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Study Effects of Ginseng under Immobility Stress on AST, CPK, CPK-MB, LDH, ALT and Troponin of Blood Serum on Male Rats

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ABSTRACT

Ginseng is a perennial herb that has been used for medicinal purposes in China and other Asian countries for centuries. Ginseng and its constituents have been shown to exhibit both anti-stress and antioxidant activity, and to exert various benefits relating to stress and the immune system. As a fluid liquid, blood is one of the most important biologic fluids of the body in which under physiological and pathologic conditions, its compounds are subject to changes and fluctuations. For this study, 24 adult male rats were randomly selected then the rats were divided into three groups of 8 rats. In this experiment, the first (Treatment) and second (Ginseng treatment) groups were transferred daily into the Restrainer and were under Immobility stress for 2 hours per day during 15 days. For ginseng group ginseng 500mg/kg (Ginsin capsule) was given daily after immobility stress. The treatment group and control group were given water instead of ginseng each day. After 15 days, blood sampling was taken on the 15th day from groups. In this research AST, CPK, CPK-MB, LDH, ALT and Troponin was analyzed then we found out, there was a significant difference on AST parameter between treatment group and ginseng treatment group so ginseng reduces the serum AST level but there was no significant difference between control, treatment and ginseng treatment on AST, CPK, CPK-MB, LDH, ALT and Troponin parameters.

KEY WORDS: Rat, Immobility stress, Blood, Serum, Biochemistry

INTRODUCTION

Ginseng is a perennial herb that has been used for medicinal purposes in China and other Asian countries for centuries [26]. Ginseng (*Panax. sp.)* is valuable in Chinese medicine and plays an important role in folk medicine in East Asia. Ginseng glycopeptides have pharmacological effects, e.g., immunomodulatory, anti-tumor, anti-ulcer and hypoglycemic activities [25]. The root of Asian ginseng contains active chemical components called ginsenosides (or panaxosides) that are thought to be responsible for the herb's claimed medicinal properties. More than twenty ginsenosides have been isolated [10], and novel structures continue to be reported, particularly from *Panax quinquefolius* and *Panax japonicus* [31] ginsenosides exhibit considerable structural variation. They differ from one another by the type of sugar moieties, their number, and their site of attachment. Some sugar moieties present are glucose, maltose, fructose, and saccharose. Ginseng has both stimulatory and inhibitory effects on the CNS [24, 2], and may modulate neurotransmission. Ginsenosides Rb1 and Rg1 play a major role in these effects [28, 6]. Ginsenosides have been shown to exert anticarcinogenic effects in vitro through different mechanisms. Several ginsenosides show direct cytotoxic and growth inhibitory effects against tumor cells [29, 22].Ginseng and its constituents have been shown to exhibit both anti-stress and antioxidant activity[5, 10], and to exert various benefits relating to stress and the immune system [16, 27], and alleged ability to boost the reduced metabolism of weak patients [17, 14]. As a fluid liquid, blood is one of the most important biologic fluids of the body in which under physiological and pathologic conditions, its compounds are subject to changes and fluctuations. Hence, having normal levels of blood parameters and investigating the manner of their change can be helpful for identifying problems and determining organs' health .Normal values of biochemical parameters of blood and investigating them and determining changes can assist us in identifying different physiological and pathological states.

MATERIALS AND METHODS

For this study, 24 adult male rats (Wistar rats) were randomly selected and weighed (The average body weight 180 to 220 gram). Then the rats were divided into three groups of 8 rats so that the weighted average of the two groups showed no significant differences. During the entire period, feeding was performed on the ad libitum basis.

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Feed was analyzed and the results are given in Table (1-1). The consumed water was the city tap water which was re-refined using carbon and sand filters. Water was analyzed and the results are given in Table (1-2). The environment was exposed to 12-hour lighting and 12-hour dark during the experiment for each group. The room temperature was 22±2 Degrees Celsius during the experimental period. In this experiment, the first (Treatment) and second (Ginseng treatment) groups were transferred daily into the Restrainer and were under Immobility stress for 2 hours per day during 15 days. For ginseng group ginseng 500mg/kg (Ginsin capsule, each capsule contains: Ginseng rhizoma 250mg equivalent to 7mg Ginsenosides as Rg1, produced by Goldaru) was given daily after immobility stress (the drug was given by gavage). The treatment group and control group were given water instead of ginseng by gavage each day.

Table 1-1: Food Analysis and ingredients

Food Analysis	
Crude Protein (%)	13.00
Crude Fat (%)	4.00
Crude Fiber (%)	2.00 (Min*1)
Crude Fiber (%)	5.00 (Max*2)
Moisture (%)	12.0
Calcium (%)	0.7 (Min)
Calcium (%)	1.00 (Max)
Phosphorus (%)	0.78
Copper (mg/kg)	20
Vitamin A (IU/kg)	10,000
Vitamin D (IU/kg)	1,200
Vitamin E (IU/kg)	125

Ingredients: Barley, corn, wheat bran, meal types, oilseeds, sugar beet pulp, other additives/*1 Minimum and *2 Maximum

Table1-2: Water analysis

Composition	**water**
Calcium(mg/l)	20-30
Magnesium(mg/l)	4-8
Sodium(mg/l)	15-20
Potassium(mg/l)	2-5
Sulphate(mg/l)	10-20
Chloride(mg/l)	10-20
Nitrate(mg/l)	2-4
Total hardness(mg/l)	60-80
PH	6.8-7.2

Blood sampling and serum analysis

After 15 days, blood sampling was taken on the 15th day from groups. The blood was added into the serum tube manufactured by Euro Tube ® Company. After clotting, the blood was centrifuged with the speed of 3000 rpm for 10 minutes and the serum was removed. In this study Creatin phosphokinase (CPK), Creatin Phosphokinase of Muscle and Brain (CPK-MB), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and Lactate Dehydrogenase (LDH) review was performed using Kinetik method, and all the introducing kits in this study are manufactured by Pars Azmoon ® Company. Troponin I review was performed using ELISA kits (IVD). ELISA kits were from Humasis ® Company (one step troponin I whole blood test).

Statistical Analysis

All raw data of this experiment was investigated by SPSS software version 15.00. The ANOVA and TUKEY HSD tests were used to analyze the data. Data with 5% level ($X<0.05$) of significance were considered statistically significant mean and standard deviation (st.d) was used to evaluate the data.

RESULTS

The results of serum biochemical parameters have been placed in table (2-1) and the results of ANOVA and TUKEY HSD tests have been placed in table (2-2).

Table (2-1): Blood biochemical parameters analysis Results (Mean ± Std.Deviation).

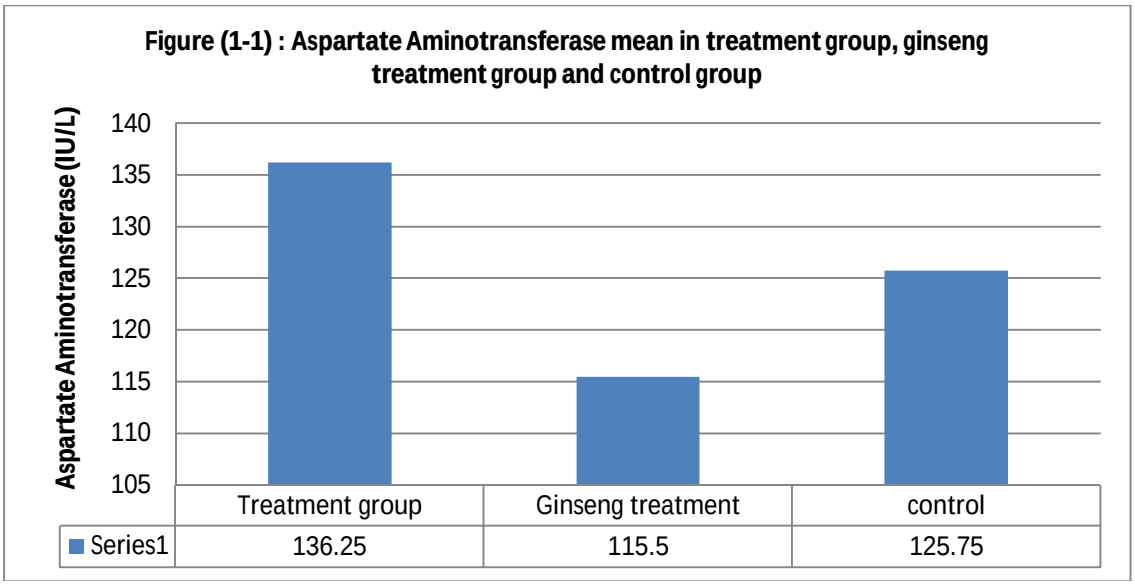
	Experiment groups		
Parameters	**Treatment**	**Ginseng treatment**	**Control**
AST(IU/L*)	136.25±21.413	115.50±12.928	125.75±13.145
CPK(IU/L)	872.50±392.851	639.25±225.968	759.25±280.801
CPK-MB(IU/L)	473.75±279.531	293.50±59.534	310.00±97.054
LDH(IU/L)	2220.25±1519.236	1086.00±294.253	1178.25±590.828
ALT(IU/L)	78.75±8.328	82.00±20.213	79.50±10.043

*IU/L: International Unit per liter

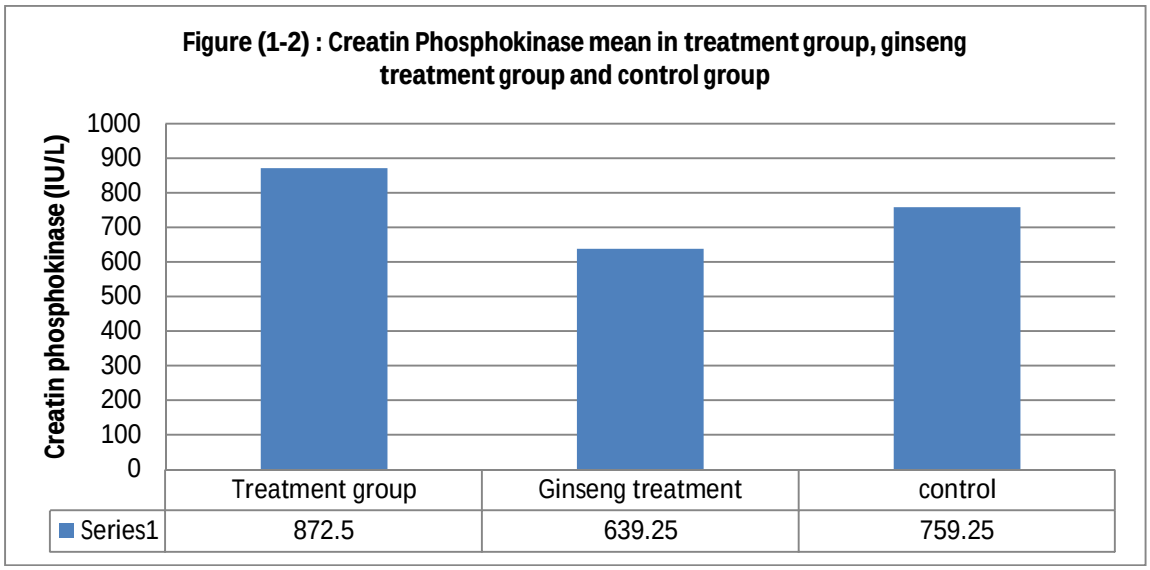
Table (2-2): Results of ANOVA and TUKEY HSD tests of blood biochemical parameters analysis

Parameter	**(I) Case**	**(j)Case**	**Sig**	**P-value**
	Control	Treatment	0.418	-
AST		Ginseng treatment	0.434	-
(Aspartate Aminotransferase)	Treatment	Control	0.418	-
IU/L		Ginseng treatment	0.048	0.048
	Ginseng treatment	Control	0.434	-
		Treatment	0.048	0.048
	Control	Treatment	0.745	-
CPK		Ginseng treatment	0.719	-
(Creatin Phosphokinase)	Treatment	Control	0.745	-
IU/L		Ginseng treatment	0.304	-
	Ginseng treatment	Control	0.719	-
		Treatment	0.304	-
	Control	Treatment	0.169	-
CPK-MB		Ginseng treatment	0.980	-
(Creatin Phosphokinase-	Treatment	Control	0.169	-
Muscle and Brain)		Ginseng treatment	0.121	-
IU/L	Ginseng treatment	Control	0.980	-
		Treatment	0.121	-
	Control	Treatment	0.098	-
LDH		Ginseng treatment	0.980	-
(Lactate Dehydrogenase)	Treatment	Control	0.098	-
IU/L		Ginseng treatment	0.068	-
	Ginseng treatment	Control	0.980	-
		Treatment	0.068	-
	Control	Treatment	0.994	-
ALT		Ginseng treatment	0.931	-
(Alanine Aminotransferase)	Treatment	Control	0.994	-
IU/L		Ginseng treatment	0.887	-
	Ginseng treatment	Control	0.931	-
		Treatment	0.887	-

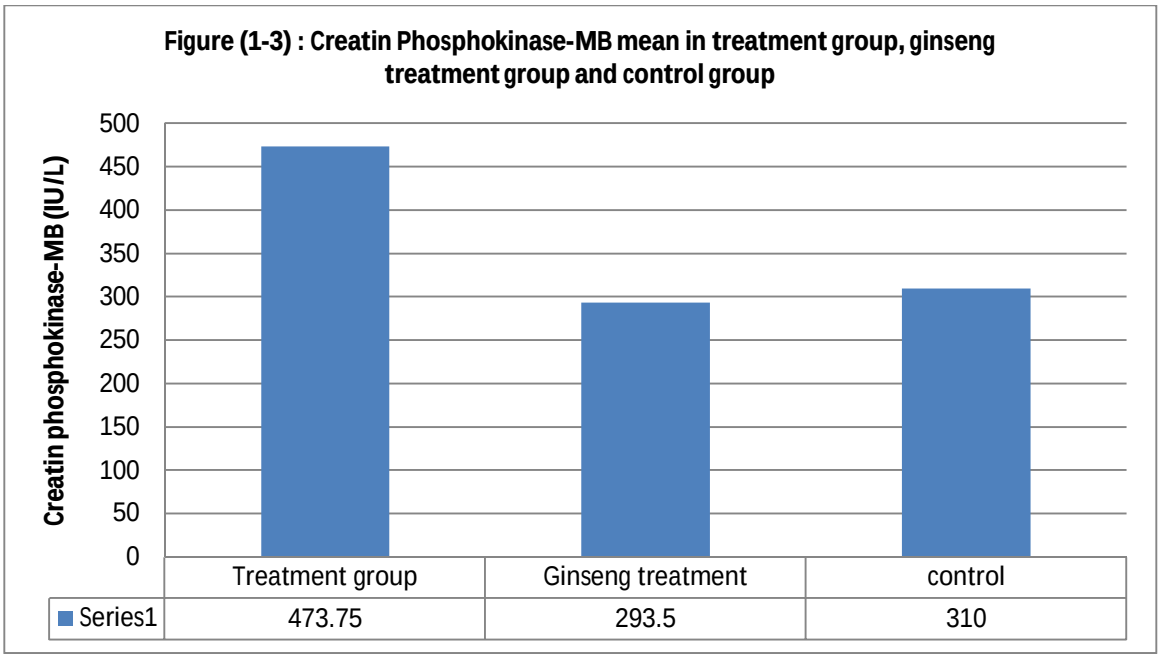
In this research we found out, there was a significant difference on AST parameter between treatment group and ginseng treatment group so ginseng reduces the serum AST level ($p<0.05$). There was no significant difference between treatment group and control group also there was no significant difference between ginseng treatment and control group on AST parameter ($p<0.05$). Column chart of AST are given on figure (1-1). The highest level of blood serum AST was on treatment group also the lowest level of blood serum AST was on ginseng treatment group.



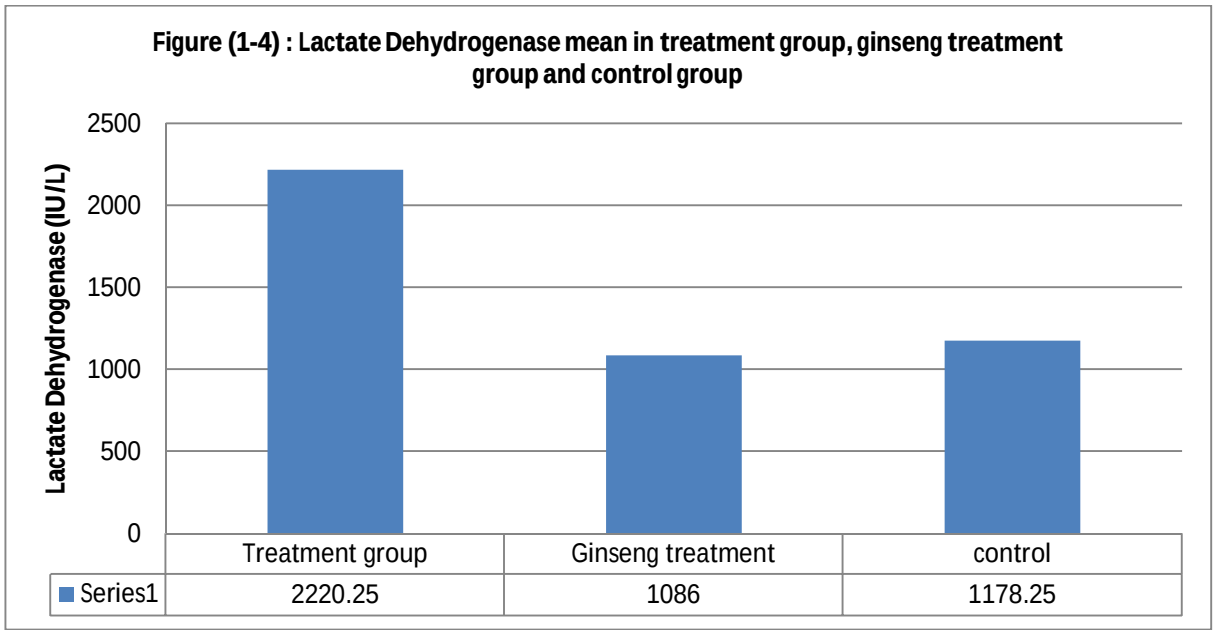
There was no significant difference between control, treatment and ginseng treatment on CPK (Creatin phosphokinase) parameter ($p<0.05$). Column chart of CPK are given on figure (1-2). The highest level of blood serum CPK was on treatment group also the lowest level of blood serum CPK was on ginseng treatment group.



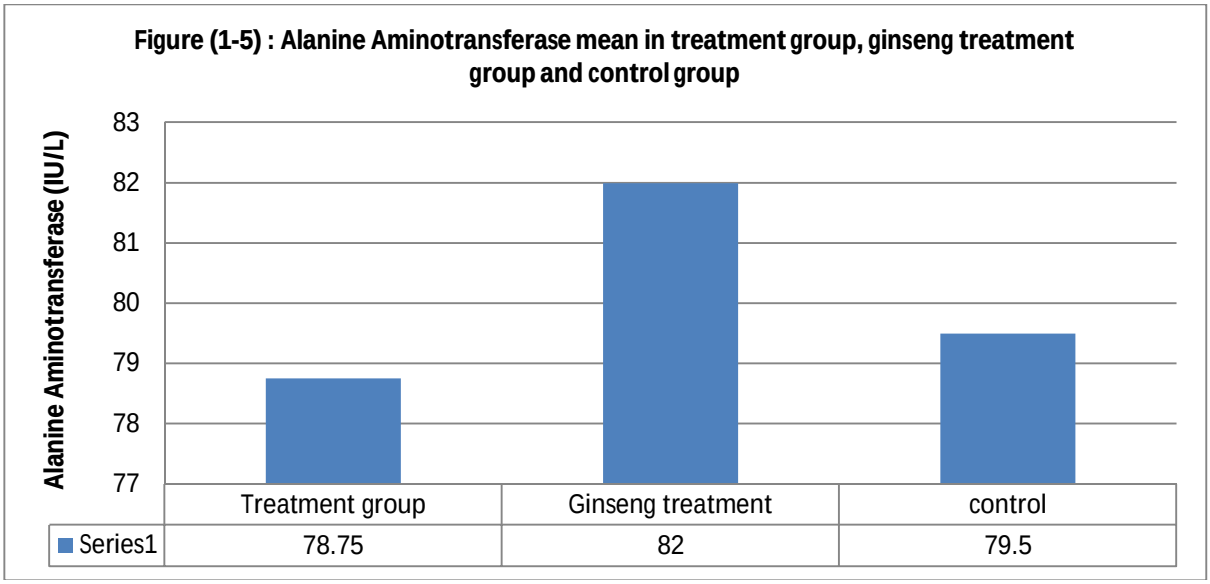
There was no significant difference between control, treatment and ginseng treatment on CPK-MB (Creatin phosphokinase muscle and brain) parameter ($p<0.05$). Column chart of CPK-MB are given on figure (1-3). The highest level of blood serum CPK-MB was on treatment group also the lowest level of blood serum CPK-MB was on ginseng treatment group.



There was no significant difference between control, treatment and ginseng treatment on LDH (Lactate Dehydrogenase) parameter ($p<0.05$). Column chart of LDH are given on figure (1-4). The highest level of blood serum LDH was on treatment group also the lowest level of blood serum LDH was on ginseng treatment group.



There was no significant difference between control, treatment and ginseng treatment on ALT (Alanine Aminotransferase) parameter ($p<0.05$). Column chart of ALT are given on figure (1-5). The highest level of blood serum ALT was on ginseng treatment group also the lowest level of blood serum LDH was on treatment group.



Result of troponin ELISA (Enzyme-Linked Immunosorbent Assay) test was negative on control group, treatment group and ginseng treatment group.

DISCUSSION

There are two major categories of liver enzymes: leakage enzymes and cholestatic enzymes [5]. Leakage enzymes are enzymes that leak into the plasma when hepatocyte injury or death occurs. Therefore, high activities in serum are an indication of hepatocellular injury [5, 15]. Commonly measured leakage enzymes include the following:

• Alanine aminotransferase (ALT; also alanine transaminase)
• Aspartate aminotransferase (AST; also aspartate transaminase)
• Sorbitol dehydrogenase (SDH)
• Lactate dehydrogenase (LDH)

Cholestatic enzymes are enzymes for which synthesis is increased as a result of bile retention or administration of drugs. Bile retention usually results from intrahepatic or extrahepatic bile duct obstruction. Commonly measured cholestatic enzymes include the following:

• Alkaline phosphatase (ALP)
• Gamma-glutamyltransferase (GGT; also gamma-glutamyltranspeptidase) [8].

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are enzymes found mainly in the liver, but also found in red blood cells, heart cells, muscle tissue and other organs, such as the pancreas and kidneys [11]. AST and ALT formerly are called serum glutamic oxaloacetic transaminase (GOT) and serum glutamic pyruvic transaminase (GPT), respectively. AST or ALT levels are a valuable aid primarily in the diagnosis of liver disease. Although not specific for liver disease, it can be used in combination with other enzymes to monitor the course of various liver disorders. When body tissue or an organ such as the liver or heart is diseased or damaged, additional AST and ALT are released into the blood stream, causing levels of the enzyme to rise [12, 7]. Therefore, the amount of AST and ALT in the blood is directly related to the extent of the tissue damage. On the other hand, the ratio of AST to ALT (AST/ALT) sometimes can help determine whether the liver or another organ has been damaged [23, 13, 7].

AST and ALT are also biological catalyst. Therefore, the assay of AST and ALT activity all based on the following enzyme reactions included original and succeeding reactions [12, 13]. Where GlOX is glutamate oxidase, POP is pyruvate oxidase, and OAC is oxalacetate decarboxylase.

Num	Enzyme or PH	Reactions
(1)	AST	*L-aspartate + a-ketoglutarate → Oxalacetate+ L-glutamate*
(2)	ALT	*L-alanine + a-ketoglutarate → Pyruvate + L-glutamate*
(3)	OAC	*Oxalacetate → Pyruvate + CO_2*
(4)	POP	*Pyruvate + O_2 + Phosphate → Acetyl phosphate + CO_2 + H_2O*
(5)	GLOX	*L-glutamate + O_2 → a-oxogluatrate + NH_3 + H_2O_2*
(6)	PH 7.8	*Oxalacetate + NADH + H^+→ malate + NAD^+*
(7)	PH 7.4	*Pyruvate + NADH + H^+→ L- lactate + NAD^+*

In this research we found out, there was a significant difference on AST parameter between treatment group and ginseng treatment group so ginseng reduces the serum AST level. There was no significant difference between treatment group and control group also there was no significant difference between ginseng treatment and control group on AST parameter also there was no significant difference between control, treatment and ginseng treatment on ALT (Alanine Aminotransferase) parameter.

LDH (also LD) can be found in high concentration in heart, liver and skeletal muscle [21]. Lactate dehydrogenase can do process oxideation and reduction [8].LDH has five isoenzymes. LD1 and LD2 are primarily located in cardiac muscle, whereas LD5 is primarily located in liver and skeletal muscle. By determining the specific isoenzyme increased in serum, the source of the cellular injury can be identified [29, 30, and 31]. Lactate dehydrogenase (LDH) catalyses the reduction of pyruvate to lactate by this reaction:

$$Pyruvate + NADH + H^+ \leftrightarrow Lactate + NAD^+$$

There was no significant difference between control, treatment and ginseng treatment on blood serum LDH level in this experiment between all control, treatment and ginseng treatment groups.

Creatine phosphokinase (CPK), aspartate transaminase (AST), and lactate dehydrogenase (LDH) have been used to evaluate muscle disorders in dogs, cats, ruminants, and horses [8, 9]. Alanine transaminase (ALT) has been used as a muscle specific enzyme in ruminant and horses because very little is present in liver [14, 20]. Serum activities increase with degenerative and necrotic lesions but do not increase with muscle atrophy or neoplasia [8].

CPK is highly specific for muscle injury. Although CPK is present in low amounts in intestine, uterus, kidney, and urinary bladder, a substantial increase in serum CPK activity is almost always an indication of skeletal or cardiac muscle degeneration or necrosis [8, 14, 9]. CPK activity increases within a few hours of onset of muscle necrosis [20]. CPK has a short half-life in plasma. As a result, CPK activity returns to normal within 24 to 48 hours after cessation of muscle injury. Therefore a persistent increase in serum CPK activity can be interpreted as continued muscle injury. CPK enzyme has three CPK-M, CPK-MB and CPK-B isoenzymes that most of cells contain CPK. But there is enough CPK-MB only in the heart and skeletal muscles that varies through the confusions related to these organs [15, 20]. There was no significant difference between control, treatment and ginseng treatment on CPK-MB (Creatin phosphokinase muscle and brain) parameter. The highest level of blood serum CPK-MB was on treatment group also the lowest level of blood serum CPK-MB was on ginseng treatment group.

Serum levels of cardiac enzymes and isoenzymes are essential to the diagnosis or exclusion of myocardial damage. A new set of serum assays have been developed for the detection of cardiac injury [4]. Cardiac troponin I is specific for cardiac tissue and is detected in the serum only if myocardial injury has occurred. This test has improved sensitivity and specificity over CPK-MB in the diagnosis and exclusion of myocardial injury [18, 1]. The troponin I assay allows early identification and stratification of patients with chest pain suggestive of ischemia, allows identification of patients that present 48 hours to 6 days after infarction, and identifies patients with false positive elevations in CPK-MB [19].

In a research conducted by Saleh (2012) adult male albino rats were divided into five groups, a control and four experimental groups; each of them contains five rats. The experimental animals were injected with 40 mg/kg body weight of streptozotocin daily for 2 successive days to induce diabetes. The first group of diabetic rats was considered as a diabetic group and left without treatment. The second group was injected i.p with 500 mg/kg body weight of taurine daily for one month and served as diabetic plus taurine group. In the third group, ginseng was given orally at a dose of 400 mg/kg body weight daily for the same previous period. The last group received both taurine and ginseng treatments at the aforementioned doses and through the same routes for one month. In the current work, the maximum improvement occurred in cardiac status parameters, (AST), (CPK) and (LDH) activities and the levels of serum endothelin-1 and TNO in the diabetic animals group which was treated with both taurine and ginseng [25]. In other research conducted by Arundhati et al. (1998) animals were divided into four groups. Each group comprised of 20 rats. Group I acted as control and received plain boiled water in the dose of 1 ml/100 gm body weight each. Group II, III and IV received the extract of Ginseng and Ashwagandha in the doses of 8.50 mg/kg, 12.75 mg/kg and 17.00 mg/kg respectively. The doses administered were the fractions of LD50 of the

combination, approximating 4, 6 and 8 times the therapeutic dose. In Arundhati et al. (1998) research, AST and ALT of rats did not show any significant toxic effect [3].

Conclusion

There was a significant difference on AST parameter between treatment group and ginseng treatment group so ginseng reduces the serum AST level but there was no significant difference between control, treatment and ginseng treatment on AST, CPK, CPK-MP, LDH, ALT and Troponin parameters.

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