Original Article

Responses of liver and renal function markers against arjuna tree extract in induced Hyperlipidemia Rats

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ABSTRACT

Cholesterol rich diets become more favorable nowadays, may be because of it makes food tastier but in long term, fatty diets possess fatty liver and chronic kidney disease leading to more series status like Diabetes and Heart disease if not controlled by healthy strategies like switching to salubrious diets. Ancient peoples have benefits from extraction of *Teminali arjuna* as antioxidant and anti-hypercholesterolemia agent. The data inquiry provides the liver and kidney protective roles of *Terminalia arjuna* ethanolic extract in chow (5% cholesterol+0.5% cholic acid) induced hyperlipidemia rats. The liver and renal function tests assess by using Biolabo kit/France and the excremental rats designed into 3 groups (Control, hyperlipidemia rats and T.arjuna treated hyperlipidemia rats). In The current inquiry, Rats fed on chow had significantly higher values of (SGOT, SGPT, serum creatinine, ALP and Blood urea) and the values of (S.albumine, S.globuline and total protein) cutback significantly in compare to control rat groups. the biomarkers of renal function and hepatocellular activity in induced hyperlipidemia rats significantly affected by abating T.arjuna extract in their diet. Notably, the level of Uric acid, blood sugar and amylase enzyme significantly cutback in induced hyperlipidemia rats treated with extract of T.arjuna bark. Terminalia arjuna bark extract (500 mg/kg body weight) could be used as active antilipidemia and efficient liver and kidney protective agents in obese patients or long term fatty diet consumers. As shown to have positive feedback on hepatic and renal functions and become able to cut off high levels of Uric acid, blood urea and amylase enzyme in induced hyperlipidemia rats.

Keywords: lipid rich foods, Hyperlipidemic liver and kidney, *T. arjuna*, Biochemial tests.

Introduction

Cholesterol rich foods including Beef, egg yolk, poultry, Butter are considered as main sources of Animal steroids [1]. The direct proportional of high cholesterol diet on the total cholesterol of a consumer has been declared by a cohort investigation [2]. Consuming fat rich diets lead to initiate dyslipidemia, obesity, fatty liver, kidney dysfunction and Heperlipidemia [3]. Hyperlipidemia explained as major risk factor in progression of Coronary heart disease, liver injury and renal dysfunctionality [4].

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The major roles of the liver include protein synthesis, metabolism, oxidation and lipid spreading, can be majority impaired by the cholesterol accumulation causing fatty liver diseases (cirrhosis, hepatocellular carcinoma and liver failure) through Hypoxic and nitric oxide signal transduction procedure [5]. Malnutrition with high cholesterol content Also cause lowered glomerulosclerosis, glomerular enlargement, and glomeruli loss in rats with blood pressure. Another study also added that fatty diet may cause renal dysfunction due to histopathological deformities like dilatation, tubular defects, inflammation of the kidney [6]. Those kidney damages will affect kidneys to function properly as excretory organ of waste products and toxic substances, also extracellular fluid volume, serum osmolality and electrolyte concentrations will be imbalanced [7]. Thus Using lipid lowering agent became necessity but Designing suitable anti-hyperlipidemia drugs with minimum adverse effects possessing challenges among pharmaceutical companies. Herbal treatment as alternative may have better

influence on the health with less side effect. A plant called Terminalia arjuna has been used by the ancient peoples for many medical purposes because of its important active constituents like flavonoids, glycosides, Terpenes and tannins. T.arjuna comes from combretaceae family, originates from a place called Uttar Pradesh, Madhya Pradesh and Duccan region. [8]. The most important part of T.arjuna were thought to be its stem bark, which serve as main center of plant isosterols, glycosides and flavonoid [9]. Previous studies have explained the vital role of Flavonoids as hypolipidemic, antioxidant and anti-inflammatory agent. Glycoside was another active ingredient accommodated sufficiently in T.arjuna barks, which has medicinal property as protective agents of hepatic cells [10]. The present study has conducted to observe the physiological change of liver and renal function markers of chow induced hyperlipidemia rats fed on ethanolic extract of Terminalia arjuna barks, the physiological changes estimated by comparing biochemical status of experimented groups.

Materials and Methods

Plant Materials: Terminalia arjuna barks were purchased from India (Madurai District, Tamil Nadu), and the recognized and authenticated by the Department of Plant Sciences, University of Madras [vide voucher no 031].

Extraction of the plant

The Air dried bark of T.arjuni were pulverized to get powder form by extraction with ethyl alcohol (90%) in hot continuous percolation over 72 hours using Soxhlet apparatus. The gained solvent vacuum distillated and evoporized to get a semisolid mass of dark brownish red shiny crystal-like residue of 13.89% (w/w) yield [11].

Preparation of Tested Animals

In this experiment, forty male albino rats were used aged 8-10 weeks and about 200-250 grams in weight. The housing and breeding of rats were done in the animal house of biology department, college of science education, salahaddin university during period (25-july-2014 and 2-February-2019). Every four or five animals were kept in each cage under laboratory condition of 22±2 °C and 12h light: 12h dark [12]. At first period, animals fed on standard rat pellet and tap water ad libitum [13]. For initiation of hyperlipidemia status, for six weeks the rates were fed on chow (5% cholesterol+0.5% cholic acid). As known to be most familiar animal models used for observing lipid lowering effect of a particular agent [14].

Experimental design

The design of the work project has divided rats into five caged groups, each cage contained eight rats. The first rat group fed only on standard diet (Control). The second group considered as the (model) fed only on the chow (5% cholesterol+0.5% cholic acid) for six weeks. The third group chosen to (Terminali arjuna rats) fed on diet containing chow (5% cholesterol+0.5% cholic acid) and ethanolic extract Terminalia arjuna bark at 500 mg/kg body weight.

Estimation of liver function markers

Evaluation of Liver Functions done through estimating the Serum Alkaline phosphatase(ALP), Serum GOT (Glutamic Oxaloacetic Transferase), GPT (Glutamic phosphate transferase), TSB (Total serum billirubin) by using Biolabo reagent kit/France, Estimation of Total Protein, Albumin and Globulin also done through Biolabo reagent kit/France [15].

Determination of Renal Function Tests

Determination of Blood Urea Nitrogen, Serum Creatinine and Gama Glutamyle Transferase (GGT) Based on the method followed by [16]. The estimation of Creatinine Kinase (CK) done based on the procedure done by Biolabo reagent kit/France/ Cobas –USA, the photo metrically measured rate of formation of NADPH is directly proportional to the CK activity [17].

Estimation of Lactate Dehydrogenase (LDH) and **Blood glucose** done by using Biolabo reagent kit/France/ Cobas – USA [18].

Estimation of α-Amylase: To find its concentration same laboratory instructions were applied as previously performed by [19].

Statistical Analysis

All data are expressed as mean ± standard. The software (SPSS Version 19) was used to find the error of means and statistical analysis. Statistically the $p<0.05$ was considered to be significant at which changes in the statistics were found using Duncan test for multiple comparisons after ANOVA.

Results

The present data showed that the serum ALT of the control group (42.15±3.09 IU/L) was significantly different from hyperlipidemic rats (57.98±6.01 IU/L). However, value of serum ALT in Terminalia arjuna (41.81±3.57 IU/L) were significantly decreased ($p<0.05$) in comparison to the untreated hyperlipidemic rats. The serum levels of AST in hyperlipidemic rats (154.30±10.45 IU/L) had significant changed in compare with control groups (139.75±7.11 IU/L), but the hyperlipidemic rats treated with T.arjuna bark extract(149.87±9.23 IU/L) showed no significant changes (Table 1). The test results of ALP evaluation indicated that hyperlipidemic rats (605.89±60.67 IU/L) had significantly increased ALP levels in compare to the control group (412.03±43.33 IU/L), in addition, the serum ALP levels in Terminalia arjuna treated group (454.63±40.41 IU/L) have shown non-significant decreased ($P<0.05$) changes in comparison to the untreated hyperlipidemic rats (Table 1).

The total bilirubin was found to be siginificantly higher (0.22±0.05 mg/dl) in compare in induced hyperlipidemic

(0.07±0.01 mg/dl) rats with control groups. But its level did not change when the hyperlipidimic rates treated with T.arjuna bark extract (0.12±0.03 mg/dl) in compare with model group rats (Table 1).The total protein in the present study had significantly decreased levels in hyperlipidemic rats group (5.44±0.13 g/dl) in compare with group rats (6.18±0.22 g/dl). However, the level didn't change when the hyperlipidemia rats treated with *Terminalia arjuna* (5.87±0.19 g/dl) in compare to untreated model rats (Table 1). The serum albumin in the current experiment observed to be non-significantly different between control group (3.94±0.06 g/dl) and hyperlipidemic rat model (3.51±0.09 g/dl). But the serum albumin value in *Terminalia arjuna* treated rats (4.32±0.25 g/dl) noticed to be significantly increased ($p<0.05$) in compare with the model hyperlipidemic rats. The result also presented the serum globulin as to be non-significantly different between *T.arjuna* Treated and Untreated rats. (Table 1).

Table 1: Effects of Terminalia arjuna on some markers of Liver Function in Hyperlipidemic Rats

Parameters	G1 (Control)	G2 (Hyperlipidemic) Rats	G3 *(Terminalia arjuna)*
GPT/ALT (IU/L)	42.15±3.09 ab	57.98±6.01 a	41.81±3.57 b
GOT/AST (IU/L)	139.75±7.11 b	154.30±10.45 a	149.87±9.23 ab
ALP (IU/L)	412.03±43.33 b	605.89±60.67 a	454.63±40.41 ab
T.S.B (mg/dl)	0.07±0.01 b	0.22±0.05 a	0.12±0.03 ab
Total Protein (g/dl)	6.18±0.09 a	5.44±0.13 b	5.87±0.19 ab
S. Albumin (g/dl)	3.94±0.06 ab	3.51±0.09 b	4.32±0.25 a
S. Globulin (g/dl)	2.25±0.07 ab	1.92±0.11 ab	1.55±0.38 b

The same letters within column mean no significant differences and the different letters mean significant differences.

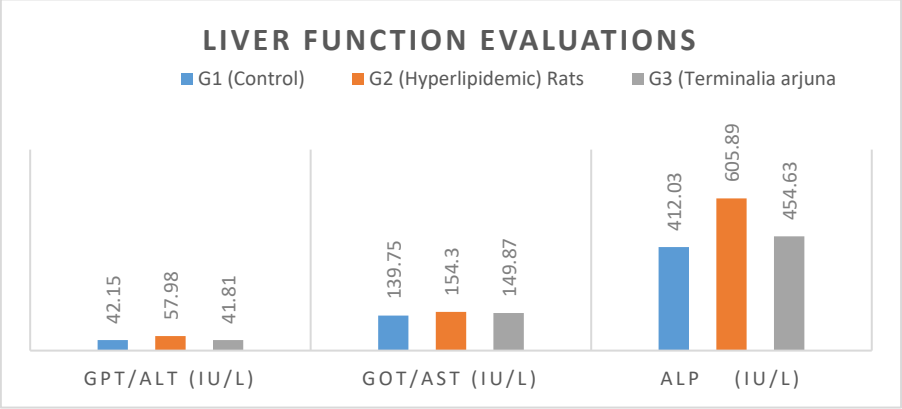

Figure 1: Shows the concentrations of liver function tests between control, hyperlipidemia and Terminalia arjuna groups.

The current investigation showed that the level of Blood Urea in hyperlipidemia rats (46.77±1.39 mg/dl) changed significantly in compare with control groups (28.71±2.28 mg/dl), while its level didn't change in *T.arjuna* treated rats (40.52±2.78 mg/dl) in compare with Untreated model rats (Table 2). The Creatinine phosphate kinase levels were observed to be significantly ($p<0.01$) elevated in hyperlipidemic group (0.53±0.02 mg/dl) in compare with control group (0.47±0.02 mg/dl). Treating hyperlipidemia rats with T.arjuna bark extract had no significantly changes on this elevation. In addition, the level of S.Creatinine, LDH and GGT didn't show any significant changes among all tested groups (Table 2).

Table 2: Effects of Terminalia arjuna, on some markers of Renal functions in Hyperlipidemia Rats

Parameters	G1 (Control))	G2 (Hyperlipidemic) Rats	G3 *(Terminalia arjuna*
Blood Urea (mg/dl)	28.71±2.28 c	46.77±1.39 a	40.52±2.78 ab
S. Creatinine (IU/L)	0.47±0.02 b	0.53±0.02 ab	0.48±0.02 b

CPK (U/L)	249.85±33.17 b	436.00±50.69 a	341.00±19.24 ab
LDH-P (U/L)	358.71±34.54 a	444.57±59.35 a	350.28±24.74 a
GGT (U/L)	0.142±0.01 a	0.571±0.02 a	0.285±0.02 a

The same letters within column mean no significant differences and the different letters mean significant differences.

The conducted work showed that the serum blood glucose significantly risen in hyperlipidemic rats (192.42±7.99 mg/dl) in compare to control rats (122.14±3.15 mg/dl). Whereas, rats treated with Terminalia arjuna bark extract had significantly ($p<0.05$) lowered serum blood glucose 128.71±7.05 mg/dl in compare to hyperlipidemic rats (Table 3).

The Uric acid test results showed to be significantly higher in induced hyperlpidemic rats (4.01±0.19 mg/dl) in compare to control group (2.14±0.18 mg/dl). Notably this elevated uric acids in induced hyperlipidemia rats become significantly decreased ($p<0.01$) when the rats treated *T.arjuna* barks (2.82±0.24 mg/dl) (Table 3).

The Serum amylase analysis showed significant increased changes in hyperlipidemic rats (866.94±11.66 su/dl) in compare to control rats (478.08±71.33 su/dl). But Treating hyperlipidemia rats with Terminalia arjuna bark extract significantly ($p<0.05$) lowered serum amylase level (540.53±50.66 su/dl) (Table 3).

Table 3: Effects of *Terminalia arjuna*, on Blood glucose, S.Uric acid and Amylase concentration in Hyperlipidemia Rats.

Parameters	G1 (Control)	G2 (Hyperlipidemic) Rats	G3 (Terminalia arjuna)
Blood Glucose (mg/dl)	122.14±3.15 b	192.42±7.99 a	128.71±7.05 b
S. Uric Acid (mg/dl)	2.14±0.18 b	4.01±0.19 a	2.82±0.24 b
Amylase (su/dl)	478.08±71.33 b	866.94±11.66 a	540.53±50.66 b

The same letters within column mean no significant differences and the different letters mean significant differences.

Discussion

Cholesterol rich foods linkage to the risks of Cardiovascular diseases become initiated by a research article for a long time ago [20]. accretion of cholesterol in the arteries induces plaque buildup and arterial blockage causing a chronic condition called atherosclerosis [21]. The release of cellular enzymes (SGOT, SGPT and ALP) into the serum can serve as primary signs of hepatic damages [22].

The observed data inquiry, illustrated the adequate force of T. arjuna on the Liver function biomarkers. the T.arjuna bark extract significantly decreased GPT values in induced hyperlipidemic rats, but the values for GOT, ALP and total serum bilirubin didn't change significantly in T.arjuna treated rats. In accordance, a project by [23] demonstrated that the parameters of liver activity decreased significantly in T.arjuna treated hyperlipidemia rats and recovering of hepatic cells occurred through cell permeability restoring. Achieved yield acknowledged by [24]. In contrast, a previous article published by [25] depicted that the addition of 200 mg/kg of Terminalia arjuna extract to rat's diet significantly decreased the level of AST, ALT, ALP, Bilirubin.

The empirical outcome exhibited significant decline for the total protein and serum albumin amount in untreated hyperlipidemia rats but treating hyperlipidemia rats with ethanolic extract of T.arjuna the values significantly risen for S. albumin and total protein . These was agreed by [26]. As exhibited, the values for Serum globulin didn't expressed any differences by treating hyperlipidemia rats with ethanolic extract of T.arjuna. likely, previous laboratory effort by [27] established that the Extraction of T.arjuna significantly reduced liver damages.

The dietary rich cholesterol significantly increased the level of blood urea and Creatinine phosphate kinase in hyperlipidemic rats and Using ethanolic extract of T.arjuna bark reduced this elevation non- significantly. Also the level of S. creatinine, LDH and GGT have decreased non-significantly among all the experimented groups. A study by [28] expected excellent recovery of renal function in hyperlipidemia rabbits treated with T.arjuna extract because of the renal tubules ability to regenerate. The inquiry delineated acknowledged by [29] revealing that devouring precise amount of T.arjuna bark extract possessed significant kidney protective potentials.

The Conducted inquiry also implemented the significant aftermath of T.arjuna bark extract have on decreasing the levels of Blood glucose, Uric acid and Amylase enzyme in induced hyperlipidemia rats after they were significantly increased to due consuming high cholesterol diets. Same result found by [30] who published a research article on the effectiveness of T.arjuna in abating the intensity of serum creatinine, blood urea and Uric acids in T.arjuna hyperlipidemia rats. Similarly, Alike probe by [31] stated a significant cutback of blood glucose in induced diabetic rats treated with ethanolic extract of T.arjuna barks.

Conclusion

The outcome of the present inquiry can be shrinkage by suggesting the fatty diets initiats fatty liver and kidney damage as seen increased peculiar signs of that damage by elevating liver tests (GOT, GPT and ALP) and renal function tests (Blood urea and serum creatinine) in induced fatty liver rats, the protein yield (Total protein, S.albumine, and A.glubuline) also decreased. T.arjuna bark extract played as effective medicinal agent in dropping off levels of the liver activity tests (AST, ALT and ALP) and lowerd the renal testing parameters non-significantly in model high cholesterol rats. T.arjuna bark could be used as anti-proliferation agents for acute kidney injury because of its significant capabilities in reducing oxidative stress markers like Uric acid.

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