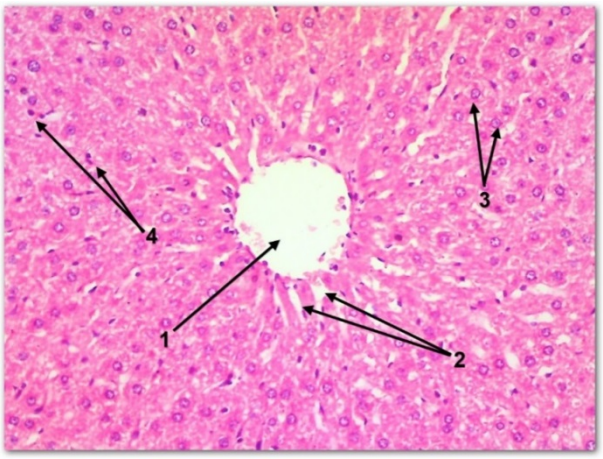

Fig. 14: A transverse section in rat liver from the eight weeks AlCl3+Curcuma group shows no bleeding in the central vein (1), expansion of sinusoids around the central vein (2), normal hepatocytes nucleus (3) and atrophy of hepatocytes nucleus (4).X400, H&E.

DISCUSSION

The data showed that AlCl3 increase serum glucose levels significantly in all eight weeks of experiment (Table 1). This agrees with Abdel-Wahab, 2012 [17] who stated that the administration of AlCl3 increased blood glucose level in rats which may indicate disruption in carbohydrate metabolism. The results were in the same line with [18]. Aluminum chloride-induced hyperglycemia and that may be attributed to enhanced breakdown of liver glycogen, its subsequent increased glucose production and decrease glucose utilization [19]. Hayden, 2002 [20] recorded that oxidative stress was a major pathogenic link to both insulin resistance and the dysfunction of the pancreatic β-cells through the formation of amyloid proteins, which not only prevents the release of insulin into the circulation, but also destroys the insulin secreting β-cells.

Several studies revealed the benefits of medical plants like curcumin which showed hypoglycemic effect [21]. The present study recorded that treatment with curcumin caused a significant decrease in serum glucose in all experiment period except for the fourth week, also treatment with curcumin along with aluminum chloride decreased serum glucose significantly in all eight weeks compared to AlCl3 group. The hypoglycemic effect of curcumin may be attributed to curcumin induces electrical activity in rat pancreatic β-cells by activating volume-regulated anion channel, and led to depolarization of cell membrane potential, generation of electrical activity, and enhanced insulin release [22]. Shao et al., 2012 [23] suggested that curcumin improves whole body glucose disposal by both stimulation of insulin sensitivity and inhibition of hepatic gluconeogenesis.

In this study AlCl3 exposure caused a decrease of total protein and albumin level in all eight weeks of experiment, (Table 2&3). The inhibitory effect of AlCl3 on protein profile is in agreement with the finding of [24]. These changes may refer to degeneration of renal tubular cells by AlCl3accumulation leading to nephrotoxicity [25]. Aluminum chloride accumulate in liver of AlCl3-treated rats [26]. Thus, it is likely that the tissue burden of AlCl3 have caused disturbances in protein metabolism [27]. Tripathi et al., 2009 [28] found that the significant decrease in the concentrations of total proteins in rats treated with AlCl3 particularly the albumin could be attributed to nutrition or reduction of the protein synthesis in the liver which could be due to reduced enzymes of protein synthesis in liver.

There was a significant increase in total protein and albumin of curcumin and AlCl3+curcumin group in most of experimental period. This finding was supported by the finding of [29] who said that the addition of turmeric ameliorated the adverse effects of aflatoxin B1 (a secondary metabolites of various Aspergillus spp. which has hepatotoxic effect) on serum total protein and albumin. Venkatanarayanaet al., 2012 [30] reported that Curcumin treatment significantly improved the concentrations of total proteins and albumin in plasma. This effect may be related to the antioxidant properties of curcumin [31].

In this study AlCl3 exposure caused a significant increase in total cholesterol and triglycerides in all weeks of experiment (Table 4&5). This data is in agreement with [32] & [33] who recorded that AlCl3 increased cholesterol and triglyceride levels compared to the controls. Newairy et al., 2009 [19] demonstrated that accumulation of AlCl3 in the liver may lead to a disturbance of lipid metabolism and elevation in lipid profile. Also, administration of AlCl3 increased lipid peroxidation and significantly affect various membrane-bound enzymes loss of membrane integrity which altered lipid metabolism and were closely associated with hyperlipidemia and/or hypercholesterolemia due to hepatic dysfunction.

The results showed a significant decrease in total cholesterol and triglycerides levels in curcumin treated group in all eight weeks, and a significant decrease in the group treated with curcumin alone or with AlCl3 compared to AlCl3 group. These results were confirmed by [34] who revealed that curcumin significantly lower total cholesterol, triglycerides. Curcumin was effective in inhibiting lipid synthesis, storage, and stimulating fatty acids degradation, these effects mediated by regulating the activities of several key enzymes and the expression of transcription factors that regulate lipid metabolism [35].

The current study showed a significant increase in bilirubin level of AlCl3 exposed group in all eight weeks of experiment (Table 6). This was in agreement with [19] who found that bilirubin was increased due to AlCl3 administration which cause liver injury. AbuAita, 2014 [36] found that increased level of bilirubin in the AlCl3 administered rats may be due to the destructive effect of AlCl3 on erythrocyte and this was in agreement with the

present results. The obtained results coincide with the previous study of [37]. Moreover, Mangood et al., 2012 [38] found that the induction rate of serum bilirubin was associated with free radical production.

The current results showed a significant decrease in bilirubin in curcumin and AlCl3+curcumin group in all eight weeks of experiment. The results agree with the findings of [15] who noticed that after administration of curcumin, a significant decline in bilirubin which ameliorate the increase in total bilirubin levels after injection of thioacetamide, which caused liver injury in rats. Vinay et al., 2016 [39] stated that administration of curcumin significantly prevented the elevation in total bilirubin, by maintaining the integrity of cell membranes (antioxidant property). They concluded that Curcuma protects against ethanol induced hepatotoxicity and hepatic damage.

The activities of serum liver function enzymes: alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma glutamyle transferase (GGT) were increased by the AlCl3in all eight weeks of experiment (Table 7, 8, 9 & 10). This was in agreement with the studies of [40] who reported that the increased activity of intracellular enzyme ALT in serum of mice that were treated with AlCl3indicates significant liver cellular damage. They suggested that chronic AlCl3 exposure induce hapatoxicity manifested by elevation of liver function enzymes [41]. Aluminum chloridetoxicity lead to the accumulation in liver[42] and lead to discharge of its enzymes content to the circulation [43].Kumar et al., 2009 [44] demonstrated that theses enzymes increases in serum when cellular degeneration or destruction occurs in liver. These enzymes caused alterations in liver function, such increase could be a sign of impaired liver function.

The current study showed a significant decrease in ALP, AST, ALT and GGT levels of curcumin treated group compared to control, and a significant decrease of AlCl3+curcumin group compared to AlCl3 group in most weeks of experiment. These findings are in agreement with the findings of [45] found that AST, ALT, ALP and GGT levels declined significantly in rats after administration of curcumin to counter the elevation due to paracetamol. This means curcumin has hepatoprotective effect and antioxidant properties against hepatotoxins. Rukkumani et al., 2003 [46] concluded that curcumin, by scavenging or neutralizing free radicals, inhibits peroxidation of membrane lipids and maintains cell membrane integrity and their function.

Histological structures of liver of the AlCl3intoxicated rats (fig. 2-6) showed distorted portal area and oedema, bleeding in the portal vein, fibrosis around portal area and vacuolar degeneration of hepatocytes. Abdel-Wahab, 2012 [17] studies revealed that liver sections from rats administered AlCl3 showed distorted liver architecture: Marked necrosis and degeneration of hepatocytes, centrilobular necrosis and congestion of the central vein, vacuolization of hepatocytes, dilatation and congestion of the blood sinusoids in addition to infiltration of inflammatory cells were observed.

Histological structures of liver in the animals treated with Curcuma longa (fig. 7-10) showed a normal tissue structure of liver which resembles the control group, while Studying the histological structure of liver in the AlCl3+Curcuma group (fig. 11-14) showed that there was no bleeding in the central vein, expansion of sinusoids around the central vein, normal hepatocytes nucleus and atrophy of hepatocytes nucleus. Haghighi et al., 2013 [15] noticed an inflammation in hepatic lobules in thioacetamide treated animals, while in Curcumin Group, even a moderate portal inflammation was still present, but when compared to the thioacetamide group, it was significantly less. Also curcumin protection of liver from inflammatory condition may be due to its anti-inflammatory effect [47].

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