Evaluation of the Potential Cardio Protective Effects of Sechium edule (Chayote Fruit) Extract on Male Wistar Rats Subjected to Cadmium-Induced Toxicity

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Abstract:

Cardio toxicity, a major health concern linked to heavy metal accumulation, particularly Cadmium (Cd) chloride, induces oxidative stress and disrupts heart function. This study investigated the potential ameliorative effects of ethanol extracts from Schism elude (S.E.) fruits on Cd-induced oxidative stress in male Westar rats. Daily administration of Cd (4mg/kg) for 5 weeks resulted in oxidative stress, evidenced by elevated lipid peroxidation and altered antioxidant status. Treatment with S.E. extract (200mg/kg and 400mg/kg) demonstrated significant reductions in serum total cholesterol, triglycerides, and low-density lipoprotein cholesterol, coupled with increased high-density lipoprotein cholesterol. The extract reversed Cd-induced elevations in serum ALT, lipid peroxidation, & improved enzymatic and no enzymatic antioxidant levels in the heart. S.E. extract also regulated serum Na^+ and K^+ ion levels and improved abnormal ECG parameters induced by Cd, indicating enhanced heart function. Histopathological analysis revealed marked improvements in the structural features of the heart, kidney, and liver in S.E. extract-treated groups compared to the Cd control group. These findings suggest that Schism elude may hold promise as a novel treatment for cardio toxicity resulting from cadmium exposure.

Keywords: *Cardiotoxicity, Cadmium, Sechium edule, cholesterol, triglycerides.*

1. Introduction:

Cardio toxicity, often induced by heavy metal exposure like cadmium (Cd), poses severe health risks Cd, [1] a non-essential heavy metal, is highly toxic and associated with various diseases. [2-5] Its mechanism involves oxidative tissue damage, reactive oxygen species production, and disruption of cellular functions. Herbal medicines, with known cardiovascular benefits, offer a potential safer alternative. [6-8]

The study focuses on *Sechium edule* (S.E.), a plant widely used in Ayurvedic medicine, renowned for its diverse phytoconstituents. With significant diuretic, nephroprotective and anti-inflammatory etc. [9-12] properties, S.E. is investigated for its potential in countering cadmium (Cd)-induced cardiotoxicity in Wistar rats. Cd, a major public health concern, infiltrates ecosystems through various sources, posing severe health risks. Cd toxicity, [14,15] associated with oxidative damage, impacts organs and tissues, leading to cardiomyopathy and heart failure. Synthetic drugs carry risks, emphasizing the need for safer alternatives. Herbal medicines, including S.E., gain importance for cardiovascular health. This study explores S.E.'s cardioprotective effects, providing insights into its therapeutic potential against Cd-induced cardiovascular harm. [16-19]

2. Materials & Methods:

2.1. Plant material:

Fruits of Sechium edule (S.E.) were sourced from Spencer, Haldia, and the local market in Haldia, West Bengal. Taxonomic authentication at the Regional Research Institute (Ayurveda), Bangalore, assigned the voucher specimen reference number (RRCBI/MCW/7/2008) for future use.

2.2. Preparation of the extract:

Sechium edule (S.E.) fruit extract preparation involved cleaning, drying, and powdering. The coarse powder underwent petroleum ether treatment, maceration in ethanol, and distillation. The resulting ethanolic extract, a dark mass, was stored for further use, ensuring removal of impurities and preservation of bioactive compounds. [20-23]

2.3. Phytochemical investigation:

Preliminary phytochemical screening of the ethanolic extract of *Sechium edule* (S.E.) fruits done for identification of the presence of alkaloids, phenolics, flavonoids, saponins, carotenoids, carbohydrates, and glycosides.

2.4. Experimental animals:

Male albino Wistar rats (180-220g) will be used, housed in controlled conditions with a 12h light-dark cycle, sanitized cages, and standard diet access. After a week of acclimatization, experiments following CPCSEA guidelines and IAEC approval will commence.[24]

2.5. Drugs and Chemicals:

Cadmium chloride, vitamin C, ketamine HCl, and assay kits for total cholesterol, triglycerides, SGOT, SGPT, ALP, total protein, serum urea, sodium, potassium ions, and creatinine will be purchased. All other chemicals used will be of analytical reagents grade from commercial sources. [25, 26]

2.6. Oral Toxicity Test:

According to OECD 423 guidelines, Wistar rats, after overnight fasting, will receive a single oral dose (2000 mg/kg b.w.) of S.E. fruit extract. Food will be withheld for 3-4 hrs post-administration. Rats will be observed for 30 min initially, periodically for the first 24 hrs (with emphasis on the first 4 hrs), and daily for 14 days. Observations will cover skin, fur, eyes, mucous membranes, respiratory and circulatory functions, autonomic responses, and central nervous system parameters. Mortality, if any, will be recorded over the two-week period. [27,28]

2.7. Induction of Cardiotoxicity:

Male Wistar rats, rendered cardiotoxic, received oral Cd (4mg/kg) for 5 weeks. Cd (90 mg), dissolved in sterile water (30 ml), was administered orally (0.25 ml) via an intragastric tube throughout the 5-week period.

2.8. Experimental design:

Male Wistar rats, post one-week acclimatization, were divided into five groups (n=6). Pre-treatment with S.E. fruit extract (200 and 400 mg/kg; p.o.) was done for 3 weeks, followed by Cd administration (4 mg/kg; p.o.) for 5 weeks. Groups received clean water, Cd, Vit-C + Cd, S.E. (200 mg/kg) + Cd, and S.E. (400 mg/kg) + Cd, respectively. Treatments were administered orally using an intra-gastric tube for 56 days. On the 56th day, after a 24-hour fast, blood was collected for biochemical analysis, and animals were euthanized for further assessments. [29]

3. Result:

3.1. Preliminary phytochemical investigation:

In preliminary phytochemical analysis of an alcoholic fruit extract S.E showed the presence of carbohydrates, proteins, flavonoids, saponins and tannins.

3.2. Acute oral toxicity test:

In toxicity study, no mortality occurred during 48 hours of observation with the selected dose 2000mg/kg p.o. As the ethanolic extract of S.E fruits were found to be tolerated up to a dose level of 2000mg/kg p.o. The extract was considered to be safe and dose ranges 400mg/kg p.o. ($1/5^{th}$ of the extract) and 200mg/kg p.o. ($1/10^{th}$ of the extract) was selected for the present study.

3.3. In Vivo Activity:

3.3.1. Effect of alcoholic fruit extract ofS.E on lipid profile in Cd- induced cardiotoxic rats.

A. Effect of administration of Cd (4mg/kg; p.o.) on lipid profiles in rats.

Total cholesterol, Triglyceride, high density lipoprotein (HDL-C), low density lipoprotein (LDL-C) and very low-density lipoprotein (VLDL-C) levels in vehicle treated rats (Group-I) were found to be 64.09±2.46, 46.81±1.10 36.79±1.68, 20.67±0.43 and 8.56±0.22 respectively. In Cd (4mg/kg) treated (Group II) the serum level of total cholesterol, Triglyceride, HDL-C, LDL-C and VLDL-C were found to be 79.55±1.41, 117.59±3.83, 15.75±0.73, 38.04±0.82 and 23.53±0.76 respectively. Thus, Cd significantly increased the levels of total cholesterol, Triglyceride, LDL-C and VLDL-C and decreased HDL-C level.

B. Effect of administration of Vit-C (50mg/kg; p.o.) on lipid profiles in Cd-induced cardiotoxic rats.

Total cholesterol, triglyceride, HDL-C, LDL-C and VLDL-C levels in Vit–C (50mg/kg) treated rats (Group III) were found to be 66.59±1.26, 63.03±1.74, 28.53±0.68, 25.13±0.23 and 12.61±0.35 respectively. The above values have significantly decreased the levels of total cholesterol, triglyceride, LDL-C, and very VLDL-C and HDL-C value have increased significantly in group-III when compared to group-II.

C. Effect of administration of lower dose of alcoholic fruit extract ofS.E (200mg/kg; p.o.) on lipid profiles in Cd-induced cardiotoxic rats.

Total cholesterol, triglyceride, HDL-C, LDL-C, and VLDL-C levels in lower dose of S.E. (200mg/kg) treated rats (Group IV) were found to be 73.33±1.94, 68.59±1.88 26.76±2.19, 32.23±0.09 and 114.12±0.37 respectively. The above values have significantly decreased the levels of total cholesterol, triglyceride, LDL-C and VLDL-C values and HDL-C value have increased significantly when compared to group-II.

D. Effect of administration of higher dose of alcoholic fruit extract ofS.E. (400mg/kg; p.o.) on lipid profiles in Cd-induced cardiotoxic rats.

Total cholesterol, triglyceride, HDL-C, LDL-C and VLDL-C levels in higher dose of S.E. (400mg/kg) treated rats (Group V) were found to be 71.37±1.46, 64.49±2.80, 32.51±2.29, 26.61±0.51 and 13.49±0.55 respectively. The above values have significantly decreased the levels of total cholesterol, triglyceride, LDL-C and VLDL-C values and HDL-Cs value have increased significantly when compared to group-II.

Table 1: Effect of alcoholic fruit extract ofS.E on lipid profile Cd-induced cardiotoxic rats.

Groups	**Treatment**	**Total cholesterol (mg/dL)**	**Triglyceride (mg/dL) s**	**HDL-C (mg/dL)**	**LDL-C (mg/dL)**	**VLDL-C (mg/dL)**
I	Control	64.09±2.46	46.81±1.10	36.79±1.67	20.67±0.43	8.562±0.22
II	Cd (4mg/kg; p.o.)	79.55±1.41$^{\#\#}$	117.59±3.83$^{\#\#}$	15.75±0.73$^{\#\#}$	38.04±0.82$^{\#\#}$	23.53±0.76$^{\#\#}$
III	Vit-C (50 mg/kg; p.o.) +Cd	66.59±1.26**	63.03±1.74**	28.53±0.68**	25.13±0.23**	12.61±0.35**
IV	S .E. (200 mg/kg;p.o.) +Cd	73.33±1.94**	68.59±1.88**	26.76±2.19**	32.23±0.09**	114.12±0.37*
V	S .E. (400 mg/kg; p.o.) +Cd	71.37±1.46**	64.49±2.80**	32.51±2.29**	26.61±0.15*	13.49±0.55**

Values are expressed as Mean ± SEM, n=6; $^{\#\#}$ P<0.01 considered statistically significant as compare to normal control group; *** P<0.001, ** P<0.01 and *P<0.05 considered statistically significant when compared to Cd treated group.

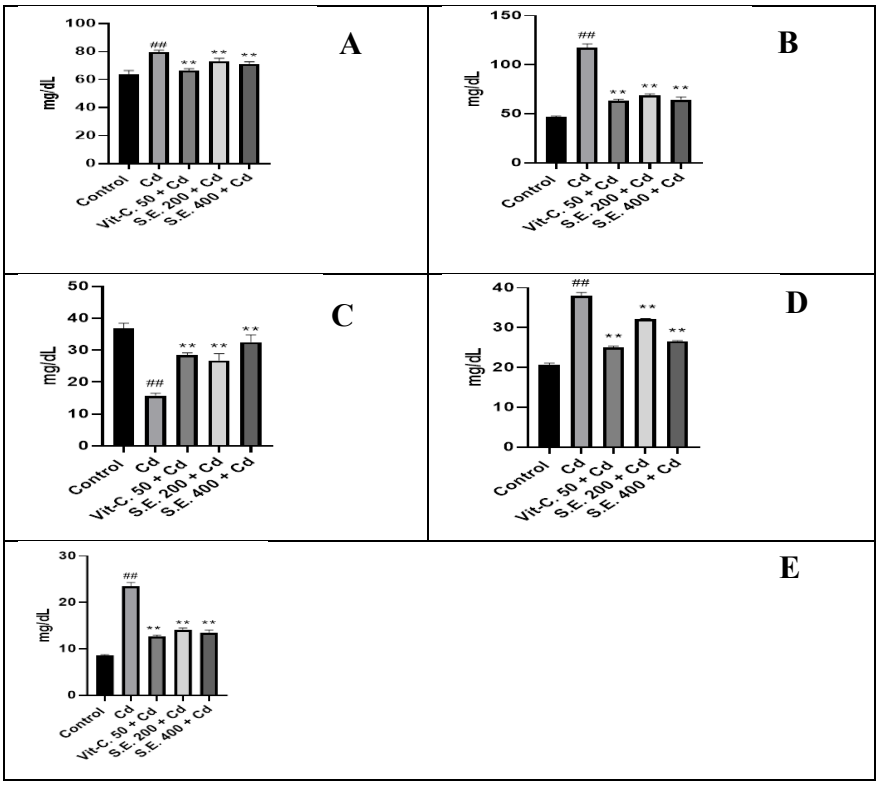

Figure 1: Effect of alcoholic fruit extract ofS.E. on A. cholesterol B. Triglyceride C. HDL-C D. LDL-C E. VLDL-C level in Cd-induced cardiotoxic rats.

3.3.2. Effect of alcoholic fruit extract ofS.E. on serum lactate dehydrogenase (LDH), creatine phosphokinase (CPK), Serum glutamic oxaloacetic transaminase (SGOT), SGPT, and total protein levels pyruvic transaminase (SGPT) and total protein levels in Cd- induced cardiotoxic rats.

A. Effect of administration of Cd (4mg/kg; p.o.) on serum cardiac markers in rats.

Serum LDH, CPK, SGOT, SGPT and total protein levels in vehicle treated rats (Group-I) were found to be 139.39±6.412, 32.98±3.08, 25.09±2.55, 26.31±0.99, and 7.12±0.39 respectively. In Cd (4mg/kg) treated rats (Group II) the LDH, CPK, SGOT, SGPT and total protein were found to be 455.60±41.11, 62.08±3.25, 180.20±11.72, 96.40±3.94 and 5.04±0.133 respectively. Thus, in Cd treated rats (Group-II) significantly increased the levels of serum LDH, CPK, SGOT and SGPT and decreased total protein level.

B. Effect of administration of Vitamin-C (50mg/kg; p.o.) on serum cardiac marker in Cd-induced cardiotoxic rats.

Serum LDH, CPK, SGOT, SGPT and total protein levels in Vit-C (50mg/kg) treated rats (Group-III) were found to be 150.36±12.01, 36.29±1.64, 117.88±2.75, 58.96±1.94 and 6.81±0.12 respectively. The above values have significantly decreased the level of LDH, CPK, SGOT and SGPT and increased total protein level when compared to group-II.

C. Effect of administration of lower dose of alcoholic fruit extract ofS.E (200mg/kg; p.o.) on serum cardiac marker in Cd-induced cardiotoxic rats.

Serum LDH, CPK, SGOT, SGPT and total protein levels in rats treated with alcoholic fruit extract ofS.E. (200mg/kg) treated rats (Group-IV) were found to be 246.09±5.91, 39.81±2.49, 128.76±4.95, 77.47±1.05 and 6.20±0.11 respectively. The above values have significantly decreased the level of LDH, CPK, SGOT and SGPT and increased total protein level when compared to group-II.

D. Effect of administration of higher dose of alcoholic fruit extract ofS.E. (400mg/kg; p.o.) on serum cardiac marker in Cd-induced cardiotoxic rats.

Serum LDH, CPK, SGOT, SGPT and total protein levels in alcoholic fruit extract ofS.E. (400mg/kg) treated rats (Group-V) were found to be 196.64±4.48, 38.56±2.58, 124.01±2.99, 64.30±2.23 and 6.23±0.09 respectively. The above values have significantly decreased Serum LDH, CPK, SGOT and SGPT and increased total protein level when compared to group-II.

Table 2: Effect of alcoholic fruit extract ofS.E. on biochemical parameter LDH, CPK, SGOT, SGPT and total protein in Cd-induced cardiotoxic rats.

Groups	**Treatment**	**LDH (U/L)**	**CPK (U/L)**	**SGOT (IU/L)**	**SGPT (IU/L)**	**Total protein (gm/dL)**
I	Control	139.39±6.41	32.98±3.08	25.09±2.55	26.31±0.99	7.12±0.39
II	Cd (4mg/kg;p.o)	455.60±41.11$^{\#\#}$	62.08±3.25$^{\#\#}$	180.20±11.72$^{\#\#}$	96.40±3.94$^{\#\#}$	5.04±0.13$^{\#\#}$
III	Vit-C (50mg/kg; p.o) +Cd	150.36±12.01**	36.29±1.64**	117.88±2.75**	58.96±1.94**	6.81±0.12**
IV	S.E. (200mg/kg ;p.o) +Cd	246.09±5.91**	39.81±2.49**	128.76±4.95**	77.47±1.05**	6.20±0.11**
V	S.E. (400mg/kg ;p.o) +Cd	196.64±4.48**	38.56±2.58**	124.01±2.99*	64.30±2.23**	6.23±0.09**

Values are expressed as mean ± SEM, n=6; ## P<0.01 considered statistically significant as compare to normal control group; ***P<0.001, **P<0.01 and * P<0.05 considered statistically significant when compared to Cd group.

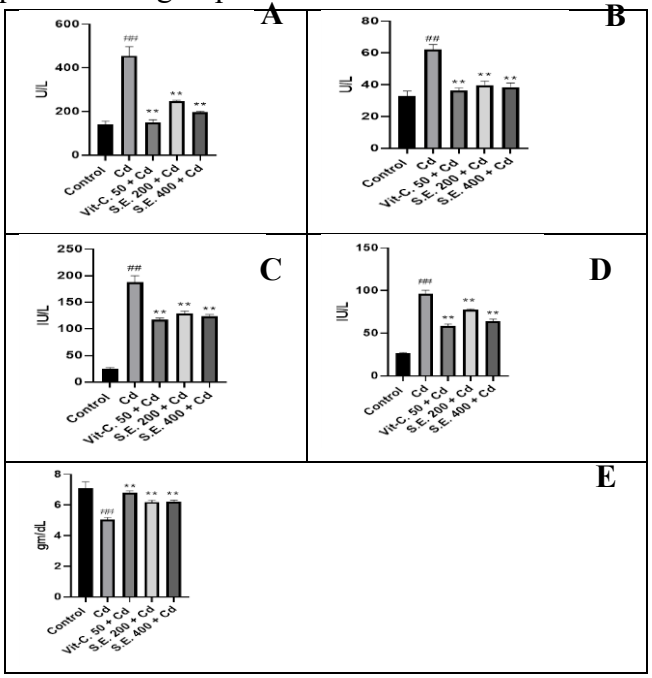

Figure 2: Effect of alcoholic fruit extract ofS.E. on A. LDH, B. CPK, C. SGOT, D. SGPT, E. Total protein level in Cd-induced cardiotoxic rats.

3.3.3. Effect of alcoholic fruit extract ofS.E. on blood urea, creatinine, alkaline phosphatase (ALP), sodium (Na^+) and potassium (K^+) levels in Cd-induced cardiotoxic rats.

***A. Effect of administration of Cd (4mg/kg; p.o.) on serum level of cardiotoxic rats*.**

Blood urea, creatinine, ALP, Na^+ and K^+ levels in vehicle treated rats (Group-I) were found to be 24.06±1.03, 0.174±0.007, 14.28±1.40, 45.32±1.90 and 3.95±0.13 respectively. In Cd (4mg/kg) treated rats (Group II) the serum levels of urea, creatinine, ALP, Na^+ and K^+ were found to be 45.16±2.04, 0.752±0.03, 75.84±6.42, 141.69±15.62 and 6.06±0.61 respectively. Thus, in Cd treated rats (Group-II) significantly increased the levels of blood urea, serum creatinine, ALP, Na^+ and K^+.

B. Effect of administration of Vit-C (50mg/kg; p.o.) on serum levels in Cd-induced cardiotoxic rats.

Blood urea, creatinine, ALP, Na^+ and K^+ levels in Vit-C (50mg/kg) treated rats (Group-III) were found to be 28.43±1.55, 0.401±0.018, 16.95±1.63, 65.08 ±1.24 and 3.77±0.51 respectively. The above values have significantly decreased blood urea, creatinine, ALP, $Na^+$and K^+ level when compared to group II.

C. Effect of administration of lower dose of alcoholic fruit extract ofS.E. (200mg/kg; p.o.) on serum levels in Cd-induced cardiotoxic rats.

Blood urea, creatinine, ALP, Na^+ and K^+ levels in lower dose of ethanolic extract of fruits S.E. (200mg/kg) treated rats (Group-IV) were found to be 38.38±1.67, 0.324±0.037, 19.03±1.51, 87.27±2.12 and 4.26±0.26 respectively. The above values have significantly decreased for blood urea, creatinine, ALP, Na^+ and K^+ level when compared to group-II.

D. Effect of administration of higher dose of alcoholic fruit extract ofS.E. (400mg/kg; p.o.) on serum levels in Cd-induced cardiotoxic rats.

Blood urea, creatinine, ALP, Na^+ and K^+ levels in higher dose of ethanolic extract of fruits S.E. (400mg/kg) treated rats (Group-IV) were found to be 35.63±1.31, 0.314±0.019, 17.25±1.05, 82.98±2.52 and 3.53±0.18 respectively. The above values have significantly decreased for blood urea, creatinine, ALP, Na^+ and K^+ level when compared to group-II.

Table 3: Effect of alcoholic fruit extract ofS.E. on biochemical parameter Blood urea, serum creatinine, alkaline phosphatase, sodium (Na+) and potassium (K+) in Cd- induced cardiotoxic rats.

Groups	**Treatment**	**Urea (mg/dL)**	**Creatinine (mg/dL)**	**ALP (KA/dL)**	**Na^+ (mmol/L)**	**K^+ (mmol/L)**
I	Control	24.06±1.03	0.174±0.007	14.28±1.40	45.32±1.90	3.95±0.13
II	Cd (4mg/kg; p.o.)	45.16±2.04$^{\#\#}$	0.752±0.029$^{\#\#}$	75.84±6.42$^{\#\#}$	141.69±15.62$^{\#\#}$	6.06±0.61$^{\#\#}$
III	Vit-C (50mg/kg; p.o.) +Cd	28.43±1.55**	0.401±0.018**	16.95±1.63**	65.08±1.24**	3.77±0.51**
IV	S.E. (200mg/kg; p.o.) +Cd	38.38±1.67*	0.324±0.037**	19.03±1.51**	87.27±2.12**	4.26±0.26**
V	S.E. (400mg/kg; p.o.) +Cd	35.63±1.31**	0.314±0.019**	17.25±1.05**	82.98±2.52**	3.53±0.18**

Values are expressed as mean ± SEM, n=6; $^{\#\#}$ P<0.01 considered statistically significant as compare to normal control group; ***P<0.001, **P<0.01 and * P<0.05 considered statistically significant when compared to Cd group.

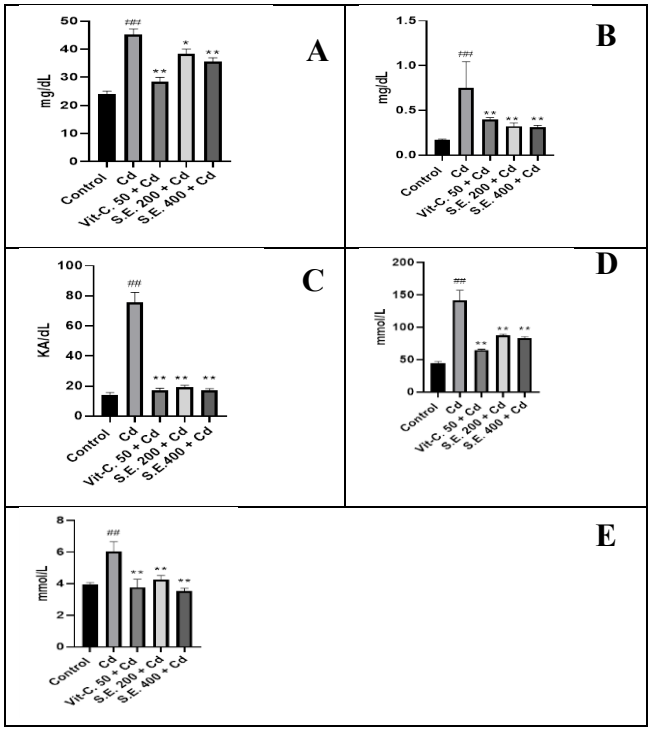

Figure 3: Effect of alcoholic fruit extract ofS.E. on A. Urea, B. Creatinine, C. ALP, D. Na^+, E. K^+ level in Cd-induced cardiotoxic rats.

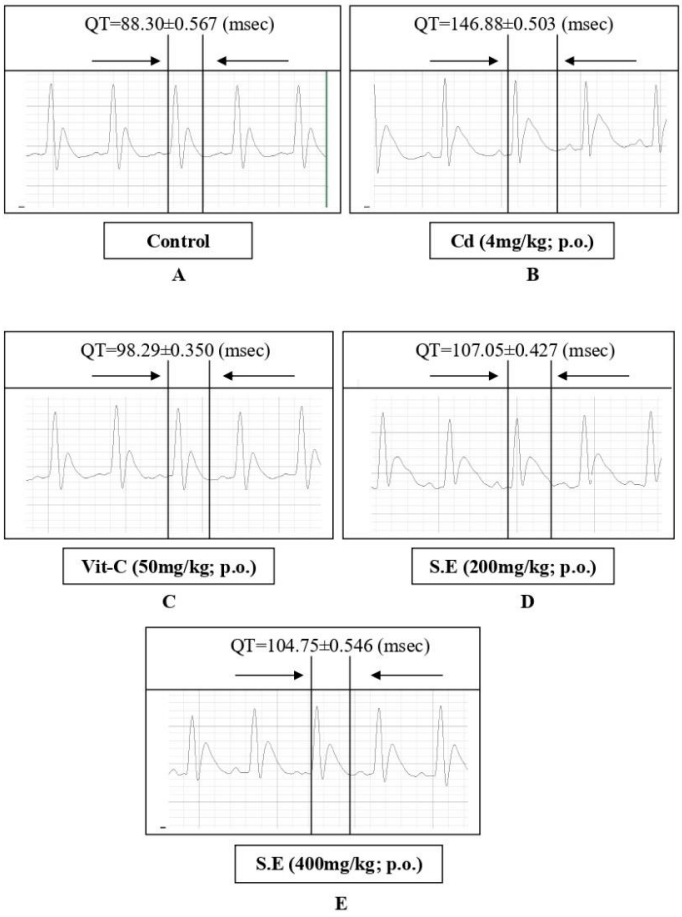

Figure 4: A-E Effect of S.E. on ECG in QT interval in Cd-induced cardiotoxic rats.

3.3.4. Effect of alcoholic fruit extract ofS.E. on ECG in QT interval of heart in Cd-induced cardiotoxic rats.

A. ***Effect of administration of Cd (4mg/kg; p.o.) on QT interval in rats.***

QT interval in vehicle treated rats (Group-I) were found to be 82.93±0.392, 85.26±0.445 and 88.30±0.567 respectively on day 1st, 30th and 56th day. In Cd (4mg/kg) treated rat (Group-II) the QT interval was found to be 87.33±0.567, 122.45±0.627 and 146.88±0.503 respectively on day 1st, 30th and 56th day. Thus, in Cd treated rats (Group-II) the QT interval was significantly increased over a period of 56th days when compared to (Group-I).

B. Effect of administration of Vit-C (50mg/kg; p.o.) on QT interval in Cd-induced cardiotoxic rats.

QT interval in rats, treated with Vit-C (50mg/kg) in (group-III) were found to be 86.34±0.336, 91.40±0.533 and 98.29±0.0350 respectively on day 1st, 30th and 56th day. The above values were significantly decreased from day 30th to 56th day when compared to (Group-II).

C. Effect of administration of lower dose of alcoholic fruit extract ofS.E. (200mg/kg; p.o.) in Cd-induced cardiotoxic rats.

QT interval in rats treated with lower dose of alcoholic fruit extract ofS.E. (200mg/kg) in (Group-IV) were found to be 82.64±0.455, 97.22±0.456 and 107.05±0.427 respectively on day 1st, 30th and 56thday. The above values were significantly decreased from day 30th to 56th day when compared to (Group-II).

D. Effect of administration of higher dose of alcoholic fruit extract ofS.E. (400mg/kg; p.o.) in Cd-induced cardiotoxic rats.

QT interval in rats treated with higher dose of alcoholic fruit extract ofS.E. (400mg/kg) in (Group-V) were found to be 87.51±0.321, 96.50±0.601 and 104.75±0.546 respectively on day 1st, 30th and 56thday. The above values were significantly decreased from day 30th to 56th day. when compared to (Group-II).

Table 4: Effect of alcoholic fruit extract ofS.E. on ECG in QT interval of heart in Cd-induced cardiotoxic rats.

Groups	**Treatment**	**QT interval (msec)**		
		Day 1	**Day 30**	**Day 56**
I	Control	82.93±0.392	85.26±0.445	88.30±0.567
II	Cd (4mg/kg; p.o.)	87.33±0.567$^{\#\#}$	122.45±0.627$^{\#\#}$	146.88±0.503$^{\#\#}$
III	Vit-C (50mg/kg; p.o.) + Cd	86.34±0.336	91.40±0.533**	98.29±0.350**
IV	S.E (200 mg /kg; p.o.) + Cd	82.64±0.455**	97.22±0.456**	107.05±0.427**
V	S.E (400 mg /kg; p.o.) + Cd	87.51±0.321	96.50±0.601**	104.75±0.546**

Values are expressed as mean ± SEM, n=6; $^{\#\#}$ P<0.01 considered statistically significant as compare to normal control group; ***P<0.001, ** P<0.01 and * P<0.05 considered statistically significant when compared to Cd group.

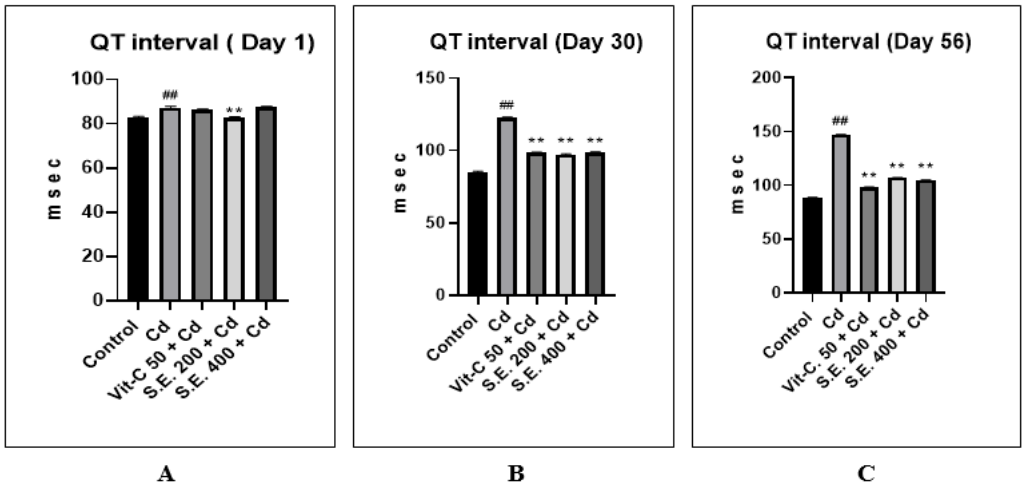

Figure 4: A-C Effect of alcoholic fruit extract ofS.E. on ECG in QT interval of heart in Cd-induced cardiotoxic rats.

3.3.5. Effect of alcoholic fruit extract ofS.E. on ECG in QTc interval in Cd- induced cardiotoxic rats:

A. Effect of administration of cadmium (4mg/kg; p.o.) on QTc interval in rats.

QTc interval in vehicle treated rats (Group-I) were found to be 71.61±0.15, 71.90±0.20 and 72.60±0.36 respectively on day 1st, 30th and 56thday. In Cd (4mg/kg) treated rat (Group-II) the QTc interval were found to be 73.88±0.35, 81.98±0.51 and 88.36±0.21 respectively on day 1st, 30th and 56thday. Thus, in Cd treated rats (Group-II) the QTc interval was significantly increase over a period of 56th days when compared to (Group-I).

B. Effect of administration of Vit-C (50mg/kg; p.o.) on QTc interval in Cd- induced cardiotoxic rats:QTc interval in rats treated with Vit-C (50mg/kg) in (group-III) were found to be 73.37±1.6, 72.23±0.99 and 74.62±0.25 respectively on day 1st, 30th and 56thday. The above values were significantly decreased from day 30th to 56th day when compared to (Group-II).

C. Effect of administration of lower dose of alcoholic fruit extract ofS.E. (200mg/kg; p.o.) in Cd-induced cardiotoxic rats.

QTc interval in rats treated with lower dose of alcoholic fruit extract ofS.E. (200mg/kg) in (Group-IV) were found to be 70.86±0.16, 75.25±0.23 and 78.81±0.37 respectively on day 1st, 30th and 56th day. The above values were significantly decreased from day 30th to 56th day when compared to (Group-II).

D. Effect of administration of higher dose of alcoholic fruit extract ofS.E. (400mg/kg; p.o.) in Cd-induced cardiotoxic rats.

QTc interval in rats treated with higher dose of alcoholic fruit extract ofS.E. (400mg/kg) in (Group-V) were found to be 73.95±1.4, 76.78±0.27 and 77.42±0.59 respectively on day 1st, 30th and 56th day. The above values were significantly decreased from day 30th to 56th day when compared to (Group-II).

Table 5: Effect of alcoholic fruit extract ofS.E. on ECG in QTc interval of heart in Cd-induced cardiotoxic rats.

Groups	**Treatment**	**QTc (msec)**		
		1st day	**30th day**	**56th day**
I	Control	71.61±0.15	71.90±0.20	72.60±0.36
II	Cd (4mg/kg; p.o)	73.88±0.35##	81.98±0.51##	88.36±0.21##
III	Vit-C (50mg/kg; p.o) + Cd	73.37±0.16	72.23±0.99**	74.62±0.25**
IV	S.E (200 mg/kg; p.o) + Cd	70.86±0.16**	75.25±0.23**	78.81±0.37**
V	S.E (400 mg/kg; p.o) + Cd	73.95±0.14	76.78±0.27**	77.42±0.59**

Values are expressed as mean ± SEM, n=6; ## P<0.01 considered statistically significant as compare to normal control group; ***P<0.001, ** P<0.01 and * P<0.05 considered statistically significant when compared to cadmium group.

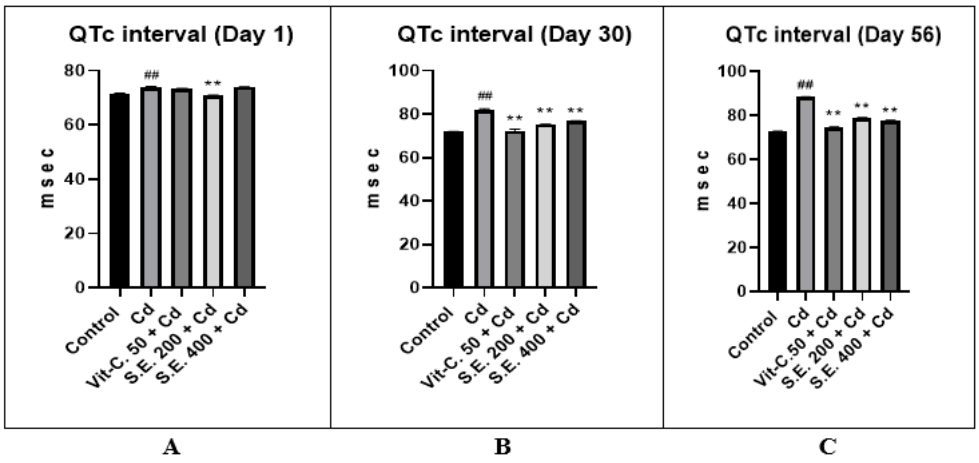

Figure 5: A-C Effect of alcoholic fruit extract ofS.E. on ECG in QTc of heart in Cd-induced cardiotoxic rats.

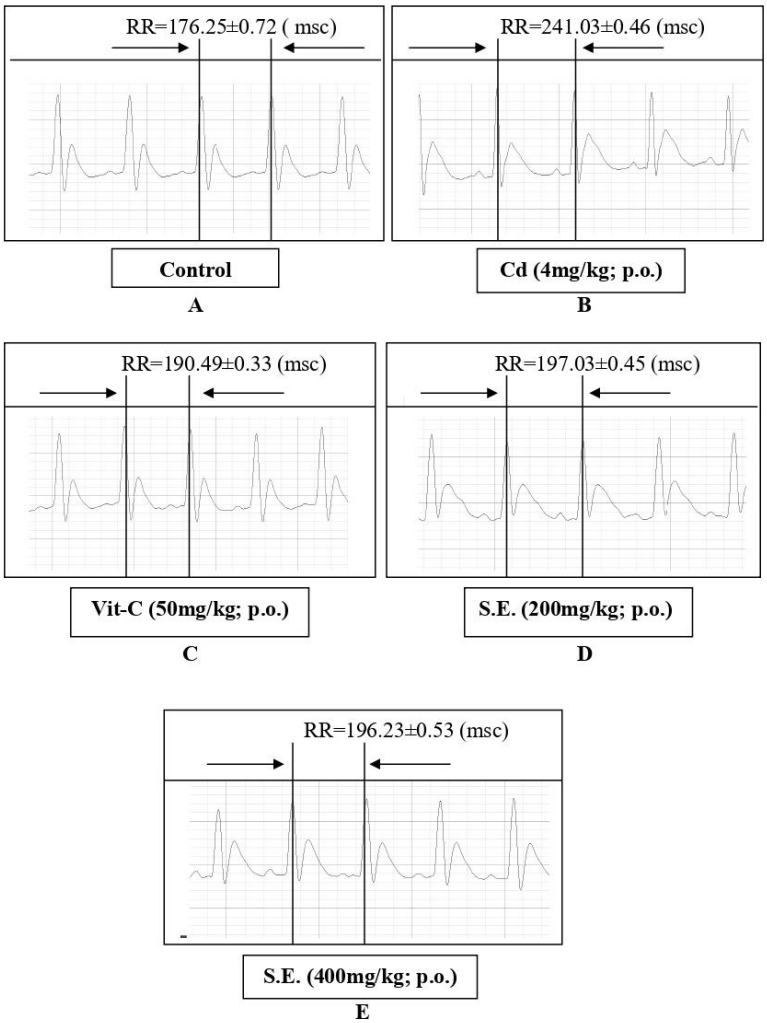

Figure 6: A-E Outcome alcoholic fruit extract of S.E. on ECG in RR interval of heart in Cd-induced Cardiotoxicity in rats.

3.3.6. Outcome alcoholic fruit extract of S.E. on ECG in RR interval of heart in Cd-induced cardiotoxic rats:

A. Effect of administration of cadmium (4mg/kg; p.o) on RR interval in rats.

RR interval in vehicle treated rats (Group-I) were found to be 168.14±0.37, 172.31±0.48 and 176.25±0.72 respectively on day 1st, 30th and 56th day. In Cd (4mg/kg) treated rat (Group-II) the RR interval was found to be 171.41±0.34, 216.80±0.46 and 241.03±0.46 respectively on day 1st, 30th and 56th day. Thus, in cadmium treated rats (Group-II) the RR interval was increase significantly over a period of 56th days when compared to (Group-I).

B. Effect of administration of Vitamin-C (50mg/kg; p.o.) on RR interval in Cd-induced cardiotoxic rats.

RR interval in rats treated with Vitamin-C (50mg/kg) in (group-III) were found to be 170.19±0.46, 184.01±2.11 and 190.49±0.327 respectively on day 1st, 30th and 56th day. The above values were significantly decreased from day 30th to 56th day when compared to (Group-II).

C. Effect of administration of lower dose of alcoholic fruit extract of S.E. (200mg/kg; p.o.) in Cd-induced cardiotoxic rats.

RR interval in rats treated with lower dose of alcoholic fruit extract ofS.E. (200mg/kg) in (Group-IV) were found to be 169.24±0.55, 187.15±0.562 and 197.03±0.46 respectively on day 1st, 30th and 56th day. The above values were significantly decreased from day 30th to 56th day when compared to (Group-II).

D. Effect of administration of higher dose of alcoholic fruit extract ofS.E. (400mg/kg; p.o.) in Cd-induced cardiotoxic rats.

RR interval in rats treated with higher dose of alcoholic fruit extract ofS.E. (400mg/kg) in (Group-V) were found to be 171.35±0.73, 186.10±0.49 and 196.23±0.53 respectively on day 1st, 30th and 56th day. The above values were significantly decreased from day 30th to 56th day when compared to (Group-II).

Table 6: Effect of alcoholic fruit extract ofS.E. on ECG in RR interval of heart in Cd-induced cardiotoxic rats.

Groups	**Treatment**	**RR interval (msec)**		
		Day 1	**Day 30**	**Day 56**
I	Control	168.14±0.37	172.31±0.48	176.25±0.72
II	Cd (4mg/kg; p.o)	171.41±0.34$^{\#\#}$	216.80±0.46$^{\#\#}$	241.03$^{\#\#}$± 0.46
III	Vit-C (50mg/kg; p.o) + Cd	170.19±0.45	184.01±2.11**	190.49±0.33**
IV	S.E (200 mg /kg; p.o) + Cd	169.24±0.55*	187.15±0.56**	197.03±0.45**
V	S.E (400 mg /kg; p.o) + Cd	171.35±0.73	186.10±0.49**	196.23±0.53**

Values are expressed as mean ± SEM, n=6; $^{\#\#}$ P<0.01 considered statistically significant as compare to normal control group; ***P<0.001, ** P<0.01 and * P<0.05 considered statistically significant when compared to Cd group.

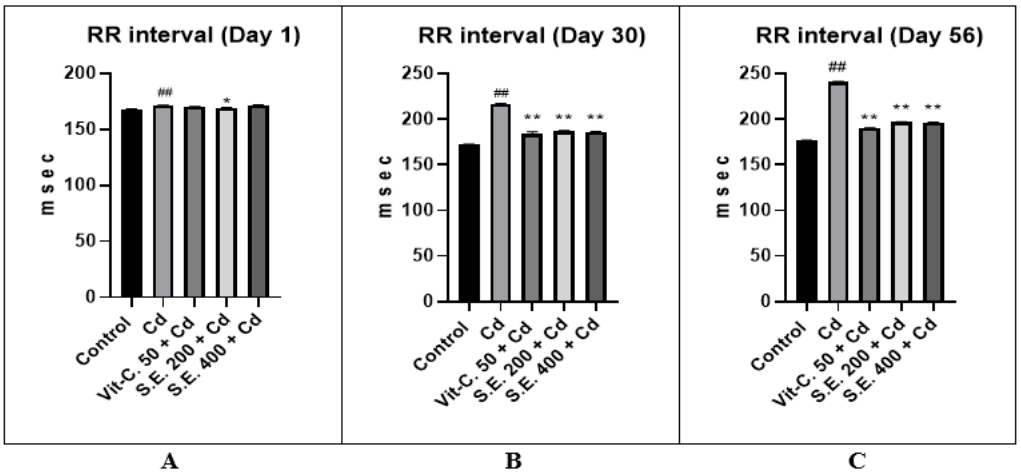

Figure 7: A-C Effect of alcoholic fruit extract ofS.E. on ECG in RR interval of heart in Cd-induced cardiotoxic in rats.

3.3.7. Outcome alcoholic fruit extract of S.E. on heart rate in Cd-induced cardiotoxic in rats:

A. Effect of administration of Cd (4mg/kg; p.o.) on heart rate in rats.

Heart rate in vehicle treated rats (Group-I) were found to be 356.84±0.80, 348.42±1.13 and 340.44±1.40 respectively on day 1st, 30th and 56th day. In Cd (4mg/kg;) treated rat (Group-II) the heart rate was found to be 350.03±0.70, 276.74±0.60 and 248.92±0.48 respectively on day 1st, 30th and 56th day. Thus, in Cd treated rats (Group-II) the heart rate was significantly decreased over a period of 56th days when compared to (Group-I).

B. Effect of administration of Vitamin-C (50mg/kg; p.o.) on heart rate in Cd-induced cardiotoxic rats.

Heart rate in rats treated with Vitamin-C (50mg/kg) in (group-III) were found to be 352.52±0.96, 326.22±3.72 and 315.77±0.76 respectively on day 1st, 30th and 56th day. The above values were significantly increased from day 30th to 56th day when compared to (Group-II).

C. Effect of administration of lower dose of alcoholic fruit extract o f S.E. (200mg/kg; p.o.) in Cd-induced cardiotoxic rats.

Heart rate in rats treated with lower dose of alcoholic fruit extract ofS.E. (200mg/kg) in (Group-IV) were found to be 344.33±0.99, 320.58±0.96 and 304.72±0.71 respectively on day 1st, 30th and 56th day. The above values were significantly increased from day 30th to 56th day when compared to (Group-II).

D. Effect of administration of higher dose of alcoholic fruit extract of S.E. (400mg/kg; p.o.) in Cd-induced cardiotoxic rats.

Heart rate in rats treated with higher dose of alcoholic fruit extract o fS.E. (400mg/kg) in (Group-V) were found to be 350.19±2.10, 322.40±0.85 and 305.76±082 respectively on day 1st, 30th and 56th day. The above values were significantly increased from day 30th to 56th day when compared to (Group-II).

Table 7: Effect of alcoholic fruit extract of S.E. on heart rate in Cd-induced cardiotoxic rats.

Groups	**Treatment**	**Heart rate (BPM)**		
		1st day	**30th day**	**56th day**
I	Control	356.84±0.80	348.42±1.13	340.44±1.39
II	Cd (4mg/kg; p.o)	350.03±0.70##	276.74±0.59##	248.92±0.48##
III	Vit-C (50mg/kg; p.o) + Cd	352.52±0.96	326.22±3.72**	315.77±0.76**
IV	S.E (200 mg/kg; p.o) + Cd	344.33±0.99	320.58±0.96**	304.72±0.71**
V	S.E (400 mg/kg; p.o) + Cd	350.19±2.10	322.40±0.85**	305.76±0.82**

Values are expressed as mean ± SEM, n=6; ## P<0.01 considered statistically significant as compare to normal control group; *** P<0.001, ** P<0.01 and * P<0.05 considered statistically significant when compared to Cd group. [BPM=Beats per minute]

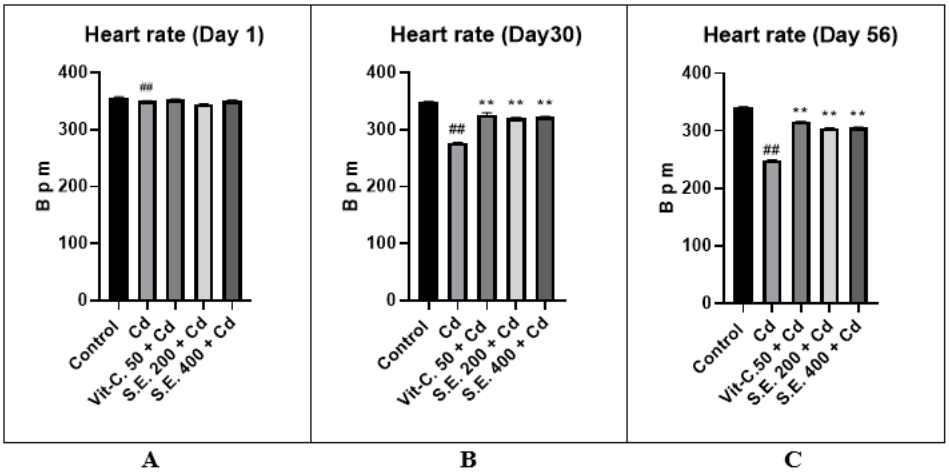

Figure 8: A-C Effect of alcoholic fruit extract ofS.E. on heart rate in Cd-induced Cardiotoxic in rats.

3.3.8. Histopathological Observation:

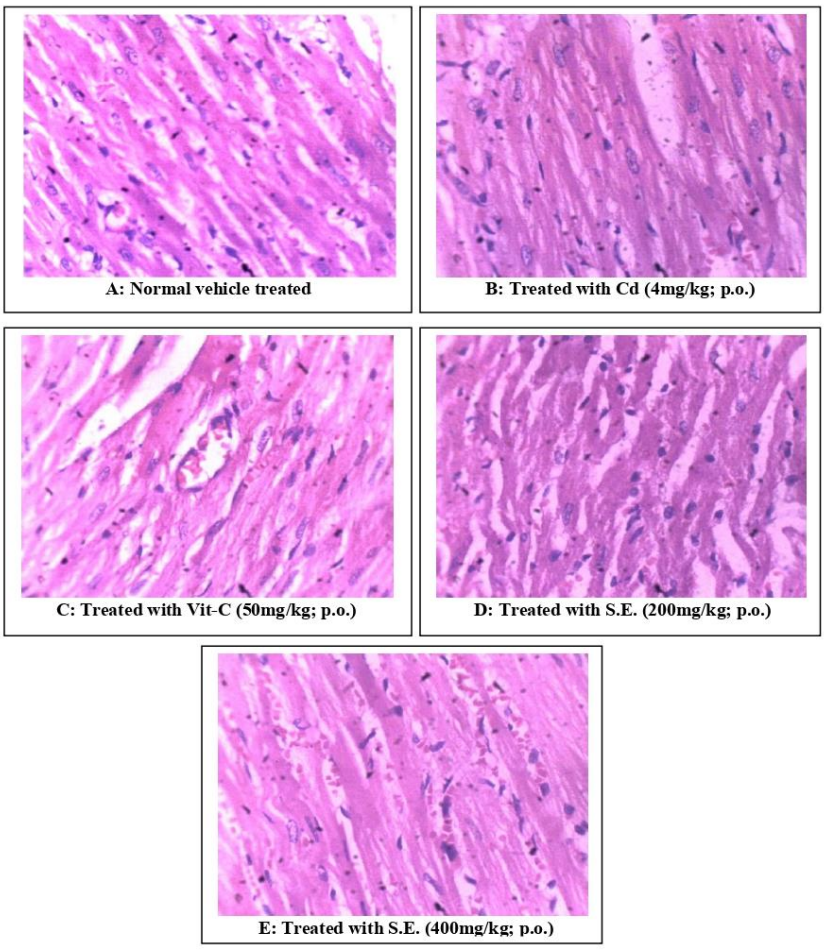

Figure 9: A-E Effect of alcoholic fruit extract ofS.E. on H & E staining of heart in Cd-induced cardiotoxic rats.

In the Cd-induced cardiotoxicity model, the hearts of normal rats exhibited intact muscle fibres, while Cd-exposed hearts showed degenerative changes, fiber necrosis, and vascular damage. Treatment with *Sechium edule* extract restored normal cardiac architecture, indicating its potential cardioprotective effects.

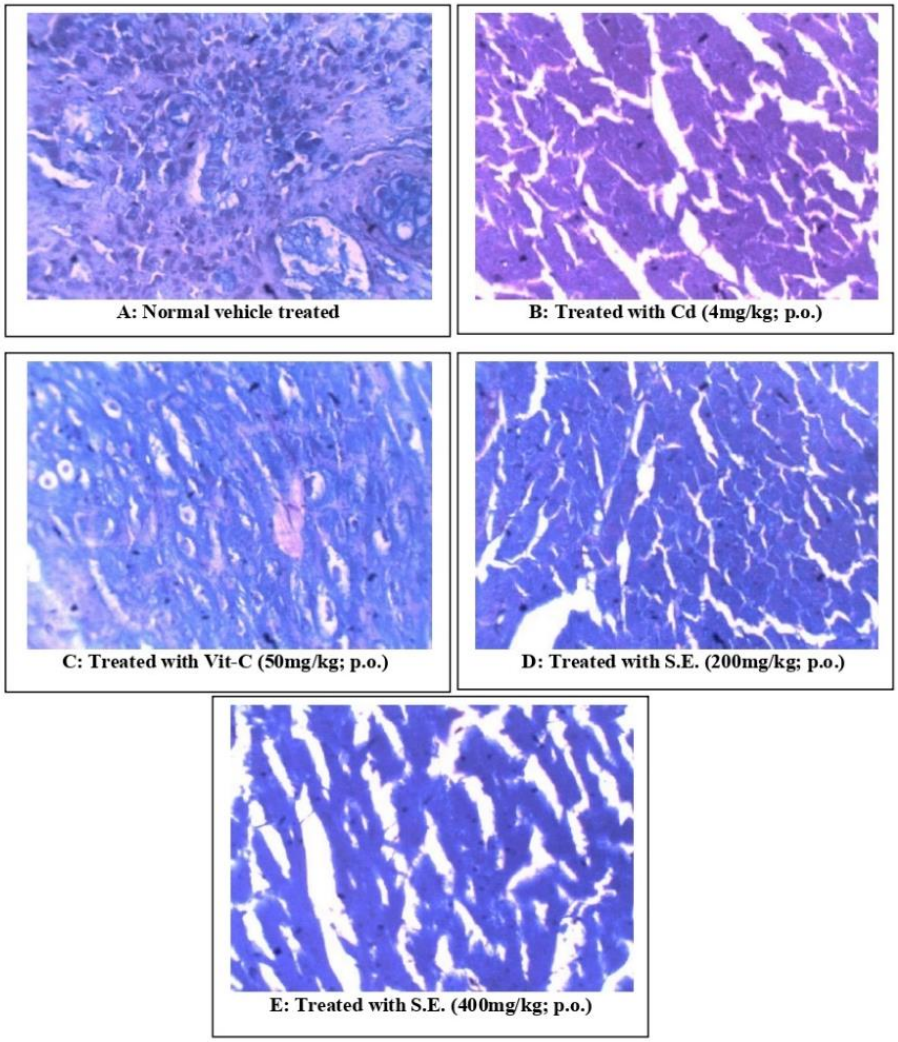

Figure 10: A-E Effect of alcoholic fruit extract ofS.E. on Masson trichrome staining of heart in Cd-induced cardiotoxic rats.

In Masson trichrome staining, normal rat hearts exhibited normal collagen distribution, while Cd-induced cardiotoxic rats showed increased collagen bundles, indicative of fibrosis. Treatment with *Sechium edule* extract and Vit-C restored normal collagen appearance and cardiac architecture, suggesting potential anti-fibrotic effects.

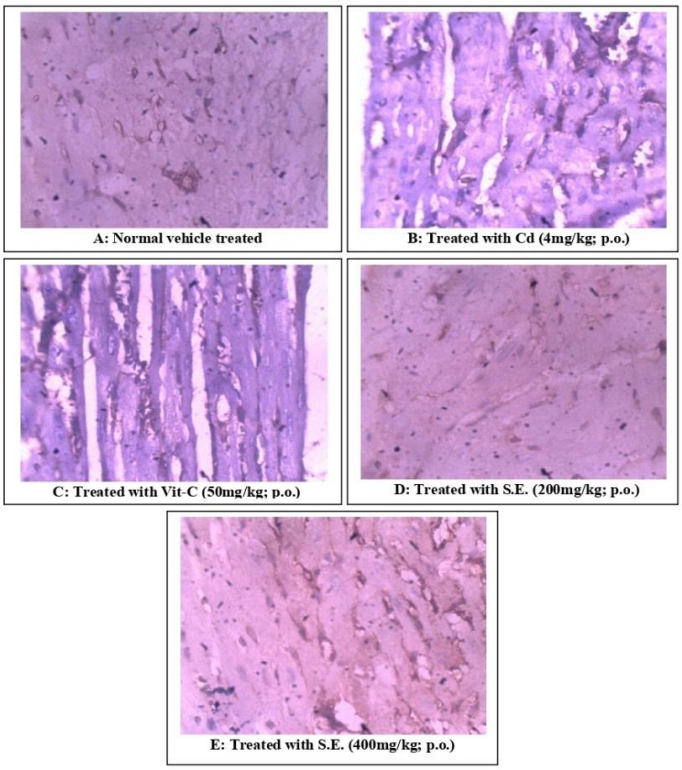

Figure 11: A-E Effect of alcoholic fruit extract ofS.E. on staining with Bcl_2 of heart in Cd-induced cardio toxic rats.

Bcl2 staining in myocardial tissue sections revealed moderate expression in normal control rats. Cd-induced group exhibited lower Bcl2 expression, while Vit-C and *Sechium edule* (S.E.) treatments showed improved expression. S.E. treatment notably increased Bcl2 expression, suggesting its potential anti-apoptotic effects in myocardial fibres compared to the Cd group.

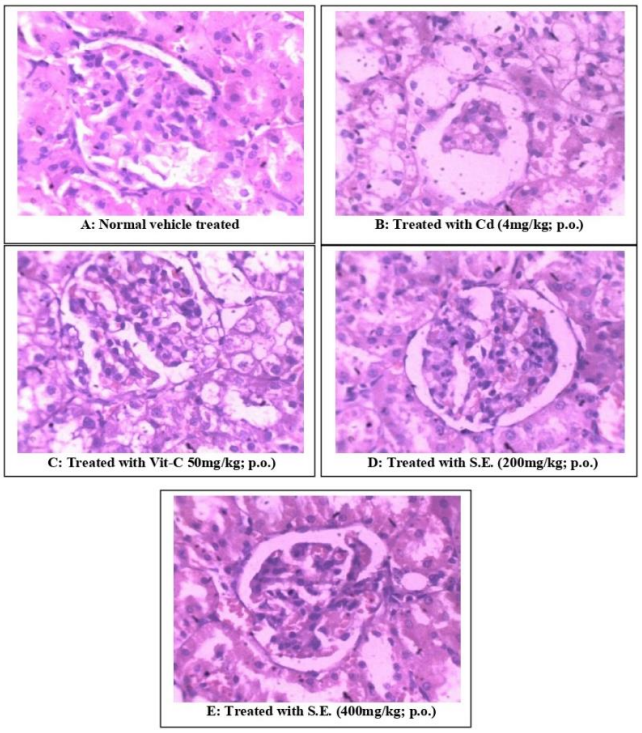

Figure 12: A-E Effect of alcoholic fruit extract ofS.E. on H & E staining of kidney in Cd-induced cardiotoxic rats.

In the Cd-induced cardiotoxic model, normal rat kidneys had intact tubules and glomeruli, while Cd-exposed kidneys showed degenerative tubules, desquamated epithelial cells, misshapen tubules, and glomerular congestion. Treatment with Vit-C and *Sechium edule* extract restored almost normal cellular architecture, indicating potential renal protective effects.

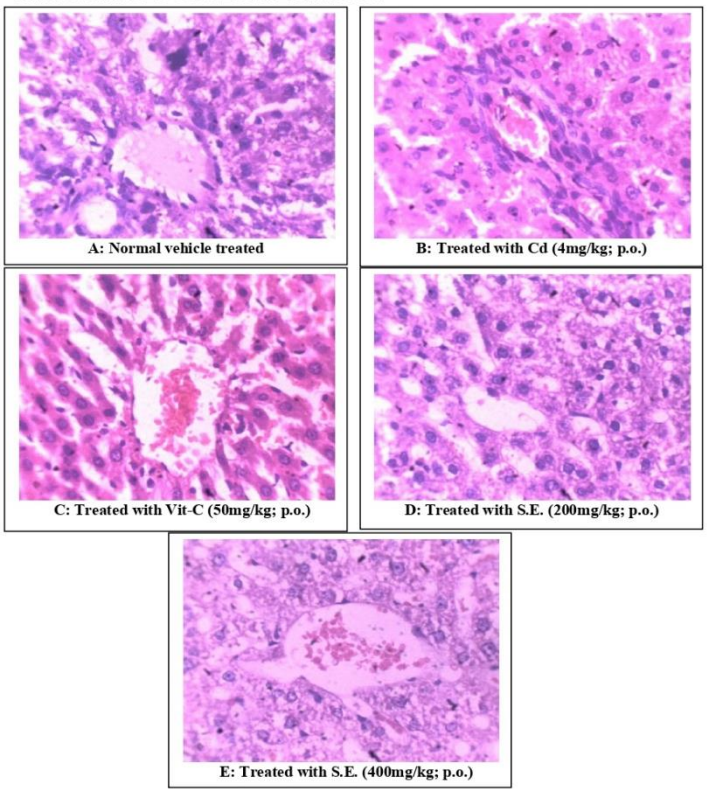

Figure 13: A-E Effect of alcoholic fruit extract ofS.E. on H & E staining of liver in Cd-induced cardiotoxic rats.

In normal rat liver, hepatic lobules with portal triads were intact. Cd exposure led to severe damage, including fatty changes, focal necrosis, Kupffer cell proliferation, and bile duct loss. Vit-C and *Sechium edule* extract treatment partially improved hepatocyte structure, reduced bile duct loss, and alleviated focal necrotic areas, indicating potential hepatoprotective effects.

4. Discussion:

The presence of heavy metal ions, even at low concentrations, poses significant health risks due to their accumulation in tissues, causing metabolic, histological, and pathological changes in humans and mammals. Occupational exposure to cadmium (Cd) induces oxidative stress, generating reactive oxygen species that can lead to damage in organs, the nervous system, and even death. Cd accumulation in the heart causes peroxidative disorders, significantly increasing membrane lipid peroxidation markers like TBARS and protein carbonyls. Cd replaces redox-active metals, increasing free iron availability and triggering the Fenton reaction, resulting in damaging hydroxyl radical production and increased membrane lipid peroxidation.

Cd's thiol-affinitive nature primarily targets cellular glutathione (GSH), depleting the GSH pool and disrupting cellular redox balance, causing oxidative stress. Sub-chronic Cd treatment in the study significantly reduced GSH concentration in the heart. Cd-induced cardiotoxicity is associated with decreased superoxide dismutase (SOD) activity, causing detrimental effects on cells, such as mitochondrial enzyme inactivation, lipid peroxidation, and reactive nitrogen species production. Glutathione reductase (GR) activity, crucial for maintaining GSH levels, was also significantly decreased in the heart.

Cd exposure elevated serum markers indicating lipid abnormalities, cardiac damage, and impaired renal function. Treatment with Sechium edule (S.E.) extract significantly ameliorated these serum markers, suggesting its potential in protecting against cardiac damage and modulating lipid abnormalities.

Markers of cardiac function, including LDH, CPK, SGOT, and SGPT, were markedly elevated in Cd-induced cardiotoxic rats, indicating cardiomyocyte necrosis. S.E. extract treatment reduced these enzyme levels, suggesting protection against cardiac muscle damage.

ECG analysis revealed increased CVD risk in Cd-induced cardiotoxic rats, with prolonged QT, QTc, and RR intervals. S.E. extract treatment significantly decreased these intervals, indicating cardiac protection. Cd-induced bradycardia was also alleviated by S.E. extract treatment. Elevated Na+ and K+ ions in Cd-induced cardiotoxic rats suggested electrolyte imbalances and potential renal dysfunction, which were significantly decreased by S.E. extract treatment, indicating protection against cardiopathy and electrolyte imbalances.

Cd-induced renal damage, evidenced by increased serum urea and creatinine levels, was prevented by S.E. extract treatment. Histochemical analysis demonstrated severe histopathological changes in Cd-induced cardiotoxic rats, partially mitigated by S.E. extract treatment. Masson trichrome staining indicated fibrosis in Cd-treated hearts, partially alleviated by S.E. extract treatment.

Cd-induced liver damage, including fatty changes, focal necrosis, Kupffer cell proliferation, and bile duct proliferation, was partially improved by S.E. extract treatment.

5. Conclusion:

The ethanolic extract of *Sechium edule* (S.E.) significantly improved lipid profiles, decreased cardiac enzymes (LDH, CPK, SGOT, SGPT), lowered blood urea, serum creatinine, ALP levels, and regulated Na+, K+ ions in Cd-induced cardiotoxic rats. ECG parameters were normalized, and histopathological improvements were observed in the heart, liver, and kidney. S.E. exhibits potential antioxidant effects against Cd-induced cardiotoxicity.

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