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# Effect of some flavonoids on atherogenicity in streptozotocin‑induced diabetic rats

*EL-Alfy, E. A.* [1,2] *, El-Taweel, HMA., Gomaa, E.A.& Abdel-Aziz, A. F.* [1 *]

[1.] *Faculty of science, Mansoura University, Mansoura, Egypt*

[2.] *Faculty of science, Mansoura University, Mansoura, Egypt*

* ***Correspondence to:*** *afaziz2012@hotmail.com, Tel: +201008764445*

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**Abstract:** This study looked into the atherogenicity of certain flavonoids in streptozotocin-induced diabetic rats, where a single and a mixed dose of Quercetin (QUE), Curcumin (CUR), and Silymarin (SIL) were administered.

**Methods:** The rats were given a single intraperitoneal (i.p.) injection of 45 mg/kg b.wt. of streptozotocin to develop diabetes. Conventional spectrophotometric methods were used to analyse serum lipid profiles, whereas standard equations were used to compute atherogenicity, atherogenic indices/coefficients, and serum lipid ratios.

**Results:** Serum total cholesterol (TC) concentrations in experimental rat groups ranged from 0.98 ± 0.04 mmol/L to 1.69 ± 0.11 mmol/L ($p < 0.05$). The concentration of serum high-density lipoprotein (HDL) in untreated diabetic rats was substantially lower ($p < 0.05$) than in treated diabetic rats. The atherogenic risk indices (ARI) of treated diabetes groups ranged from 3.88 0.79 to 6.83 0.24, while the ARI of the untreated diabetic group was 14.57 ± 0.83. The atherogenic index of plasma (AIP) versus LDL concentrations of the experimental rat groups yielded a reasonably well-fitting regression line ($R2 = 0.5723$). Flavonoid-treated diabetic groups had atherogenic protection ranging from 53.10 to 73.38%.

**Conclusion:** This study found that CUR, SIL, and a combination of the two with QUE provided diabetic rats with a disproportionately high level of protection against atherogenic consequences.

**keywords**: Diabetes mellitus, Serum lipid profile, Atherogenicity, Dyslipidemia, Flavonoids

## 1.Introduction

Diabetes is a chronic illness caused by the body's inability to either make insulin (T1DM) or use insulin effectively (T2DM). This is usually characterized by hyperglycemia, urination, increased thirst, tiredness, and the formation of wounds with delayed healing(27).

Diabetes is one of the fastest-growing diseases worldwide projected to affect 693 million people by 2045. Leading to macrovascular complications (cardiovascular disease) and microvascular complications (such as diabetic retinopathy and neuropathy, diabetic kidney disease) lead to increased blindness, mortality, and kidney failure (8). Under hyperglycemic conditions, vascular endothelial dysfunction plays a critical role in mediating both microvascular and macrovascular consequences (27)

Atherosclerosis is a common chronic inflammatory condition of the arterial wall that causes impairment and mortality. Atherosclerosis manifests as in its latter stages as a lesion of the artery wall's first layer and plaque accumulation. The rupture of atherosclerotic plaques causes thrombotic events to occur more quickly, which can be deadly. Decades of careful research have revealed that atherosclerosis has a complicated aetiology, with chronic inflammation and lipid accumulation in the artery wall as the key components (29)

Diabetes mellitus is linked to hyperlipidemia, which is a complication of the

disease (32). Lipid metabolism and hypercholesterolemia are linked to atherosclerosis. Local endothelial dysfunction, which may be produced by blood flow imbalance around the sites of arterial bifurcations, is thought to start the sequence of pathological events that leads to atherosclerosis development. The endothelium of blood vessels responds to mechanical stress by activating, which leads to the stimulation of immune system. Circulating monocytes adhere to and enter the damaged artery wall, transforming into macrophages that participate in lipid uptake via phagocytosis and give birth to foam cells, which are abundant in atherosclerotic plaques (29).

The lipid profile reflects the proportionate lipid component of the blood. Estimating blood lipid concentrations and ingredient ratios provides reliable diagnostic and prognostic information for atherogenic dyslipidemia, determining arteriosclerosis risk, and defining cardiovascular disease and death rate. Increased serum TC, TG, LDL, and VLDL concentrations over their reference ranges are frequently indicators of dyslipidemia and increased cardiovascular disease occurrence. Increased TG and LDL concentrations in the blood have been linked to an increased risk of cardiac disease. Clinical studies and empirical data, on the other hand, revealed an inverse association between serum HDL levels and the occurrence of atherogenic dyslipidemia. The atherogenic index of plasma (AIP), which is the logarithmic ratio of blood TG to blood HDL content, is a significant indicator of coronary heart disease (CHD). Atherosclerotic dyslipidemia is also determined by the ratio of serum LDL to HDL concentrations, as well as the serum [TC]/[HDL] ratio. These ratios can be used as diagnostic parameters to determine the level of cardiovascular disease (7).

Medicinal plant use has grown in popularity around the world, and it now plays a vital role in illness treatment, particularly in diabetes. Natural substances and active phytochemicals found in medicinal plants can help to enhance health and relieve illness while also giving some cancer protection and activating the immune response. The main benefits of medicinal plants appear to be their efficacy, minimal risk of side effects (when used correctly), and inexpensive cost (32). A huge number of medicinal plants contain flavonoids which are natural antidiabetic and antioxidant compounds. Moreover, containing anti-inflammatory effects (6).

Quercetin is a flavonoid compound and one of the dietary polyphenols with potent pharmacological properties, including anti-diabetic, anti-inflammatory, antioxidant, anticancer, cardioprotective, and anti-allergic properties. (4).

Among these medicinal plants, is the *Curcuma longa* plant which contains curcumin. Curcumin has pharmacological and biological effects that include anti-microbial, hypoglycemic, anti-inflammatory, cardioprotective, antioxidant, and immunomodulatory effects (28).

Additionally, curcumin has an effective role in lipoprotein metabolism and in the treatment of cardiovascular risk factors in coronary artery disease by decreasing serum triglyceride, LDL, and VLDL levels (14).

Silymarin is a mixture of active flavonoids and flavonolignans extracted from *Silybum marianum (L.) Gaertn.* Plant. The principal compounds in silymarin flavonoids and flavonolignans possess pharmacological activities as a scavenger and antioxidant properties acting against free radicals, additionally anti-diabetic (T2D) and anti-inflammatory effects (21).

We believe that single and combination medicinal flavonoid plants have various abilities to treat atherogenic dyslipidemia and lower atherogenicity risk markers in diabetic patients. As a result, this study looked into the atherogenicity of single and combined flavonoids of Quercetin (QUE), Curcumin (CUR), and Silymarin (SIL) in streptozotocin-induced diabetic rats.

## 2. Materials and methods

### 2.1 Chemicals

Streptozotocin (STZ), Quercetin (QUE), Curcumin (CUR), and Silymarin (SIL) were purchased from Sigma-Aldrich Company, USA. All the reagents and other chemicals were of high analytical grade.

**2.1.Experimental animals**

Eighty male albino rats were purchased from Theodore Bilharz Research Institute, Giza, Egypt, with an average body weight of 140-160 g. All rats were kept in well-ventilated steel cages and kept at a constant room temperature of 25 2 °C on a 12-hour light/12-hour dark cycle, with a commercial standard feed and free access to water. For acclimation to ambient circumstances, the rats were housed for two weeks.

The Ethical Committee on the Use of Animals in Research at Mansoura University in Mansoura, Egypt, gave their approval to this work. The rats were handled in compliance with the United States' established laboratory animal care practises. (26).

**2.1. Experimental diabetic induction**

All rats were starved for 12 hours before being given streptozotocin (STZ, Sigma, St. Louis, Missouri, USA). to induce diabetes. The rats were injected intraperitoneally with a freshly prepared solution of 45 mg STZ/kg b.wt, 0.2 ml of each was dissolved in 0.05 M sodium citrate buffer, pH 4.5 (15).(23).

Within 2-3 days after STZ injection, STZ-injected animals exhibited massive glycosuria and fresh blood samples were drawn from the tail vein for measuring blood glucose levels by Accu-Chek Performa (Roche Diabetes Care, Indianapolis, IN, USA)

. Only animals with an FBS level of 250 mg/dl at 72 hours after injection were declared diabetic (32).

**2.1.Experimental design**

A sum of 80 male albino rats were separated into ten groups, each consisting of eight rats:

Group1 Control rats received a standard diet.

Group2 STZ-induced Diabetic rats (induction of diabetes by a single i.p. injection of STZ, 45 mg/kg body weight).

Group3 Control rats treated with Quercetin (80 mg/kg b.wt/day) for long 40 days via oral gavage.

Group4 STZ-induced diabetic rats were treated with Quercetin (80 mg/kg b.wt/day) for long 40 days via oral gavage.

Group5 Control rats treated with Curcumin (80 mg/kg b.wt/day) for long 40 days via oral gavage.

Group6 STZ-induced diabetic rats were treated with Curcumin (80 mg/kg b.wt/day) for long 40 days via oral gavage.

Group7 Control rats treated with Silymarin (80 mg/kg b.wt/day) for long 40 days via oral gavage.

Group8 STZ-induced diabetic rats were treated with Silymarin (80 mg/kg b.wt/day) for long 40 days via oral gavage.

Group9 Control rats were treated with a mixture of Quercetin, Curcumin, and Silymarin (80 mg/kg b.wt/day) for each component for long 40 days via oral gavage.

Group10 STZ-induced diabetic rats were treated with a mixture of Quercetin, Curcumin, and Silymarin (80 mg/kg b.wt/day) for each component for long 40 days via oral gavage.

**2.1. Collection of blood**

Rats were starved overnight and then slaughtered after being sedated with diethyl ether at the end of the experiment (40 days). Blood samples were taken after a fast and allowed to clot. Standard procedures were used to determine the blood lipid profile measurements of the corresponding rat groups.

**2.1. Lipid profile**

Serum total cholesterol (22) and triglyceride (3) levels were determined spectrophotometrically using commercially available kits (SPINREACT, Spain), and serum HDL level was assessed using the method described by (13). LDL levels were calculated using (11).

$$[\mathrm{LDL}] = [\mathrm{TC}] - [\mathrm{HDL}] - \left[\frac{[\mathrm{TG}]}{5}\right] \qquad (1)$$

Burnstein & Sammaille, 1960 methods were used to compute serum VLDL concentrations, with the ratio of serum VLDL to TG concentrations set at 1:5 in fasted rats.

$$[\mathrm{VLDL}] = \left[\frac{[\mathrm{TG}]}{5}\right] \quad (2)$$

**2.1. Atherogenic risk index**

According to the Durendić-Brenesel et al., 2013 approach, the Atherogenic Risk Index (ARI) was calculated as follows:

$$\mathrm{ARI} = \frac{[\mathrm{TC}] - [\mathrm{HDL}]}{[\mathrm{HDL}]} \quad (3)$$

**2.1. Percentage protection**

The Percentage protection against atherogenicity of flavonoid treated STZ-induced diabetic rats groups (Groups 4, 6, 8, and 10) was calculated ***(Chikezie et al., 2018)***:

$$\% \text{ protection} = \frac{ARI_{STZ-Group} - ARI_{STZ-Treated\ Group}}{ARI_{STZ-Group}} x100 \quad (4)$$

where:

STZ-Group (Negative Control) = Diabetic patients who have not been treated (Group 2). STZ-Treated group = Flavonoid treated diabetic groups (Groups 4, 6, 8, and 10).

**2.1. Atherogenic risk predictor indices**

(2) presented the following Atherogenic Risk Predictor Indices:

$$AIP = Log\frac{[TG]}{[HDL]} \quad (5)$$

$$CRI-I = \frac{[TC]}{[HDL]} \quad (6)$$

$$CRI-II = \frac{[LDL]}{[HDL]} \quad (7)$$

Eq. (*5*) represents AIP (atherogenic index plasma)

Eq. (*6*) represents CRI-I (Castelli's risk index I)

Eq. ( 7) represents CRI-II (Castelli's risk index II)

**2.4.Statistical and data analyses**

The software GraphPad Prism 8.0.2 (263) was used to analyse the data. The results were presented as means ± standard deviations. Statistical significance was defined as a P-value of less than 0.05. One-way analysis of variance (ANOVA) was used for statistical multiple comparisons, followed by Tukey's test for PostHoc. Excel software (Microsoft, 365 version) was used to examine Pearson's regression analysis and correlation coefficient.

**3.Results**

Groups 1–10 had serum TG values ranging from 0.28 ± 0.01 mmol/L to 0.61 ± 0.06 mmol/L ($p < 0.05$). The lowest serum TG concentration was found in Group 8, while the highest serum TG concentration was found in Group 2 (p 0.05). In general, Group 1 had significantly lower serum TG concentrations (p 0.05) than Group 2. However, Group 2 had significantly higher serum TG concentrations ($p < 0.05$) than the other groups (3–10) (**Error! Not a valid bookmark self-reference.**) shows that serum LDL concentrations in Groups 1–10 ranged between 0.71 ± 0.02 mmol/L and 1.46 ± 0.09 mmol/L ($p < 0.05$). The highest serum LDL concentration was found in Group 2, whereas the lowest serum LDL concentration was found in Group 7. When compared to Group 7, serum LDL concentrations in Group 2 were 2.06 times higher ($p > 0.05$).

Groups 1,3–5, and 8–10 had significantly higher serum LDL values ($p < 0.05$) than Groups 6 and 7. Groups 3–10, on the other hand, had significantly lower serum LDL values ($p < 0.05$) than Group 2. **Error!** Not a valid bookmark self-reference. revealed that serum LDL concentrations in Groups 1, 3, 5, and 8 were not significantly different ($p > 0.05$). The serum VLDL concentrations of the matched rat groups were 5 times lower than **the serum** TG values (**Error! Not a valid bookmark self-reference.)** significantly lower serum TC values ($p < 0.05$) than Group 2. Similarly, serum TC values in Groups 6, 7, and 9 were significantly lower ($p < 0.05$) than those in Group 1 (**Error! Not a valid bookmark self-reference.**) shows that serum LDL concentrations in Groups 1–10 ranged between 0.71 ± 0.02 mmol/L and 1.46 ± 0.09 mmol/L ($p < 0.05$). The highest serum LDL concentration was found in Group 2, whereas the lowest serum LDL concentration was found in Group 7. When compared to Group 7, serum LDL concentrations in Group 2 were 2.06 times higher ($p > 0.05$).

**Table 1**).

Groups 1–10 had serum TC values ranging from 0.98 0.04 mmol/L to 1.69 ± 0.11 mmol/L ($p < 0.05$). Furthermore, Group 2 had the greatest serum TC concentration, while Group 7 had the least serum TC ($p < 0.05$). Group 7's serum TC concentration was 1.72-fold lower than Group 2's serum TC concentration ($p < 0.05$). There was no significant variation ($p > 0.05$) in serum TC values between groups 1, 3, 4, 5, 6, 7, 8, 9, and 10. Groups 3–10 had

Groups 1,3–5, and 8–10 had significantly higher serum LDL values ($p < 0.05$) than Groups 6 and 7. Groups 3–10, on the other hand, had significantly lower serum LDL values ($p < 0.05$) than Group 2. **Error! Not a valid bookmark self-reference.** revealed that

**Table 1**).

Serum Group 1's serum HDL concentration was 1.5 times greater than Group 2's ($p < 0.05$) (**Error! Not a valid bookmark self-reference.**) shows that serum LDL concentrations in Groups 1–10 ranged between 0.71 ± 0.02 mmol/L and 1.46 ± 0.09 mmol/L ($p < 0.05$). The highest serum LDL concentration was found in Group 2, whereas the lowest serum LDL concentration was found in Group 7. When compared to Group 7, serum

**Table 1**). Group 2 had significantly lower serum HDL concentrations ($p < 0.05$) than Groups 3–10. In comparison, serum HDL concentrations in Groups 3, 4, 7, and 10 were not significantly different ($p > 0.05$). Similarly, there was no significant difference in serum HDL concentrations between Groups 6 and 8 ($p > 0.05$). The serum HDL concentrations in Groups 5 and 9 were also low (**Error! Not a valid bookmark self-reference.**) shows that serum LDL concentrations in Groups 1–10 ranged between 0.71 ± 0.02 mmol/L and 1.46 ± 0.09 mmol/L ($p < 0.05$). The highest serum LDL concentration was found in Group 2,

**Table 1**).

The mean ± S.D. of eight (n=8) measurements. According to Tukey's test, the means in the column with the same letter are statistically different at $p < 0.05$. Values that sharing common superscript letters (a–f) in the same column differ significantly at $p < 0.05$

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serum LDL concentrations in Groups 1, 3, 5, and 8 were not significantly different ($p > 0.05$). The serum VLDL concentrations of the matched rat groups were 5 times lower than the serum TG values (**Error! Not a valid bookmark self-reference.)** LDL concentrations in Group 2 were 2.06 times higher ($p > 0.05$).

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Groups 1,3–5, and 8–10 had significantly higher serum LDL values ($p < 0.05$) than Groups 6 and 7. Groups 3–10, on the other hand, had significantly lower serum LDL values ($p < 0.05$) than Group 2. **Error! Not a valid bookmark self-reference.** revealed that serum LDL concentrations in Groups 1, 3, 5, and 8 were not significantly different ($p > 0.05$). The serum VLDL concentrations of the matched rat groups were 5 times lower than the

serum TG values (**Error! Not a valid bookmark self-reference.)**

**Table 1** Experimental rat groups' serum lipid profiles**.**

| Rat group | lipid profile of the serum (mmol/L) | | | | |
|---|---|---|---|---|---|
| | TG | TC | HDL | LDL | VLDL |
| Group 1 | 0.29 ± 0.03 [af] | 1.20 ± 0.07 [a] | 0.16 ± 0.01 [a] | 0.98 ± 0.06 [a] | 0.06 ± 0.01 [a] |
| Group 2 | 0.61 ± 0.06 [abcde] | 1.69 ± 0.11 [abcde] | 0.11 ± 0.01 [abcde] | 1.46 ± 0.09 [abcde] | 0.12 ± 0.01 [abcd] |
| Group 3 | 0.44 ± 0.06 [a] | 1.24 ± 0.07 [a] | 0.18 ± 0.01 [a] | 0.97 ± 0.06 [a] | 0.09 ± 0.01 [a] |
| Group 4 | 0.47 ± 0.01 [bf] | 1.25 ± 0.08 [b] | 0.16 ± 0.01 [b] | 1.00 ± 0.06 [b] | 0.09 ± 0.01 |
| Group 5 | 0.40 ± 0.05 [a] | 1.18 ± 0.13 [a] | 0.14 ± 0.02 [f] | 0.96 ± 0.11 [a] | 0.08 ± 0.01 [a] |
| Group 6 | 0.41 ± 0.10 [c] | 1.10 ± 0.28 [c] | 0.22 ± 0.02 [cf] | 0.79 ± 0.24 [c] | 0.08 ± 0.02 [b] |
| Group 7 | 0.40 ± 0.06 [a] | 0.98 ± 0.04 [a] | 0.18 ± 0.01 [a] | 0.71 ± 0.02 [a] | 0.08 ± 0.01 [a] |
| Group 8 | 0.28 ± 0.01 [d] | 1.21 ± 0.13 [d] | 0.21 ± 0.02 [d] | 0.95 ± 0.10 [d] | 0.05 ± 0.01 [c] |
| Group 9 | 0.28 ± 0.04 [a] | 1.03 ± 0.19 [a] | 0.15 ± 0.01 | 0.82 ± 0.18 [a] | 0.06 ± 0.01 [a] |
| Group 10 | 0.34 ± 0.02 [e] | 1.14 ± 0.14 [e] | 0.18 ± 0.01 [e] | 0.89 ± 0.14 [e] | 0.07 ± 0.01 [d] |

**Table 2** Experimental rat groups' atherogenicity and atherogenic risk predictor indices (ARPIs).

| Rat group | $\frac{[TC - HDL]}{[HDL]}$ | $Log\frac{[TC - HDL]}{[HDL]}$ | $Log\frac{[TAG]}{[HDL]}$ | $\frac{[LDL]}{[HDL]}$ | $\frac{[TC]}{[HDL]}$ |
|---|---|---|---|---|---|
| Group 1 | 6.42 ± 0.18 [agh] | 0.81 ± 0.02 | 0.25 ± 0.03 | 6.06 ± 0.16 | 7.42 ± 0.01 |
| Group 2 | 14.57 ±0.83 [abcde] | 1.16 ± 0.03 | 0.75 ± 0.01 | 13.44 ± 0.81 | 15.57 ± 0.01 |
| Group 3 | 5.95 ± 0.21 [a] | 0.77 ± 0.02 | 0.39 ± 0.04 | 5.46 ± 0.17 | 6.95 ± 0.01 |
| Group 4 | 6.83 ± 0.24 [b] | 0.83 ± 0.02 | 0.47 ± 0.01 | 6.24 ± 0.24 | 7.83 ± 0.01 |
| Group 5 | 7.67 ± 0.59 [af] | 0.89 ± 0.03 | 0.47 ± 0.02 | 7.08 ± 0.56 | 8.67 ± 0.01 |
| Group 6 | 3.88 ± 0.79 [cfg] | 0.59 ± 0.09 | 0.26 ± 0.06 | 3.51 ± 0.73 | 4.88 ± 0.01 |
| Group 7 | 4.46 ± 0.18 [ah] | 0.65 ± 0.02 | 0.35 ± 0.04 | 4.01 ± 0.21 | 5.46 ± 0.01 |
| Group 8 | 4.75 ± 0.11 [d] | 0.68 ± 0.01 | 0.12 ± 0.03 | 4.49 ± 0.10 | 5.75 ± 0.01 |
| Group 9 | 5.76 ± 1.14 [a] | 0.76 ± 0.09 | 0.27 ± 0.05 | 5.38 ± 1.10 | 6.76 ± 0.01 |
| Group 10 | 5.30 ± 0.72 [e] | 0.72 ± 0.06 | 0.28 ± 0.01 | 4.92 ± 0.70 | 6.30 ± 0.01 |

The mean ± S.D. of eight (n=8) measurements. According to Tukey's test, the means in the column with the same letter are statistically different at $p < 0.05$.

**Table 2** summarises the ARI and ARPIs. Table 2 shows that, when compared to the other experimental rat groups, Group 2 had the highest ARI, AIP, CRI-I, and CRI-II.

The ARIs of Groups 3–10 were significantly lower ($p < 0.05$) than Group 2. Specifically, the ARIs of Groups 3–10 ranged between 3.88 ± 0.79 and 7.67 ± 0.59, while the ARI of Group 2 was 14.57 ± 0.83. The ARIs of Groups 6 and 7 were, on the other hand, significantly lower ($p < 0.05$) than those of Group 1. Furthermore, the ARI of Group 5 differed significantly ($p < 0.05$) from that of Group 6. An examination of

**Table 2** revealed that the ARIs of Groups 4, 6, and 8 differed significantly ($p < 0.05$).

The logarithm of ARI of Group 2 yielded the greatest value, as shown in

**Table 2**. Furthermore, the logarithm of ARI for Groups 3–10 was between 0.59 ± 0.09, which related

to Group 6 and 0.89 ± 0.03, which corresponded to Group 5.

The linear regression study of AIP vs serum LDL in experimental rat groups (Groups 1–10) yielded a reasonably well-fitting regression line ($R^2 = 0.5723$). (**Fig. 1**). A considerable positive correlation ($r = 0.76$) was found between AIP and serum LDL values in Groups 1–10.

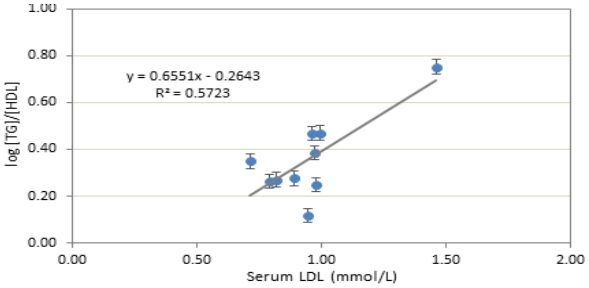


**Fig. 2** AIP vs. serum LDLvaluesinexperimental rat groups: a linear regression analysis

**Table 3** Flavonoid-treated ratgroups'percentage protection**.**

| Rat group | Flavonoid formulations administered (80 mg/kgb.wt) | % protection |
|---|---|---|
| Group 4 | QUE | 53.10 |
| Group 6 | CUR | 73.38 |
| Group 8 | SIL | 67.40 |
| Group 10 | QUE, CUR, and SIL | 63.62 |

Atherogenic protection of flavonoid-treated diabetic groups (Group 4, 6, 8, and 10) was within the range of 53.10 – 73.38

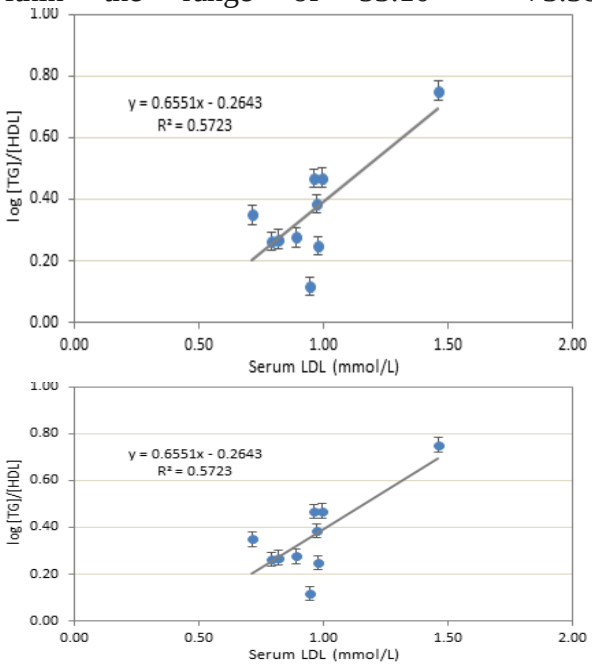


**Fig. 2** AIP vs. serum LDLvaluesinexperimental rat groups: a linear regression analysis

**Table 3**). Additionally, Group 6 exhibited the highest atherogenic protection.

## Discussion

This study found dyslipidemia in streptozotocin-induced diabetic rats, which was consistent with earlier findings. *(7) and (25)*. Animal models also demonstrated the ability of QUE, CUR, and SIL to reverse diabetic dyslipidemia. *(10); (16) and (31)*. Furthermore, epidemiological studies revealed that eating foods high in phytochemical antioxidants such as polyphenolic compounds reduced the incidence of diabetes mellitus aetiology, complications, and predisposing factors. ((1); (6) and (19).

Combinations of quercetin, curcumin, and silymarin improved faecal excretion of cholesterol, neutral sterol, and bile acids in hypercholesterolemic rats, according to previous research. *(17) and (24)* .

Individuals with high ARI, as well as atherogenicity risk predictor indices and biomarkers including AIP, CRI-I, and CRI-II, have a higher chance of developing coronary heart disease and atherosclerosis, according to clinical studies (7). Serum lipid proportions and atherogenic coefficients have been demonstrated to be stronger predictor of cardiovascular disease than isolated serum lipid measures in studies. *(15) and (20)* . Mathematically, a low ARI is obtained by lowering plasma concentrations of LDL, as well as non-esterified and esterified plasma lipids like TC and TG, and raising plasma concentrations of HDL. The strong positive correlation (r = 0.76) between AIP and serum LDL in Groups 1–10 indicated that higher serum LDL corresponded to higher AIP values and risk markers. Furthermore, the relatively tight fit regression line ($R^2$ = 0.7616) between AIP and serum LDL concentrations in Groups 1–10 indicated that serum LDL was a factor and predictor of AIP risk markers, and thus elevated serum LDL contributed to atherogenicity in diabetes.

## Conclusion

This study found that a single or combination dose of Quercetin (QUE), Curcumin (CUR), and Silymarin (SIL) provided fairly good protection against atherogenic outcomes in diabetes mellitus, which corresponded to their abilities to counter dyslipidemia. Finally, these data indicated that certain bioactive components from CUR compounds and a mixture of QUE, CUR, and SIL collaborated to enhance their ability to alleviate atherogenic dyslipidemia, as previously discussed. To extract and characterise these therapeutic biomolecules as well as understand their therapeutic action mechanisms, more research is needed to find the bioactive components that improved atherogenic dyslipidemia in diabetes mellitus.

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