CARDIOPROTECTIVE EFFECTS OF VEDICINAL-9 ON ISOPROTERENOL INDUCED MYOCARDIAL INFARCTION IN RATS

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advance the safety evaluation

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Objectives

- **Objective:** The objective of the study is to assess the effect of pre and post treatment of Vedinical-9 in isoproterenol induced myocardial infarction in rats

Experimental Design

Group	Treatment	Route	Sex (No. of animals)
G1	Isoproterenol- Single Dose	Sub cutaneous	1-6
G2	Vedicinal-9 Normal + Single Dose Isoproterenol	Oral + Sub cutaneous	7-12
G3	Vedicinal-9 Bio-enhanced + Single Dose Isoproterenol	Oral + Sub cutaneous	13-18
G4	Isoproterenol- Divided Dose	Sub cutaneous	19-24
G5	Vedicinal-9 Normal + Divided Dose Isoproterenol	Oral + Sub cutaneous	24-30
G6	Vedicinal-9 Bio-enhanced + Divided Dose Isoproterenol	Oral + Sub cutaneous	31-36

Induction of Myocardial infarction

- G1- Animals received isoproterenol at dose of 60 mg/kg body weight as a single dose by sub-cutaneous route.
- G4 - Animals received isoproterenol at dose of 85 mg/kg body weight in to two divided doses by sub-cutaneous route at interval of 24 hrs.

Observations

Following observations were recorded during experimental period;

- **Clinical Signs-** Twice a day
- **Clinical pathology evaluations-** On Day 11 blood was collected, plasma pooled and analysis of CK-MB, LDH, AST, ALT, ALT:AST, Creatinine were performed.
- **Gross Pathology Observations-** At necropsy and cross sections of formalin fixed heart.
- **Heart Weights-** Absolute heart weights recorded at the time of necropsy.
- **Histopathology-** Heart weight and histopathological observations of the heart**.**

Clinical Chemistry

Isoproterenol + Vedicinals-9 Formulation

	Group	CREAT (mg/dl)	GPT (U/L)	GOT (U/L)	CK-MB (U/L)	LDH (U/L)
Mean	G1-Single isoproterenol	0.83	135.43	113.45	137.92	410.23
SD		0.19	24.77	9.21	16.06	90.17
N		6	6	6	6	6
Mean	G2-Vedicinal-9 normal	0.81	113.33	109.78	128.93	375.47
SD		0.19	24.76	10.39	8.18	71.86
N		6	6	6	6	6
Mean	G3-Vedicinal-9 bioenhanced	0.71	89.53*	100.62	116.55*	342.70
SD		0.17	13.54	10.52	8.44	89.20
N		6	6	6	6	6

Clinical Chemistry

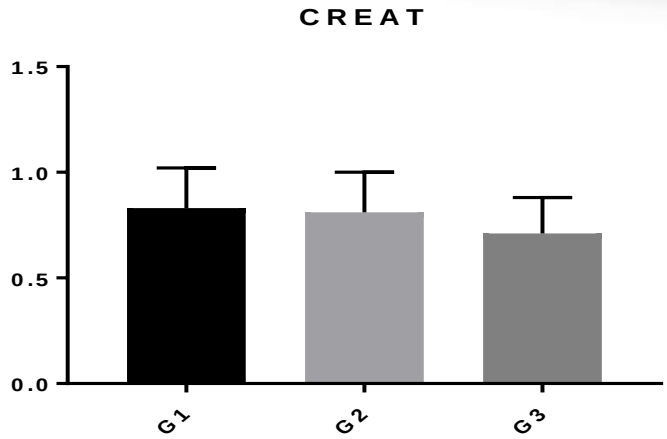
Isoproterenol + Vedicinals-9 Bio-enhanced Formulation

	GROUP	CREAT (mg/dl)	GPT (U/L)	GOT (U/L)	CK-MB (U/L)	LDH (U/L)
Mean	G4	0.68	89.55	140.70	145.14	486.28
SD		0.32	12.83	35.13	14.18	85.19
N		6	6	6	6	6
Mean	G5	0.58	100.50	116.17	133.37	407.08
SD		0.13	19.70	17.41	9.63	62.96
N		6	6	6	6	6
Mean	G6	0.58	88.95	114.13	124.97*	374.63
SD		0.17	22.20	50.86	10.02	112.95
N		6	6	6	6	6

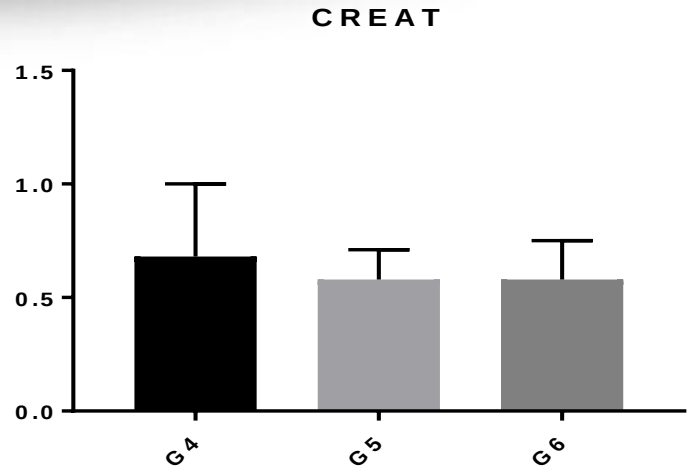
Results
Clinical Chemistry

- **Clinical pathology evaluations-**
  - Isoproterenol administration at single dose showed more damage than that caused by the divided doses of isoproterenol.
  - In the experimental group receiving single dose of isoproterenol both treatments, normal formulation and bio-enhanced formulation of Vedicinal-9 has brought the increased GPT values of all clinical chemistry parameters to normal, however the bio-enhanced more pronounced effects on these parameters compared to normal formulation.
  - Similar results observed in the experimental group receiving divided doses of isoproterenol, except for the creatinine and GPT parameters where normal formulation of vedicinal-9 has similar or no recovery effects compared to bio-enhanced formulation. For remaining parameters bio-enhanced formulation performed better than normal formulation.

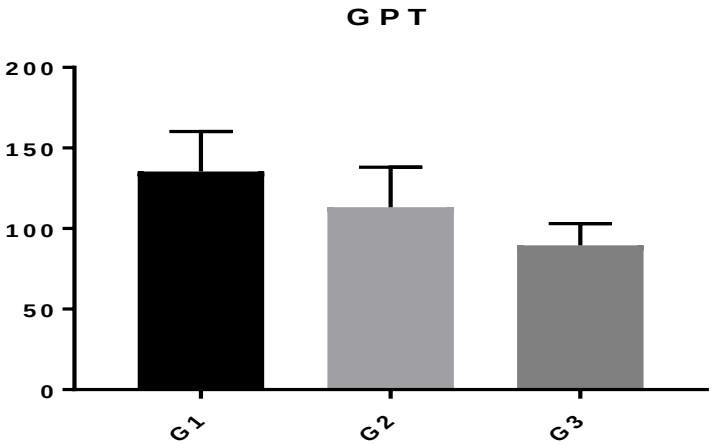
Results
Clinical Chemistry

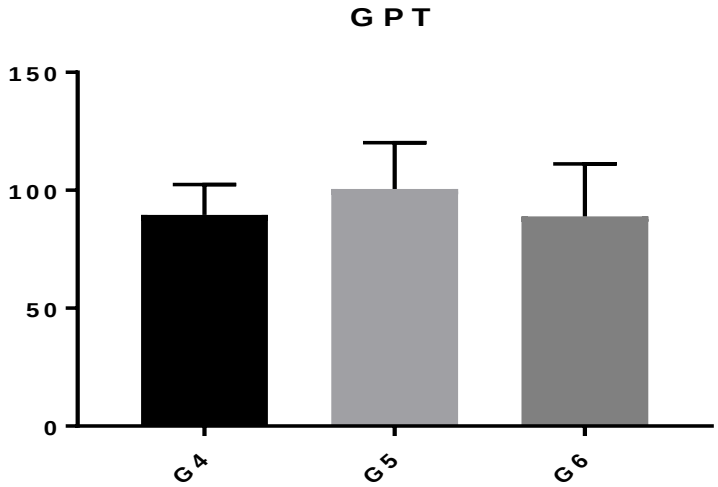


Single Dose of Isoproterenol

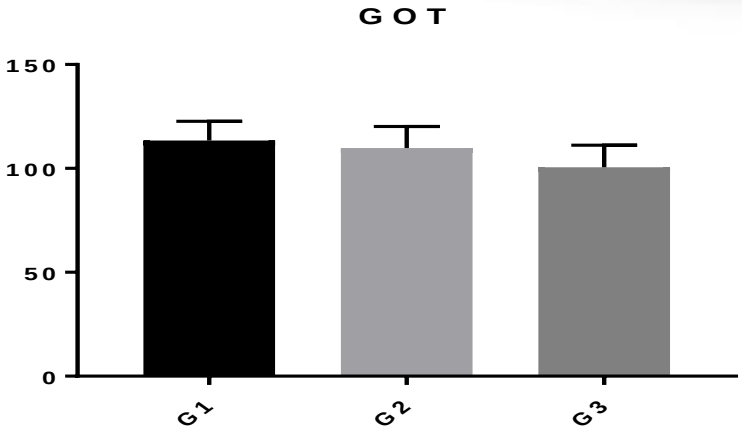


Divided Dose of Isoproterenol

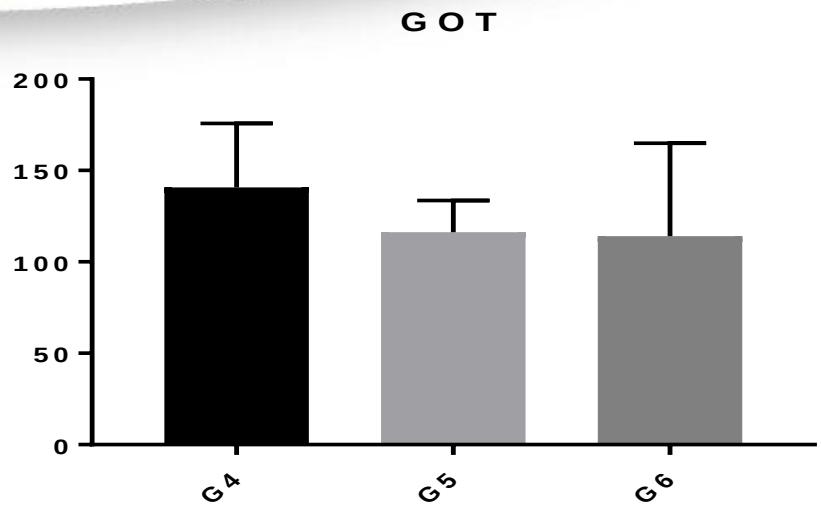




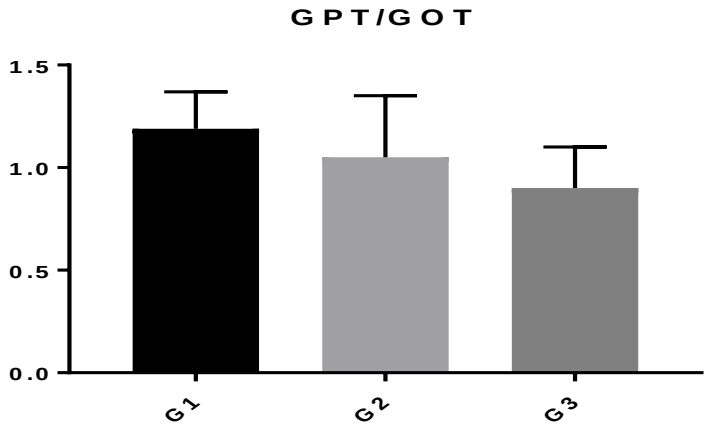
Results
Clinical Chemistry

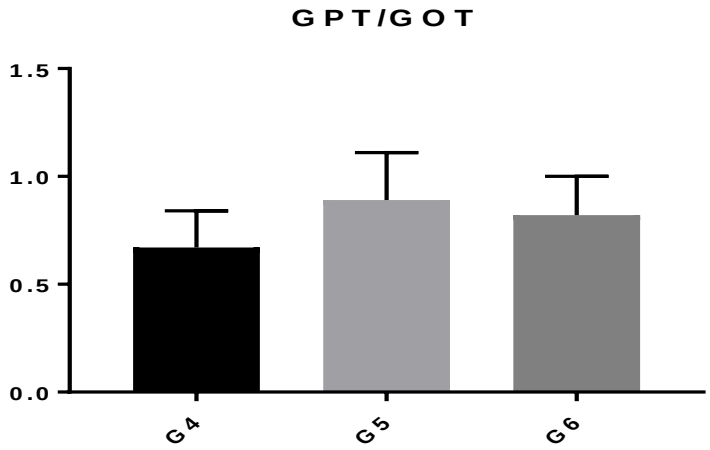


Single Dose of Isoproterenol

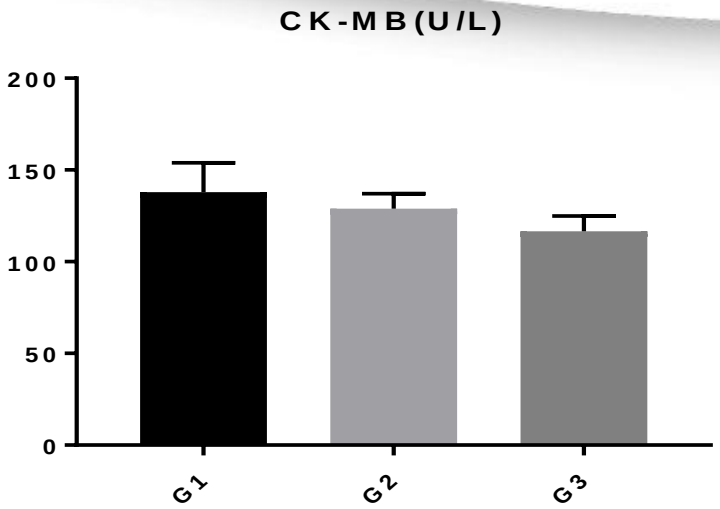


Divided Dose of Isoproterenol

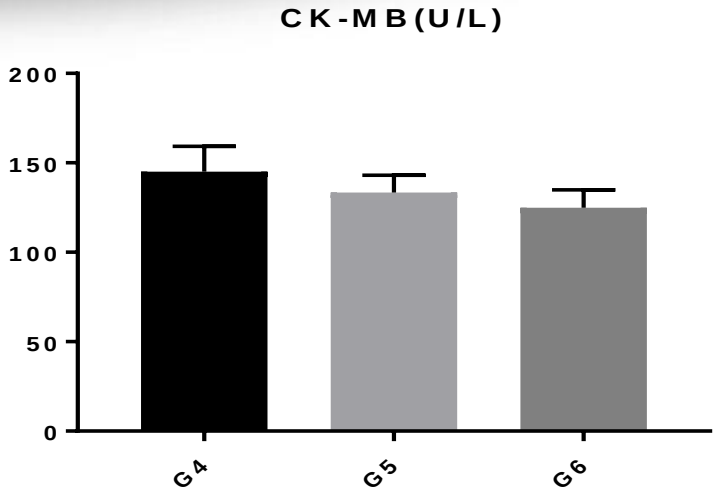




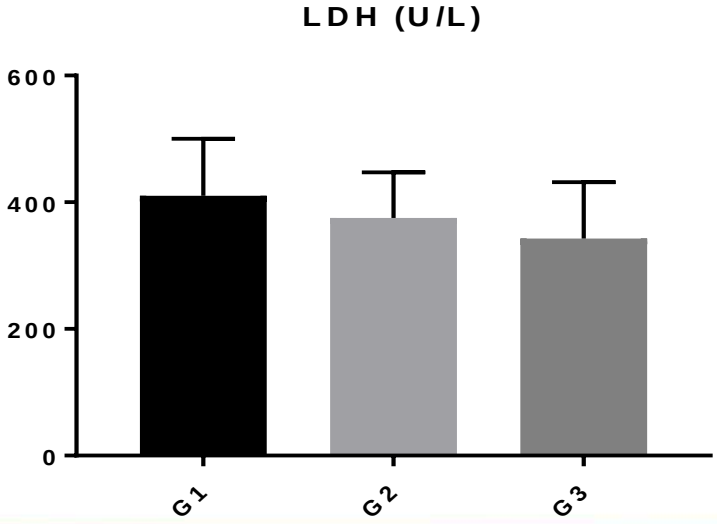
Results
Clinical Chemistry

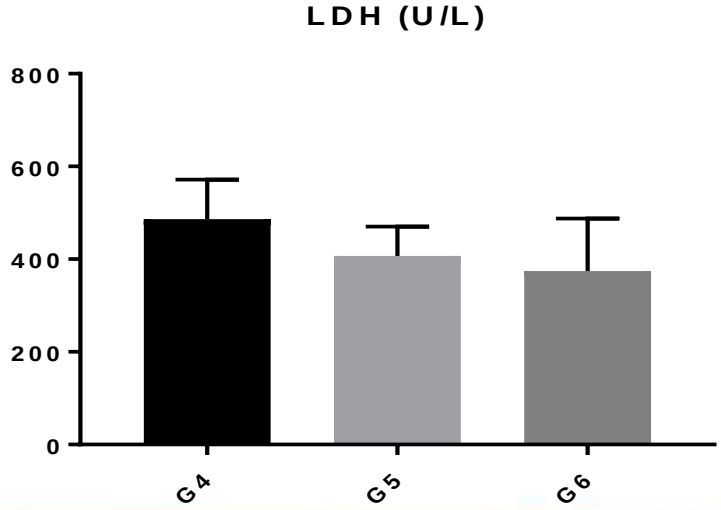


Single Dose of Isoproterenol



Divided Dose of Isoproterenol





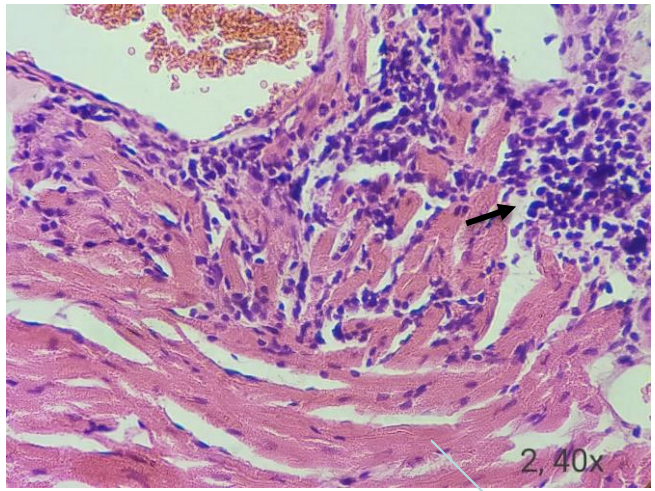
Results
Absolute Heart Weights

- The experimental group receiving Single dose of isoproterenol, bio-enhanced formulation of Vedicinal-9 reduced the heart weights. Divided doses of isoproterenol, bio-enhanced Vedicinals-9 formulation significantly increased heart weights above that of normal Vedicinals-9 formulation or only isoproterenol.

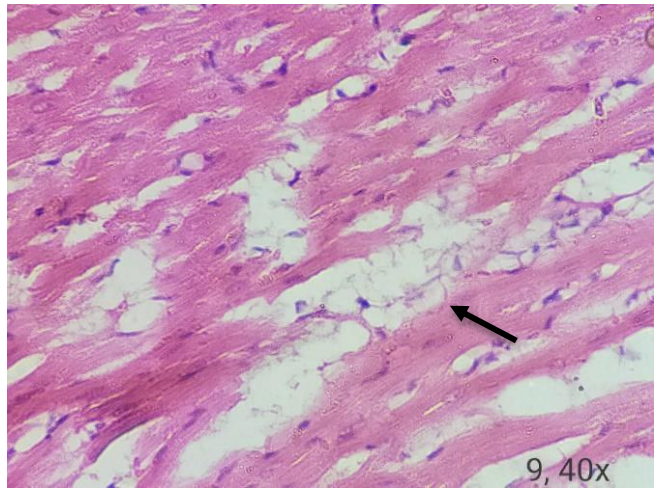
Tissue/ Findings/Sex				Females		
Dose Group	G1	G2	G3	G4	G5	G6
Dose (mg/kg)	Isoproterenol (Single Dose 60)	Vedicinals-9 (100)	Vedicinals-9 Bioenhanced (100)	Isoproterenol (Divided Dose 85)	Vedicinals-9 (100)	Vedicinals-9 Bioenhanced (100)
Number Examined	6	6	6	6	6	6
Heart						
Mean	0.75	0.76	0.71	0.72	0.77	0.78*

Results
Histopathology

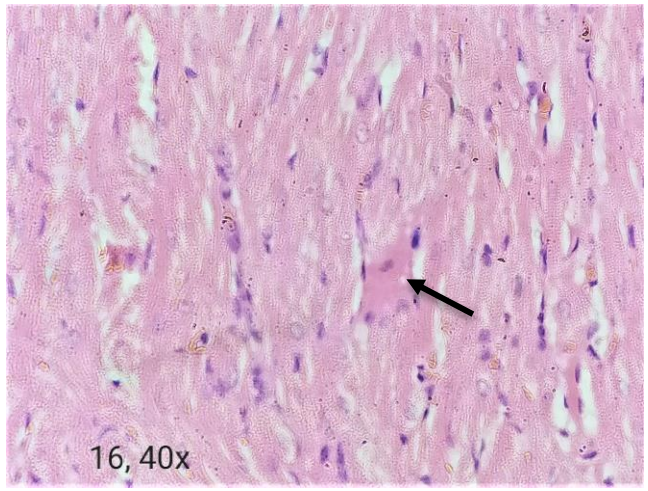
Isoproterenol + Vedicinals-9 Formulation



Group 1: Isoproterenol – Mild myocardial degeneration, infiltration of inflammatory cells, and extra-vasated RBCs. H &E, 40X



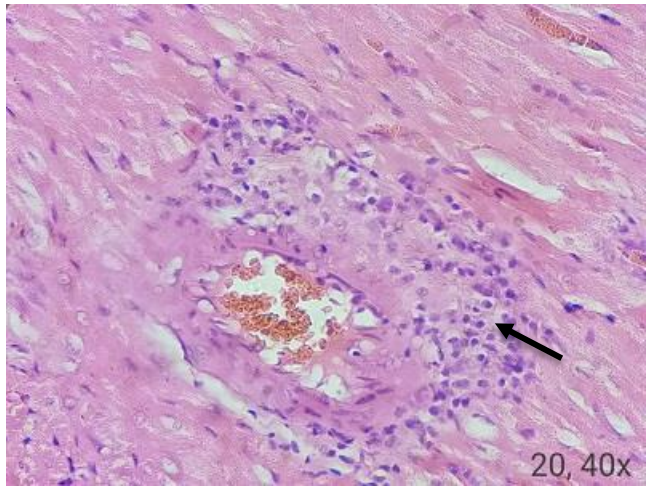
Group 2: Isoproterenol+Vedicinal-9 – Minimal myocardial degeneration, vacuolations, No infiltration of inflammatory cells, and no hemorrhages seen. H &E, 40X



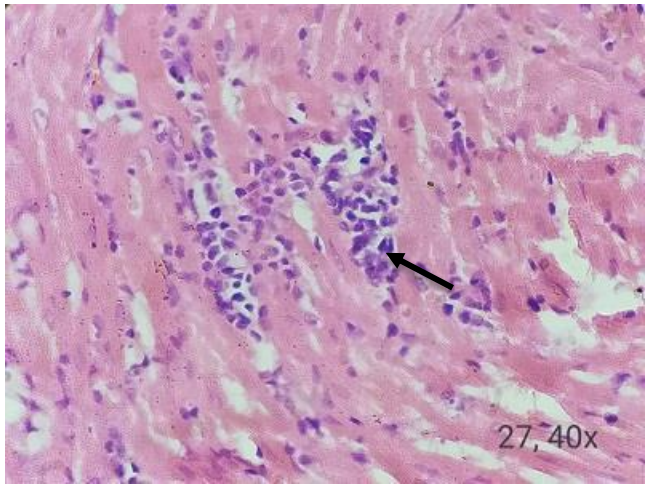
Group 3: Isoproterenol+Vedicinal-9 bioenhanced – Minimal myocardial degeneration, No infiltration of inflammatory cells, and No hemorrhages or vacuolations seen. H &E, 40X

Results
Histopathology

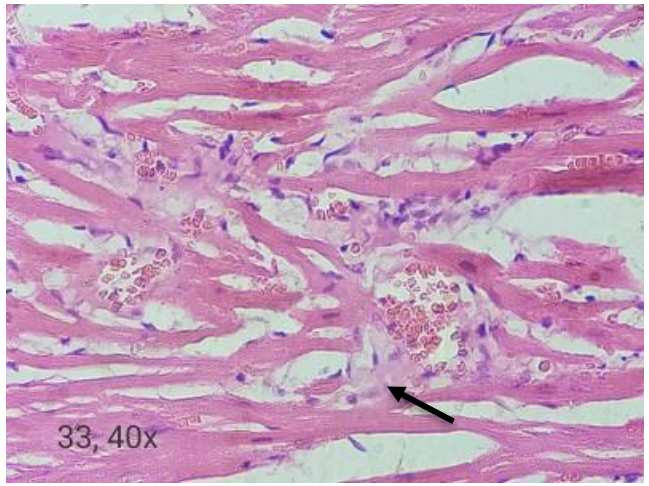
Isoproterenol + Vedicinals-9 Bio-enhanced Formulation



Group 4: Isoproterenol Divided dose– Minimal myocardial degeneration, infiltration of inflammatory cells, and extra-vasated RBCs. H &E, 40X



Group 5: Isoproterenol+Vedicinal-9 – Minimal myocardial degeneration, and minimal focal infiltration of inflammatory cells, and no haemorrhages seen. H &E, 40X



Group 3: Isoproterenol+Vedicinal-9 bioenhanced – Minimal myocardial degeneration and infiltration of inflammatory cells, and minimal focal fibrous tissue proliferation seen. H &E, 40X

Conclusions

- Based on the present study conditions, it can be concluded that the both formulations of Vedicinals-9 showed cardioprotective activity, whereas Bio-enhanced formulation performed better than that of normal Vedicinals-9 formulation.

Thank you !

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