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RESEARCH ARTICLE

Physiological Study about Rosuvastatin and Lovastatin as Compared with Quercetin in Rats (*Rattus norvegicus*)

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Abstract

The present study was accomplished to compare the role of the flavonoid quercetin with some antihyperlipidemic drugs rosuvastatin and lovastatin on lipid profile and other serum parameters of rats. In this study, five groups of eight male rats each were used. The groups were allocated as: control, cholesterol, rosuvastatin, lovastatin and quercetin groups. The animals of the control group were maintained on standard diet, while other groups were maintained on cholesterol diet 15mg/kg of diet and dosed orally and daily as follow: rosuvastatin 20 mg/kg body weight, lovastatin 15 mg, and quercetin 100 mg respectively. The results revealed that rosuvastatin and lovastatin could lower lipid profile but still significantly higher than control group while quercetin lowers them without significant difference with control. The liver enzymes were elevated by statins and they were normal and without significant difference in case of quercetin comparing with control group at ($P \leq 0.05$).

Key words: *Quercetin, Rosuvastatin, Lovastatin, Lipid, Rats.*

Introduction

Dyslipidemia and hyperlipidemia are two terms which refer usually to the raised levels of both blood cholesterol and lipids, dyslipidemia also as a term can be used to elucidate different lipoprotein metabolic disorders. In spite of considering the elevated LDL as a marker for dyslipidemia, the later can be also a marker for raised values of triacylglycerols (TAGS) and total cholesterol (TC) or vice versa the declined values of high density lipoprotein (HDL) in addition to concentrate the direction of treatment towards the cardiovascular individual risks and the raised values of LDL. [1].

Inhibitors of 3-hydroxy-3-methylglutarylcoenzyme A (HMG-CoA) reductase or as they collectively called statins, were the real revolution that invented the hypercholesterolemia treatment [2]. The exactly unique flavonoid quercetin belongs to vast family of natural compounds which consist of phenolic structures and are widely distributed in vegetables, fruits, flowers, and other plant parts [3].

These natural compounds are well established for their advantages for treatment of different diseases for ages and they are of immense varieties in plant kingdom [4]. The most fluent distributed in the plants of these flavonoids is the quercetin which includes three rings and carries five hydroxyls [5]. Quercetin presents in different fruits and vegetables like green and black tea, beans, tomato, apples and in particular in onion [6]. Researchers have mentioned that quercetin has an antioxidant activity four doubles more potent that of vitamin E [7].

Quercetin was found to have vast health benefits like genomic stabilizing effect, protection for cardiovascular system, boosting the defense and immune systems,

fighting cancer, alleviate allergy, and others [8, 9].

Materials and Methods

Animals of the Experiment

The experiment was accomplished at the animal house of the College of Medicine, Al Muthanna University. Forty male laboratory rats (*Rattus norvegicus*) of 150 – 175 g weights were used. The experiment conditions were fit for all animals. The animals were allocated and set on cages randomly for about ten days prior to the experiment to get well acclimatized. Then the experiment progressed for two months.

Protocol of Experiment

Control Group

Eight male rats were maintained on a standard diet for two months. Animals diet was an AIN1993 standard rat diet [10].

Cholesterol Group (CHO group)

Eight male rats were maintained on standard diet enriched with cholesterol as 15g/kg of diet (1.5%). Cholesterol was purchased from local medical equipment supplier and it was under the trademark of BDH England Company. The amount of cholesterol was added to the diet according to [11].

Rosuvastatin Group (Rosuvast Group)

Eight male rats were maintained on standard diet enriched with cholesterol as 15g/kg of diet (1.5%) and they were dosed orally once a day with rosuvastatin 20 mg/kg body weight by the use of oral gavage. The dose of rosuvastatin was selected according to previous studies like [12].

Lovastatin Group (Lovastat Group)

Eight male rats were maintained on standard diet enriched with cholesterol as 15g/kg of diet (1.5%) and they were dosed orally once a day with lovastatin 4 mg/ kg body weight by the use of oral gavage. The dose of lovastatin was selected according to previous studies like [13]. Rosuvastatin and lovastatin were purchased from local medical equipment supplier under trademark of Cayman Chemical Company, Canada.

Quercetin Group (Querc Group)

Eight male rats were maintained on standard diet enriched with cholesterol as 15g/kg of diet (1.5%) and they were dosed orally with quercetin (20mg) once a day by the use of oral gavage. The dose of quercetin was selected according to LD50 which is 161mg/kg body weight according to [14]. Quercetin was purchased from local medical equipment supplier and it was under a trademark of Himedia Labs, India.

Preparation of Specimens

At the end of the experiment period, rats were anaesthetized by the use of chloroform and blood samples were withdrawn from myocardium directly. Blood samples were put in gel tubes to separate and obtain sera.

Parameters of the Study

All the tests of the study were done by the use of DONGI (DONGI 120 ITALIA) device.

Statistical Analysis

ANOVA one way test was used to find out the least significant difference (LSD) among groups depending upon IBM SPSS program, version 20. The numbers in the tables refers to the means ± standard deviations and the letters on the numbers refer to the significant differences at ($P \leq 0.05$).

Results

It is obvious from Table (1) that total serum cholesterol (CHO), low density lipoprotein (LDL), and very low density lipoprotein (VLDL) were significantly elevated in the animals of cholesterol group comparing with other groups. When the antihyperlipidemic agents rosuvastatin and lovastatin (rosuvastatin and lovastatin groups) were offered, they caused a declination in CHO, LDL, and VLDL but still significantly higher than those of the control group while quercetin caused a significant decrease in these parameters comparing with other groups and there was no significant difference with the control group.

The high density lipoprotein (HDL) was significantly declined in cholesterol, lovastatin, and rosuvastatin groups comparing with control group and there was no significant difference between quercetin and control groups. For the triacylglycerols (TAGs), the cholesterol, lovastatin, and rosuvastatin groups were significantly higher than that of control while TAGs of quercetin

was significantly lower than all other groups. Considering the liver function enzymes, Table (2) reveals that the aminotransferases (AST) and (ALT) besides the alkaline phosphatase (ALP) of the cholesterol, rosuvastatin, and lovastatin groups were significantly elevated comparing with control group while quercetin shows no significant difference comparing with control group. For the bilirubin, there was significant elevation in cholesterol and rosuvastatin groups only comparing with other groups. The serum iron (Fe^{++}) was detected and showed in Table (3) which reveals that Fe^{++} was significantly declined in all groups except quercetin group comparing with the control group. Table (3) also reveals that blood sugar was declined significantly in rosuvastatin and lovastatin groups comparing with other groups. Total serum protein was not affected in all groups as it is obvious in the same table.

Table 1: Shows a comparison among antihyperlipidemic agents and quercetin on lipid profile.

GROUPS / Parameters	CHO (mg/dl)	TAGs (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Control	127 **c** ± 1.5	70.4 **d** ± 1.1	21.2 **a** ± 1.4	91.4 **c** ± 2	13.4 **d** ± 1.1
CHO	162.8 **a** ± 4.7	135.2 **a** ± 3.9	11.2 **b** ± 1.6	123.2 **a** ± 2.3	27.2 **a** ± 1.9
Lovastat	136 **b** ± 4.3	125.6 **b** ± 2.7	13.2 **b** ± 1.4	102.2 **b** ± 3.4	23.2 **b** ± 1.9
Rosuvastat	137.6 **b** ± 3.6	103.4 **c** ± 2.8	13 **b** ± 1.5	103 **b** ± 3.5	20.2 **c** ± 1.6
Querc	126 **c** ± 1.7	65.2 **e** ± 5.8	21 **a** ± 3.5	92 **c** ± 4.4	13 **d** ± 2.2
LSD	8.4	5.2	7	10.2	3

Table 2: shows a comparison among antihyperlipidemic agents and quercetin on liver enzymes

GROUPS /Parameters	AST (U/L)	ALT (U/L)	ALP (U/L)	Bilirubin (mg/dl)
Control	22 **d** ± 4.3	35.6 **c** ± 5.8	238 **b** ± 11	0.5 **B,a** ± 0.1
CHO	70.4 **b** ± 8.2	59.8 **b** ± 7.7	300.2 **a** ± 15.8	1.4 **a** ± 0.5
Rosuvastat	87.8 **a** ± 12.8	53.8 **b** ± 6.3	279.4 **a** ± 15.8	1 **a** ± 0.6
Lovastat	55.4 **c** ± 11.2	91.8 **a** ± 14	280.4 **a** ± 16.1	0.6 **B,a** ± 0.7
Querc	31.4 **d** ± 5.1	44.6 **C,b** ± 9.9	249.2 **b** ± 15.9	0.4 **B,a** ± 0.2
LSD	15	15.2	30.2	0.8

Table 3: shows a comparison among antihyperlipidemic agents and quercetin on some serum components. Different letters refer to significant differences at (P≤0.05)

GROUPS / Parameters	Urea (mg/dl)	Creatine (g/dl)	GLU mg /dl	TP g /dL	Fe^{++} mg /dL
Control	76.4 **b** ± 11.6	1.8 **b** ± 0.4	203 **B,a** ± 4.6	4.8 ± 0.8	93.8 a ± 5.2
CHO	114.8 **a** ± 10.4	2.6 **a** ± 0.5	218.2 **a** ± 7.6	4.7 ± 1.3	61 b ± 7.2
Rosuvastat	59.8 **c** ± 8.4	1.6 **b** ± 0.4	150 **c** ± 15.8	4.8 ± 1.3	60.2 b ± 15.9
Lovastat	80.4 **b** ±	1.4 **b** ±	160.6 **c** ±	6.4 ±	47 C,b ±

	16.1	0.2	14.3	1.5	10.8
Querc	74.4 **b** ± 12.2	1.6 **b** ± 0.3	208.2 **a** ± 5.4	5 ± 1.3	89.4 a ± 7.7
LSD	16.6	0.8	15.2	-----	14

Discussion

The results in this study have revealed that the use of statins, rosuvastatin and lovastatin could decrease the elevated values of CHO, LDL, TAGs and VLDL which were caused by the cholesterol diet but they were significantly higher than that of control group while quercetin decreased them to be like the values of control group without significant difference. The same was true for the HDL which was increased by statins but still significantly lowers than that of control and quercetin increased it to be without significant difference comparing to the control group.

The results also revealed that the use of statins caused significant increase in liver function enzymes AST, ALT, ALP and bilirubin beside a declination in serum Fe^{++} and glucose while quercetin caused all these parameters to be like those of control group without significant differences. These deleterious effects of statins come in line with many previous studies like [15, 17] while the role of quercetin in correcting lipid profile and liver enzymes come in line with many previous studies like [18, 20]. The high antioxidant potency of quercetin relays on the inhibition of reactive oxygen species (ROS) [21]. Thus, Quercetin provides protection to the cells against free radicals [22]. The mechanisms by which quercetin can play its role are different such as the high antioxidant potency of which like a scavenger towards the ROS with ability to do that more than that of ascorbic acid [23] and by four doubles more than that potency of vitamin E [7].Quercetin also capable of preventing LDL from being oxidized and preventing platelets from being aggregated and hence to prevent myocardial infarction throughout protection against [24]. Besides, quercetin can inhibit fat peroxidation, the enzyme xanthine oxidase and chelating of ions [25].

Cellular membranes physical properties can be changed due to hypercholesterolemia and then the increased pool of cholesterol [26] and thus the leakage of ROS through the electron system of mitochondria and the enzyme NADPH oxidase activation could be predisposed to [27]. ROS as well-known are responsible for peroxidation of lipids which might lead to imbalance status between oxidant and peroxidant mechanisms due to the resulted oxidative [28]. Hence, the above mentioned features of quercetin make it qualified to ameliorate hepatic enzymes and to lower blood lipids.

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