# Biochemical evaluation of the effect of *Rhazya stricta aqueous* leaves extract in liver and kidney functions in Rats

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**Abstract:** Rhazya *stricta* (*R. stricta*) is an important medicinal species used in indigenous medicinal herbal drugs to cure various diseases in South Asia and Middle East Countries. Over 100 alkaloids have been isolated, from *R. stricta* leaves, stems, roots and legumes and mixtures of aerial parts. The aim of this study was evaluatation of the beneficial effects of oral administration of extracts of the *R. stricta* leaves on serum lipid profile concentrations, the activity of liver enzymes and the kidney functions, using doses comparable to those applied by humans in the folkloric medicine. To achieve this goal, fifty five male Wistar rats were divided into four groups as follows: group 1 (control, n= 10) received a daily single oral dose of 0.5 ml of distilled water, groups 2, 3 and 4 (each of 15), each animal received a daily single oral dose of 0.5 ml of distilled water containing 0.1 gm/ml (group 2), 0.125 gm/ml (group 3) and 0.150 gm/ml (group 4) of the *Rhazya* leaf aqueous extract, for 18 weeks. Blood samples were collected, after an overnight fast, 1, 2, 4, 8, 12 and 18 weeks post-treatment. The aqueous extract of the *R. stricta* leaves significantly decreased concentrations of TGs, LDL-c, cholesterol, uric acid and creatinin, but increased concentration of HDL-c. It triggered all these activities without affecting liver enzyme activities or kidney functions. These findings may have a positive impact on the cardiovascular patients and may provide a new therapeutic strategy to reduce hypertriglyceridemia. [Nature and Science. 2010;8(4):136-142]. (ISSN: 1545-0740).

**Key words**: *Rhazya stricta*; lipid profile; liver enzymes; aqueous extracts; uric acid

## 1. Introduction

*Rhazya stricta* Decne (*R. stricta*), locally known as Harmal, is a member of family Apocynaceae. It is widely distributed throughout Western Asia from Yemen to Arabia, to the North West Province of India and abundantly found in various regions of Pakistan. The plant is a glabrous erect shrub with smooth central stem and dense erect branches, Western (1989) . It is widely used in traditional medicine as a reputed tonic and curative for rheumatic pain, sore throat, syphilis, diabetes, helminthiasis, inflammatory conditions, fever and other diseases , Ageel et al., (1987); Ali,et al., (1995) and Ali,et al., (1998) The leaves of the plant contain alkaloids with β-carboline nucleus (akuammidine, rhazinilam and tetrahydrosecamine), Bashir et al;., (1994). The *R. stricta* leaves have been shown to contain flavonoids, glycosides, triterpenes, tannins, volatile bases and probably other substances, Ahmed et al;., (1983) and AL-Yahya et al;., (1990). Extensive studies on the phytochemistry, Baherji et al;., (1970); Rahman et al;., (1988); Bashir et al; (1994) and Wasfi et al; (1994), antimicrobial activity Bashir et al; (1994), central nervous system depression, Ali et al; (1995) and general pharmacology and toxicity of the plant[13] have been reported. Its leaf extracts were found to cause sedation, analgesia, decreased motor activity, antidepressant-like activities, complex effects on brain endogenous monoamine oxidase activity and centrally-mediated hypotension in mice and rats, Ali, et al., (1995); Ali, et al., (2000); Tanira et al., (2000); and et al., (2000). Recently, Baeshin's team run a series of elegant experiments proving that the aqueous extract *Rhazya stricta* leaves had mutagenic activities on *wide* range of cell types including *S. cervisae*, Baeshin et al., (2005) *Aspergillus terreus*, Baeshin et al., (2008). *Allium cepa* root tip meristem, Baeshin et al., (2009) and the primary culture of human lymphoctes Baeshin et al., (submitted).

To our best knowledge, there is no documented report elucidating the effects of this plant on serum HDL-c concentrations. In light of the ample use of this plant, and as part of our ongoing research in exploring possible curable effects of some indigenous medicinal herbs in KSA, we decided to investigate the effect, if any, of the *R. stricta* leaf extract on lipid profile concentrations, especially HDL-c and HDL.

## 2-Effects of the *R. stricta* leaf aqueous extract after two weeks of treatment

The data presented in Table 2 shows that, after two weeks of treatment, the *Rhazya* extract consistently recapitulated its dose-dependent decreasing mode of action on TGs, specially in context of group 4, since it turned down concentrations of TGs to as nearly as 60% of their concentration in the control group. It also consistently increased, in a dose-dependent manner,

concentrations of HDL-c and LDL.

However, it did not significantly affect concentrations of cholesterol in all treated groups. Although a highly significantly (P<0.01) increase in activity of AST was observed in group 4, no effects was noticed for ALT or ALP. For effects of the extract on creatinine, uric acid and urea, its best effects were clearly seen in the context of group 4, where it significantly decreased concentrations of uric acid and urea; however, it did not bring effects on creatinine level. Nonetheless, it did increased concentration of creatinine in group 2.

## Materials and Methods

### 1-Materials:

### 1.1-Animals

Fifty five locally bred adult male Wistar rats, initially weighing 150-200 gm, were obtained from King Fahad Medical Research Center (KFMRC), King Abdul-Aziz University, Jeddah, KSA. They were housed in groups of five animals at a temperature of 22°C under a 12 h dark-light cycle. They were fed *ad libitum* a standard pellet diet (Grain Soils and Flourmills Organization Jeddah, KSA) and given distilled drinking water.

### *1.2-Plant material and extract preparation*

The plant was collected from a nearby area of Jeddah, KSA in May 2005. Leaves were shade-dried and ground to a fine powder with a blender. The resulting powder was stored at 4°C. Aqueous solutions were freshly prepared daily from this powder and used in all tests. Three different concentrations of the powdered leaves were prepared (0.1 gm/ml, 0.125 gm/ml and 0.150 gm/ml) by macerating 4 gm, 5 gm and 6 gm, respectively, in 40 ml distilled water for 12 h at room temperature, with occasional shaking. The extract was then filtered. The filtrate was giving directly to the rats; the aqueous extract was always administrated orally in a volume of 0.5 ml of the prepared dose.

### 2-Material and Methods:

### 2.1-Experimental design

Animals were divided into four groups and acclimatized for 4 days prior to experimentation. Group 1 (control, n= 10), each animal was given, by oral gavage, 0.5 ml distilled water. Groups 2, 3 and 4 (each of 15), each animal was given, by oral gavage, a daily single dose of 0.5 ml distilled water containing 0.1 gm/ml (group 2), 0.125 gm/ml (group 3) and of 0.150 gm/ml (group 4) of the extract, for 18 weeks.

Blood samples were collected, after an overnight fast, on weeks 1, 2, 4, 8, 12 and 18 post-treatment. At the time of the collection, information including body weights, food and water intakes as well as any abnormal physical behavior was recorded for each animal. Collected blood samples were centrifuged at 3000 rpm for 10 minutes and sera were stored immediately at - 80°C until time of analysis.

### 2.2 Biochemical assays

Sera were used for measuring concentrations of total cholesterol, high density lipoprotein (HDL-c), low density lipoprotein (LDL-c) and triglycerides (TG), for assaying activities of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP), and for determining concentrations of uric acid, urea, and creatinine. The last task was achieved by commercial kit-based enzymatic colorimetry methods (Dade Behring, USA) using an automated chemistry analyzer (Dimension R Clinical Chemistry System). These measurements were carried out in the biochemistry lab, King Abdul Aziz University Hospital (KAUH), Jeddah, KSA.

### *2.3 Statistical evaluation*

Statistical analysis was performed using SPSS 10 for Windows. The data were expressed as means ± standard deviation. Comparison of variables between groups was performed using one-way analysis of variance (ANOVA). The least significance difference test (LSD) was employed to compare means for pairs of groups. A difference was considered to be statistically significant when *P*-value ≤ 0.05.

## 3. Result Analysis

### 1-Effects of the *R. stricta* leaf aqueous extract after one week of treatment

The results are summarized in Table 1. Statistical analysis indicated that oral administration of the aqueous extract the *R. stricta* leaves significantly (*P*<0.05) decreased concentration of TGs in group 4, but it did not bring significant effect in group 2 or 3. On the other hand, it exerted a dose-dependent increasing mode on concentrations of HDL-c in all treated groups, whereas the lower dose of the extract, 0.1 gm/ml (group 2), significantly (*P*<0.05) increased HDL-c concentration, the higher doses of the extract, 0.125 gm/ml (group 3) and of 0.150 gm/ml (group 4), highly significantly (*P*<0.01) increased concentrations of HDL-c. Meanwhile, we did not observe significant (*P*>0.05) difference between all treated and control groups, regarding alterations in the concentration of LDL-c or cholesterol, neither did we notice change in activity of serum AST, ALT or ALP. In addition, serum creatinine concentration was lower in group 2 than its concentration in group 1 (control) and, finally, concentrations of uric acid and urea were significantly lower in group 4 than in control group.

**3-Effects of the *R. stricta* leaf aqueous extract after four weeks of treatment**

As shown in Table 3, TG concentrations were consistently decreased ($P$<0.05-0.01) in all treated groups compared to the control group. The extract, however, did not alter concentrations of HDL-c in all treated group, but it consistently decreased concentrations of LDL in all treated groups. Furthermore, neither did the extract alter concentrations of cholesterol, nor did it affect activity of AST, ALT, or ALP in all treated groups. Finally, the extract decreased concentration of creatinine in the context of group 4, but it did not alter concentration of uric acid or urea in any groups.

**3-Effects of *Rhazya stricta* after eight weeks of administration of treatment**

After eight weeks of treatment the extract highly significantly ($P$<0.01) augmented serum levels of TGs, especially in groups 2 and 3. It also boosted level of HDL-c in group 2; on the other hand, levels of LDL and cholesterol dwindled. In addition, the extract neither did affect activity of AST, ALT, nor ALP. The extract did not either alter concentrations of creatinine, but it significantly decreased and increased concentrations of uric acid and urea, respectively.

**4-Effects of the *R. stricta* leaf aqueous extract after twelve weeks of treatment**

Effects of the *Rhazya* extract after twelve weeks are displayed in Table 5; pair-wise comparison of TG levels in all treated and control groups show that the extract has neutralizing effect on TG levels. On the other hand, it significantly raised level of HDL-c in group 4. The extract did not affect either concentration of LDL or cholesterol; neither did it alter activity of AST, ALT nor ALP. The extract did, however, decrease activities of creatinine group 3), uric acid (groups 3 and 4) and urea (groups 2 and 3).

**Effects of the *R. stricta* leaf aqueous extract after eighteen weeks of treatment**

When we monitored effects of the *Rhazya* extract after eighteen weeks of treatment (Table. 6), we found that all treated and control animals have a more or less comparable levels for lipid profile, TGs, HDL-c, LDL and cholesterol. The same observation was noticed too for activities of the liver enzymes, AST, ALT and ALP, whereas the extract has no ability to alter their activities. Additionally, effects of the extract on concentrations of creatinine and urea were insignificant, but it significantly kept its decreasing effect on uric acid in groups 2 and 3.

**Table1: Lipid profile concentrations, Liver enzyme concentrations and kidney function test results among the groups after one week of treatment with *Rhazya stricta***

| Variable<br>n | Group 1<br>Control<br>10 | Group 2<br>(0.1gm/ml)<br>15 | Group 3<br>(0.125gm/ml)<br>15 | Group 4<br>(0.150gm/ml)<br>15 | *P*-value |
|---|---|---|---|---|---|
| **Triglycerides(mmol/l)** | 1.02±0.27 | 0.82±0.25 | 1.02±0.25 | 0.72±0.30 | $<0.05^{(c)}$ |
| **HDL (mmol/l)** | 0.43±0.06 | 0.50±0.07 | 0.51± 0.08 | 0.512± 0.07 | $<0.05^{(a)}$<br>$<0.01^{(b,c)}$ |
| **LDL (mmol/l)** | 0.89±.245 | 0.94±0.219 | 0.84±0.173 | 0.88±0.23 | NS |
| **Cholesterol (mmol/l)** | 1.79±0.21 | 1.72±0.43 | 1.81±0.24 | 1.70±0.22 | NS |
| **AST (U/L)** | 85.1±12.06 | 72.07±14.59 | 71.80±24.69 | 72.27±30.49 | NS |
| **ALT (U/L)** | 53.8±7.67 | 51.8±10.04 | 54.80±8.43 | 58.53±11.81 | NS |
| **ALP (U/L)** | 198.6±19.8 | 172.87±36.0 | 205.8±60.02 | 221.47±38.99 | NS |
| **Creatinine (umol/l)** | 31.89±4.48 | 28±4.62 | 30.40±4.39 | 32.20±4.78 | $<0.05^{(a)}$ |
| **Uric acid (U/L)** | 61.70±25.62 | 49±15.80 | 70.66±23.69 | 39.40±19.45 | $<0.05^{(c)}$ |
| **Urea ( umol/l)** | 7.52±0.95 | 6.82±0.83 | 6.87±0.86 | 6.32±1.03 | $<0.01^{(c)}$ |

Values were represented as the mean ± SD; the data were statistically analyzed using ANOVA followed by LSD test. (a: control vs. group 2, b: control vs. group 3, c: control vs. group 4).
*P*- value ≤ 0.05 was used as a criterion of significance.
*P*- value ≤ 0.01 was used as a criterion of highly significance.
NS: Not significant

**Table2: Lipid profile concentrations, Liver enzymes concentrations and kidney function test results among the groups after two weeks of treatment with *Rhazya stricta***

| Variable<br>N | Group 1<br>Control<br>10 | Group 2<br>(0.1gm/ml)<br>15 | Group 3<br>(0.125gm/ml)<br>15 | Group 4<br>(0.150gm/ml)<br>15 | *P*-value |
|---|---|---|---|---|---|
| **Triglycerides(mmol/l)** | 1.0± 0.23 | 0.86± 0.21 | 0.93± 0.20 | 0.61± 0.20 | $<0.001^{(c)}$ |

| | | | | | |
|---|---|---|---|---|---|
| **HDL (mmol/l)** | 0.49± 0.07 | 0.52± 0.08 | 0.54± 0.08 | 0.56± 0.07 | <0.05[c] |
| **LDL (mmol/l)** | 0.83± 0.28 | 0.88± 0.16 | 0.86± 0.15 | 1.03± 0.11 | <0.05[c] |
| **Cholesterol (mmol/l)** | 1.78± 0.26 | 1.79± 0.21 | 1.83± 0.19 | 1.87± 0.22 | NS |
| **AST (U/L)** | 86.6± 22.65 | 86.8± 13.97 | 98.13± 17.88 | 108.83± 15.76 | <0.01[c] |
| **ALT (U/L)** | 61.5± 12.71 | 62.2± 9.78 | 56.6± 17.5 | 66.31± 7.94 | NS |
| **ALP (U/L)** | 177.8± 19.53 | 160.4± 18.29 | 186.46± 17.79 | 172.9± 28.78 | NS |
| **Creatinine (umol/l)** | 33.6± 3.06 | 35.8± 3.73 | 37.86± 5.01 | 32.76± 5.13 | <0.05[b] |
| **Uric acid (U/L)** | 79.4± 26.60 | 79.4± 18.48 | 68.5± 23.17 | 61.61± 16.41 | <0.05[c] |
| **Urea ( umol/l)** | 7.72± 1.05 | 7.59± 0.99 | 7.09± 0.83 | 6.11± 0.87 | <0.001[c] |

Values were represented as the mean ± SD; the data were statistically analyzed using ANOVA followed by LSD test. (a: control vs. group 2, b: control vs. group 3, c: control vs. group 4).
*P*- value ≤ 0.05 was used as a criterion of significance.
*P*- value ≤ 0.01 was used as a criterion of highly significance.
NS: Not significant

**Table3: Lipid profile concentrations, Liver enzymes concentrations and kidney function test results among the groups after four weeks of treatment with *Rhazya stricta***

| **Variable**<br>**n** | **Group 1 Control**<br>**10** | **Group 2 (0.1gm/ml)**<br>**15** | **Group 3 (0.125gm/ml)**<br>**15** | **Group 4 (0.150gm/ml)**<br>**15** | ***P*-value** |
|---|---|---|---|---|---|
| **Triglycerides (mmol/l)** | 1.16± 0.49 | 0.89± 0.14 | 0.81± 0.17 | 0.86± 0.34 | <0.05[a,c]<br><0.01[b] |
| **HDL (mmol/l)** | 0.50± 0.07 | 0.49± 0.06 | 0.53± 0.08 | 0.52± 0.07 | NS |
| **LDL (mmol/l)** | 0.28± 0.06 | 0.23± 0.044 | 0.24± 0.038 | 0.24± 0.036 | <0.05[a,b,c] |
| **Cholesterol (mmol/l)** | 1.96± 0.23 | 1.7± 0.46 | 1.79± 0.19 | 1.78± 0.19 | NS |
| **AST (U/L)** | 74± 44.25 | 90.13± 24.03 | 95.08± 18.49 | 83.77± 15.02 | NS |
| **ALT (U/L)** | 62.3± 7.65 | 62.73± 8.6 | 63.57± 7.9 | 59.57± 4.69 | NS |
| **ALP (U/L)** | 189.4± 53.83 | 179.2± 34.85 | 194± 20.46 | 181.92± 29.02 | NS |
| **Creatinine (umol/l)** | 36± 6.48 | 34.2± 6.39 | 38.29± 4.64 | 30.85± 6.04 | <0.05[c] |
| **Uric acid (U/L)** | 63.6± 30.02 | 51.73± 15.63 | 92.5± 44.65 | 60.75± 32.64 | NS |
| **Urea ( umol/l)** | 7.47± 1.18 | 6.89± 1.12 | 7.19± 0.92 | 6.96± 1.09 | <0.05[c] |

NS: Not significant
Values were represented as the mean ± SD; the data were statistically analyzed using ANOVA followed by LSD test. (a: control vs. group 2, b: control vs. group 3, c: control vs. group 4).
*P*- value ≤ 0.05 was used as a criterion of significance.
*P*- value ≤ 0.01 was used as a criterion of highly significance.
NS: Not significant

**Table 4: Lipid profile concentrations, Liver enzymes concentrations and kidney function test results among the groups after eight weeks of treatment with *Rhazya stricta***

| **Variable**<br>**n** | **Group 1 Control**<br>**10** | **Group 2 (0.1gm/ml)**<br>**15** | **Group 3 (0.125gm/ml)**<br>**15** | **Group 4 (0.150gm/ml)**<br>**15** | ***P*-value** |
|---|---|---|---|---|---|
| **Triglycerides (mmol/l)** | 0.39± 0.07 | 0.46± 0.08 | 0.46± 0.06 | 0.40± 0.05 | <0.01[a,b] |
| **HDL (mmol/l)** | 0.49± 0.05 | 0.57± 0.05 | 0.52± 0.07 | 0.48± 0.06 | <0.01[a] |
| **LDL (mmol/l)** | 0.25± 0.02 | 0.24± 0.06 | 0.21± 0.02 | 0.19± 0.03 | <0.05[b]<br><0.001[c] |
| **Cholesterol (mmol/l)** | 1.94± 0.4 | 2.1± 0.25 | 1.72± 0.15 | 1.71± 0.23 | <0.05[b,c] |
| **AST (U/L)** | 127.4± 24.57 | 120.79± 23.16 | 147.5± 44.06 | 127.8± 19.54 | NS |
| **ALT (U/L)** | 55.8± 8.01 | 58.79± 9.7 | 62.71± 8.2 | 57.73± 7.14 | NS |

| | | | | | |
|---|---|---|---|---|---|
| **ALP (U/L)** | 140.3± 23.86 | 140.71± 24.56 | 150.21± 18.91 | 131.6± 20 | NS |
| **Creatinine (umol/l)** | 41.1± 5.69 | 38.79± 4.88 | 43.57± 4.79 | 39.07± 6.97 | NS |
| **Uric acid (U/L)** | 88. 7± 34.27 | 64.71± 16.79 | 76.86± 21.89 | 69.4± 18.26 | $<0.05^{(a,c)}$ |
| **Urea ( umol/l)** | 5.26± 0.66 | 5.61± 0.71 | 6.03± 0.59 | 5.69± 0.82 | $<0.05^{(b)}$ |

Values were represented as the mean ± SD; the data were statistically analyzed using ANOVA followed by LSD test. (a: control vs. group 2, b: control vs. group 3, c: control vs. group 4).
*P*- value ≤ 0.05 was used as a criterion of significance.
*P*- value ≤ 0.01 was used as a criterion of highly significance.
NS: Not significant

**Table 5: Lipid profile concentrations, Liver enzymes concentrations and kidney function test results among the groups after twelve weeks of treatment with *Rhazya stricta***

| **Variable**<br>**n** | **Group 1 Control**<br>**10** | **Group 2 (0.1gm/ml)**<br>**15** | **Group 3 (0.125gm/ml)**<br>**15** | **Group 4 (0.150gm/ml)**<br>**15** | ***P*-value** |
|---|---|---|---|---|---|
| **Triglycerides(mmol/l)** | 0.40± 0.07 | 0.45± 0.09 | 0.46± 0.07 | 0.44± 0.06 | NS |
| **HDL (mmol/l)** | 0.42± 0.04 | 0.48± 0.06 | 0.48± 0.06 | 0.50± 0.06 | $<0.05^{(a,b)}$<br>$<0.01^{(c)}$ |
| **LDL (mmol/l)** | 1.1± 0.22 | 1.03± 0.17 | 0.97± 0.14 | 1.12± 0.12 | NS |
| **Cholesterol (mmol/l)** | 1.73± 0.21 | 1.72± 0.18 | 1.68± 0.21 | 1.82± 0.18 | NS |
| **AST (U/L)** | 127.1± 31.22 | 127.3± 33.37 | 121.77± 24.19 | 123.5± 24.18 | NS |
| **ALT (U/L)** | 61.3± 6.3 | 63.42± 12.22 | 59.64± 13.31 | 64.28± 7.64 | NS |
| **ALP (U/L)** | 127.7± 20.83 | 121.17± 12.15 | 133.43± 17.1 | 128± 21.89 | NS |
| **Creatinine (umol/l)** | 49.4± 9.05 | 45.83± 3.1 | 42.14± 3.21 | 51.86± 5.20 | $<0.01^{(b)}$ |
| **Uric acid (U/L)** | 77.9± 17.69 | 72.58± 16.08 | 60.86± 16.03 | 60.79± 14.96 | $<0.05^{(b,c)}$ |
| **Urea ( umol/l)** | 6.47± 0.81 | 5.63± 0.73 | 6.21± 0.66 | 5.72± 0.83 | $<0.05^{(a,c)}$ |

Values were represented as the mean ± SD; the data were statistically analyzed using ANOVA followed by LSD test. (a: control vs. group 2, b: control vs. group 3, c: control vs. group 4).
*P*- value ≤ 0.05 was used as a criterion of significance.
*P*- value ≤ 0.01 was used as a criterion of highly significance.
NS: Not significant

**Table6: Lipid profile concentrations, Liver enzymes concentrations and kidney function test results among the groups after eighteen weeks of treatment with *Rhazya stricta***

| **Variable**<br>**n** | **Group 1 Control**<br>**10** | **Group 2 (0.1gm/ml)**<br>**15** | **Group 3 (0.125gm/ml)**<br>**15** | **Group 4 (0.150gm/ml)**<br>**15** | ***P*-value** |
|---|---|---|---|---|---|
| **Triglycerides (mmol/l)** | 0.52± 0.06 | 0.49± 0.19 | 0.52± 0.06 | 0.49± 0.08 | NS |
| **HDL (mmol/l)** | 0.45± 0.06 | 0.48± 0.07 | 0.48± 0.07 | 0.49± 0.05 | NS |
| **LDL (mmol/l)** | 1.13± 0.19 | 1.18± 0.23 | 1.11± 0.16 | 1.12± 0.13 | NS |
| **Cholesterol (mmol/l)** | 1.77± 0.18 | 1.75± 0.55 | 1.82± 0.21 | 1.86± 0.14 | NS |
| **AST (U/L)** | 142.3± 57.34 | 125.69± 32.15 | 118.43± 22.60 | 142.07± 54.16 | NS |
| **ALT (U/L)** | 69.9± 17.58 | 65± 14.66 | 63.64± 10.95 | 73.57± 21.76 | NS |
| **ALP (U/L)** | 123.3± 25.05 | 115.15± 20.85 | 115.29± 11.72 | 122.23± 20.94 | NS |
| **Creatinine (umol/l)** | 41.56± 7.97 | 45.83± 6.45 | 44.93± 5.06 | 39.86± 4.11 | NS |
| **Uric acid (U/L)** | 66.60± 23.54 | 54.92± 8.50 | 45.86± 6.2 | 54.36± 13.42 | $<0.01^{(b,c)}$ |
| **Urea ( umol/l)** | 6.17± 2.12 | 6.69± 1.95 | 7.44± 0.69 | 6.85± 0.74 | NS |

Values were represented as the mean ± SD; the data were statistically analyzed using ANOVA followed by LSD test. (a: control vs. group 2, b: control vs. group 3, c: control vs. group 4).
*P*- value ≤ 0.05 was used as a criterion of significance.
*P*- value ≤ 0.01 was used as a criterion of highly significance.
NS: Not significant.

## 4. Conclusions

*Rhazya stricta* is commonly used in folk medicine of the Arabian Peninsula for the treatment of many diseases. Therefore, we decided to elucidate the effect, if there any, of the *R. stricta* on blood lipid indices. Our findings indicated that the aqueous extract of the *R. stricta* leaves significantly decreased concentrations of TGs, LDL-c, cholesterol, uric acid and creatinin, but increased concentration of HDL-c. It triggered all these activities without affecting liver enzyme activities or kidney functions. In many studies, relatively large doses of the plant extract were used to determine the pharmacological and toxicological actions, Tanira *et al*.,(1996) and Adam,*et al*.,(2002) . Therefore, it was necessary to study the biochemical effects of this plant using low doses, in other words, doses comparable to those applied in folk medicine. The present study confirmed the low toxic potential of the plant extract. Our study showed that the daily oral administration of single doses of the extract of plant leaves (0.1, 0.125 and 0.150 gm/ml) for 18 weeks, did not produce significant changes in the activity of serum AST, ALT and ALP, neither did the extract produced significant rise in the concentrations of uric acid, urea nor creatinine. Therefore, kidney functions have not been affected by such treatment. Paradoxically, another study reported emergence of hepatonephrotoxicity for chicken grown on 100 g/kg *Rhazya stricta* diet after 4 and 7 weeks of treatment, Al-Homidan *et al.*,(2002).One possible explanation for emergence of this toxicity is the dosage effect, where applying as high as 100 g/kg *Rhazya stricta* diet elicited toxicity consequences. Our work demonstrates for the first time that the aqueous extracts of *Rhazya stricta* significantly reduced serum TG, LDL-c, cholesterol, uric acid and creatinine levels and increased HDL-c concentrations. These results indicated that the aqueous extracts of *Rhazya stricta* are effective on improving blood lipids status without bringing about a significant hepato- or nephro-toxicity. The mechanisms by which aqueous extracts of the plant leaves reduced serum lipids are unclear. Other point, our data seemed to contradict a study of report Adam *et al*.,(2002) who found that cholesterol levels were elevated in sheep fed on 0.25 g/kg/day *Rhazya stricta* leaves for 42 days. This is could be due to the relatively high dose of the plant extract. Another study reported that chronic treatments of rats or mice with *Rhazya stricta* lyophilized extract at oral doses of 0.5, 1, or 2 g/kg for 28 days produced no significant effect on any of the hematologic or biochemical indices measured Tanira et al., (1996). This suggests that the method of extraction is affecting the plant leaves. Most researches have used lyophilized extract containing about 18.3% of the original material and aqueous solutions were prepared from this lyophilized product Rasheed et al.,(1994) and Ali et al.,(1999). It has been reported previously that the leaves of the plant contain volatile bases and probably other substances, Ahmed et al.,(1983)and AL-Yahya et al.,(1990), which might alter ratio/properties of the other constituents of the extract prepared from the lyophilized leaves using a freeze drier. Confirming to this notion is that freeze-drying may diminish some medicinal plant actions, Abascal et al.,(2005).Therefore, researchers and practitioners should carefully consider how the use of freeze-dried material may affect pharmacological and clinical study results.

In conclusion, the marked hypotriglyceridemic and hypocholesterolemic effect of this plant may have therapeutic implications on patients with hypertriglyceridemia and hypercholesterolemia. However, more work is needed , with the world growing interest in complementary and alternative medicinal investigations, to explore possible mechanisms of action of *Rhazya stricta* leaves in human cardiovascular disorders, using the same method of extraction that has been used by humans in the folk medicine. Furthermore, the mutagenicity of the leaf extract demonstrated by

Baeshin's *et al(2005),and submitted).*, should be taken in consideration , as how to be avoided during therapeutic implications.

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