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Hypolipidemic Effects of Diaceto-Dipropyl-Disulphide on Alloxan Diabetic Rats

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Abstract

Dyslipidemia is one of the major derrangement observed in type 2 diabetes mellitus which further leads to various life threatening complications. Certain herbal disulphides/thiols are known to cater a solution towards regulation of this diabetes mellitus induced dyslipidemia. It is known that Diallyl Disulphide (DADS), a component of garlic extract possess hypolipidemic activities and may have therapeutic applications, but the metabolite of DADS, acrolein is toxic and poses certain disadvantages. Certain modified /altered disulphides, shown to possess significant hypolipidemic action with lesser toxic effects. In the present study, we tried to establish the hypolipidemic activities of Diaceto-Dipropyl-Disulphide (DADPDS), a synthetic modified disulphide in alloxan diabetic rats. The results show a significant decrease in plasma cholesterol (60

Index terms— Diaceto Dipropyl Disulphide, hypolipidemic, alloxan diabetes.

1 Introduction

iabetes mellitus is a systemic metabolic disease characterized by hyperglycemia, hyperlipidemia, hyperaminoacidemia and hypoinsulinemia that results from decrease in both insulin secretion and insulin action (1). Dyslipidemia, a complication associated with diabetes mellitus leads to profound alteration in the concentration and composition of lipid profile in the body which lead to the increase in the lipid concentration in the liver cells (2) **??**3)(4). It is evident that during diabetes the level of total lipids, triacylglycerol and total cholesterol increases both in plasma and tissue significantly (2). There are many herbal products which are proved to have the beneficial effect in significantly lowering the lipid levels during diabetes. Garlic's sulphur compounds specifically, DADS (Diallyl Disulphide) is known to inhibit the lipogenic enzymes and reduces cholesterol and triacylglycerol synthesis (5)(6)(7)(8). Apart from these known beneficial effects of garlic and its products, there are reports that misuse or overuse of these may produce (9). Acrolein, the possible metabolite of DADS is thought to be responsible for its toxic effects (10,11). It was thought that unsaturation of DADS may be responsible for its toxic effects by giving rise to toxic product, acrolein and the hypolipidemic activity lies in its disulphide nature. Few attempts were made in the past to prepare and use certain synthetic disulphides which mimic the beneficial effects of DADS but devoid of any toxic effects (12). In the present study an attempt was made to assess the hypolipidemic effect of Diaceto-dipropyl-disulphide (DADPDS), a synthetic, modified disulphide in alloxan diabetic rats.

2 II.

3 Materials and Methods

All chemicals employed in the present study were of Analar grade (A.R). Alloxan was procured from Loba chemie and thiopropanol (3-mercapto-1-propanol) from Sigma-Aldrich Company USA. This thiopropanol was used for the preparation of Diaceto-dipropyldisulphide (DADPDS).

4 III.

5 Synthesis of Dadpds

5 grams of thiopropanol was treated with 1N iodine in potassium iodide solution drop by drop till a light yellow colour persists and the contents were dissolved in 100 ml diethyl ether. To this 10 ml ice cold acetyl chloride was added and mixed. The above mixture was kept at 10-15? C for 3 hours. The separated ether layer was washed twice with 25 ml portions of ice cold saturated sodium chloride solution. Later washed 4 times with 0.1N sodium hydroxide solution in saturated sodium chloride then washed once with 10 ml 0.1N sodium thiosulphate in saturated sodium chloride and finally washed once with 10 ml glass distilled water. Later the ether layer was clarified with anhydrous sodium sulphate and dried at 50-55?C for 30 minutes. The residue was Diaceto-Dipropyl-Disulphide. This was employed to feed rats in the present study.

6 IV.

7 Animals

Adult male albino rats weighing 150-200g randomly selected from Central animal house of the Basaveshwara Medical College, Chitradurga were employed for the present study. A commercial standard pellet diet (Amruth Rat Feed supplied by Pranav Agro D industries, Pune, India) and water was made available to animals ad libitum. Animals were maintained in a controlled environment (25±5 C?) with light-dark cycles in an experimental room simulating natural conditions. All the animals are cared according to the rules and regulations of the CPCS (Committee for the purpose of Control and Experiments on Animals), New Delhi and IAEC (Institutional Animal Ethical Committee) of Basaveshwara Medical College, Chitradurga.

V.

8 Induction of Diabetes Mellitus

The animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of freshly prepared alloxan monohydrate (150 mg/kg body weight) (13,14) in sterile normal saline . The diabetes was confirmed by examining urine sample for sugar by using standard urine glucose strips (Qualigens). The rats whose urine showed a positive test for glucose for 3 consecutive days were labelled as diabetic. The treatment with DADPDS was started on 5 th day after alloxan injection and was considered as first day of treatment.

9 VI.

10 Grouping

The rats were divided into 3 groups comprising 6 rats in each group as follows.

a) Group 1 erved as normal rats maintained on normal lab diet and water ad libitum and were received 30ml of normal saline per kg body weight daily for 30 days. b) Group 2 as diabetic control rats maintained on normal lab diet and water ad libitum and were received 30ml/kg body weight normal saline daily for 30 days.

11 c) Group 3

Served as DADPDS treated diabetic rats. The group consists of alloxan diabetic rats, maintained on normal lab diet and water ad libitum, and was received 100mg/kg body weight of DADPDS as 30ml suspension daily for 30days.

After the stipulated period, the rats of group 1, 2 and 3 were sacrificed by anaesthetizing. Blood samples were collected using heparin as an anticoagulant. Liver tissue was procured, blotted smoothly to remove blood stains and kept individually in clean dry glass beaker with aluminium foil cover at 0-4? C for further usage. Blood samples were centrifuged at 3000 rpm for 5 mins, the separated plasma was employed for estimation of lipid parameters -total cholesterol (15) and triacylglycerol (16). A part of the liver tissue was homogenized with 9 parts of chloroform-methanol mixture (1:1, v/v) for 5 mins using Potter Elvejham tissue homogenizer and the mixture was centrifuged at 3000 rpm for 5 minutes. The supernatant was employed for the estimation of lipid parameters -total cholesterol (15) and triacylglycerol (16).

Another part of liver was homogenised with 9 parts of 5% cold TCA for 5 mins, and extract was employed for estimation of thiobarbituric acid reactive substances (TBARS) (17). A third part of liver tissue was homogenized with 9 parts of cold phosphate buffer (pH -7.4) for 5 mins and centrifuged at 3000 rpm for 5 minutes and the supernatant was used for the estimation of total thiol groups (18).

VII.

12 Statistical Evaluation

Results obtained in the present study are expressed as their Mean ± SD. The data entry was carried out using Microsoft Office Excel and statistically analysed and probability (p value) was calculated by students't' test.

13 VIII.

14 Results

It is seen from the table and from the graphs given that there is a significant raise in plasma cholesterol ($p<0.001$), plasma triacylglycerol ($p<0.001$), liver tissue cholesterol($p<0.001$), liver tissue triacylglycerol ($p<0.001$), and liver TBARS levels($p<0.001$) in group 2 as compared to group 1 whereas levels of liver tissue total thiol group were significantly lowered($p<0.05$) in group 2 as compared to group 1. Further it is evident from the table and graphs that there is a significant decrease in plasma cholesterol ($p<0.001$), plasma triacylglycerol ($p<0.001$) , liver tissue cholesterol ($p<0.001$), liver tissue triacylglycerol ($p<0.001$) and in liver tissue TBARS levels ($p<0.001$) in group 3 as compared to group 2 , whereas , a moderate raise in liver tissue total thiol groups observed in group -3 rats compared to group-2 rats (refer table -1, graphs 1-6).

15 IX.

16 Discussion

Dyslipidemia which is a common abnormality associated with diabetes mellitus may be resulting from insulin deficiency (19) , a similar picture may be seen in alloxan diabetic rats as it is known that alloxan induce profound ?-cell damage of islets of Langerhans leading to insulin deficiency (20,21). Earlier it is shown by C .S. Yadav (2)that in alloxan diabetic rat , the lipid levels both in liver and plasma rise by about 48 -55% . The results depicted in table-1 agrees with this and there is an increase of 58% and 18% respectively in plasma total cholesterol and triacylglycerols and also an increase of Many herbal extracts have been employed as lipid lowering substances since long time. Garlic (Allium sativum) and its extracts are the best known for their hypolipidemic actions (5). The hypolipidemic effects of garlic has been attributed to its principle organosulphur compound, Diallyl disulphide (DADS) which is known to inhibit HMG CoA reductase and possibly reduce plasma/tissue cholesterol levels (22)(23). But the over use of garlic may induce many toxic effects (10) due to acrolein a possible metabolite of DADS.

In order to overcome this harmful effect of DADS certain synthetic disulphides with lesser to moderate hypolipidemic benefits been employed by earlier workers (24). DADPDS, a low molecular weight acetylated disulphide been employed for its hypolipidemic actions in alloxan diabetic rats in the present study. A 100 mg/kg body weight dosage of this disulphide shows a significant hypolipidemic effect ($p<0.001$) and hypocholesterolemic ($p<0.001$) effect (refer table -1 and graphs 1-6). DADPDS is a disulphide, similar to any other disulphide, undergoes reduction to its component thiols by utilizing NADPH (25) as shown below:

17 R-S-S-R + 2NADPH 2R-SH + 2NADP

Hence decreases cellular NADPH levels thereby causing a decrease in lipid and cholesterol synthesis as it is known that HMG CoA reductase, the key enzyme of cholesterol biosynthesis as well as glycerol -?dehydrogenase requires NADPH , thus a reduction in the cellular NADPH could decrease cholesterol as well as triacylglycerol synthesis. Further it is known that DADS is an inhibitor of HMG CoA reductase and decreases the activity of this enzyme hence induces hypocholesterolemia (26).

DADPDS, a synthetic disulphide employed in the present study which is similar to DADS, a small molecular weight disulphide may induces hypocholesterolemia in alloxan diabetic rats probably by inhibiting HMG CoA reductase (refer table **??**.Thus causing a decrease in plasma as well as liver tissue cholesterol(refer table-1, graph 1 & 3).

It is also known that many lipogenic enzymes are thiol enzymes (25)and the results of present study given in table 1 shows that in group 3 the total liver tissue thiol groups has significantly raised ($p<0.05$) as compared to group 2.

Suggesting that DADPDS improve the cellular thiol group status probably by reducing the free radical levels by acting as a freeradical scavenging agent (refer table **??** , graph 5 & 6).

Thus it may be concluded that DADPDS at the dosage employed in the present study has a definite hypolipidemic and hypocholesterolemic action in alloxan diabetes rats. [1] [2] [3] [4]

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Figure 1: 1 .

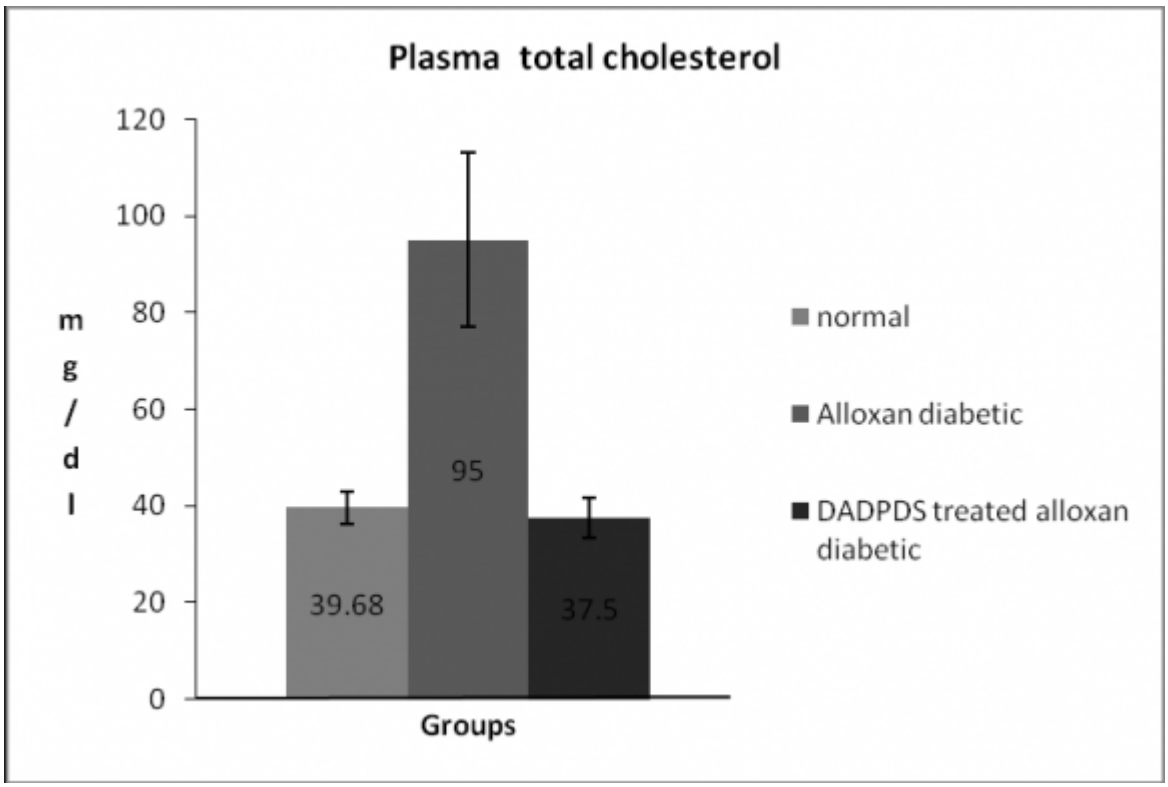

Figure 2:

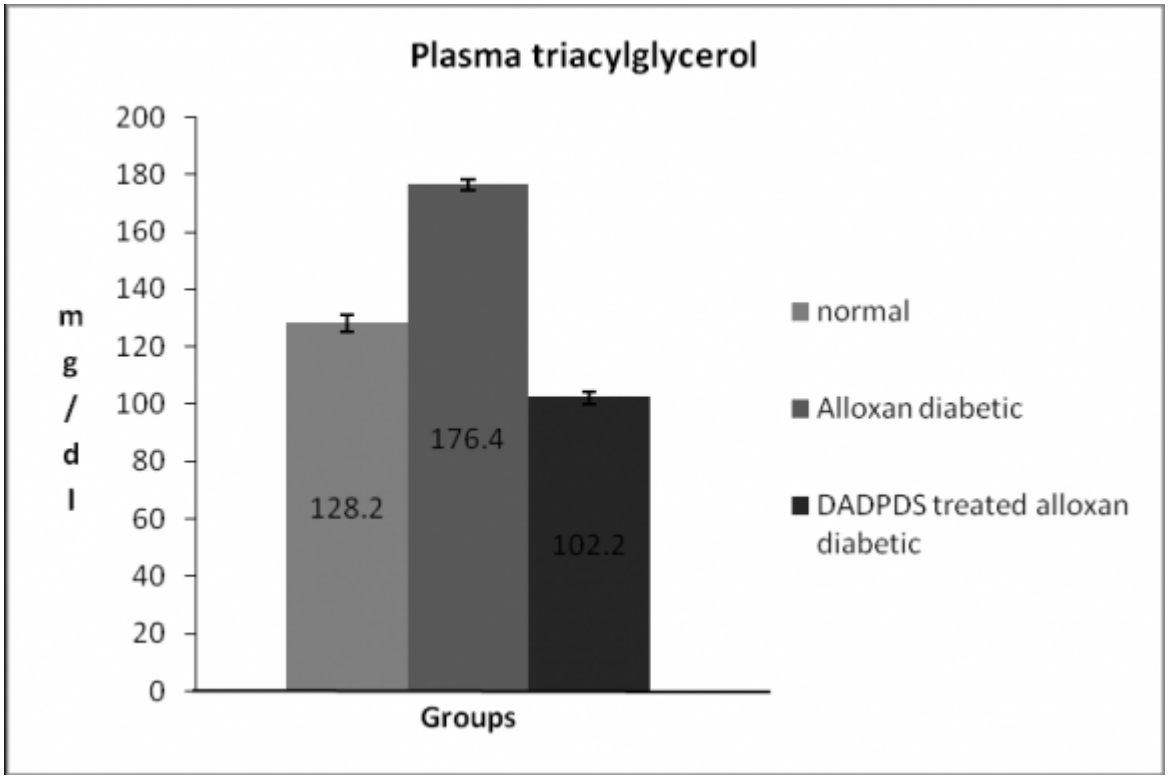

Figure 3:

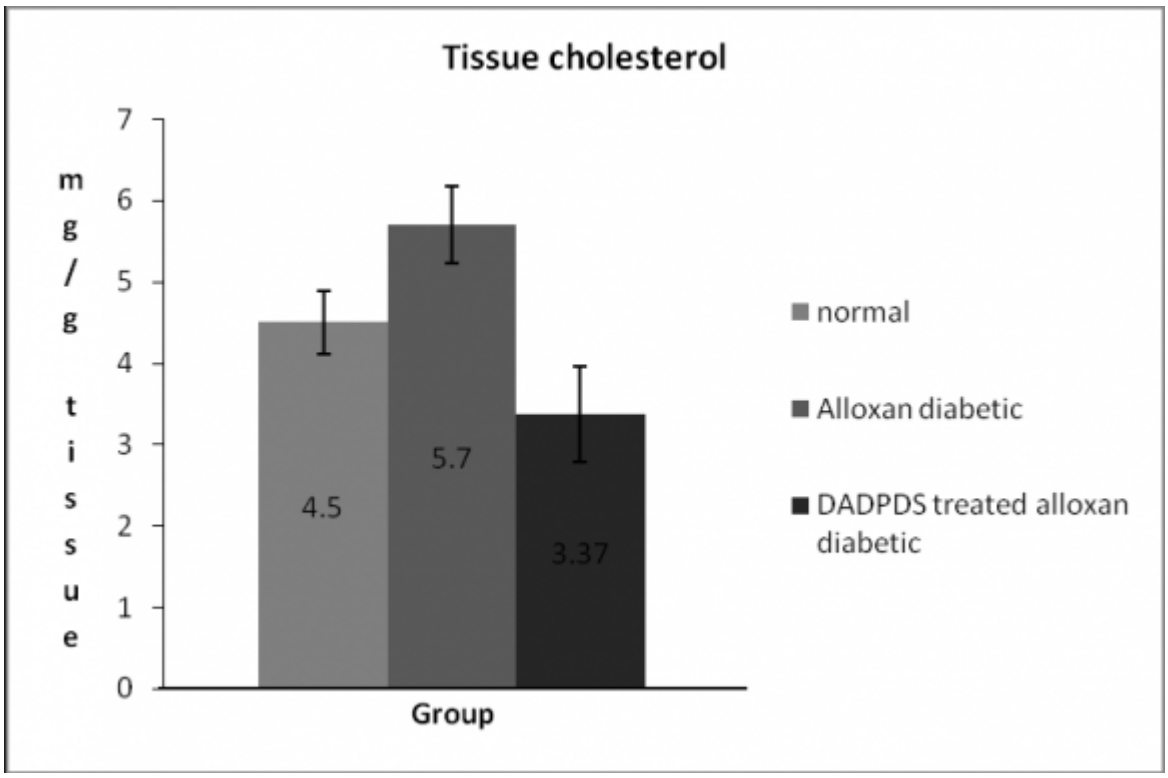

Figure 4:

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Groups	TOTAL CHOLESTEROL		TRIACYLGLYCEROL		Liver TBARS µmol/MDA/g	Liver total -SH GROUP mg/g T
	Plasma mg/dl	Tissue mg/g T	Plasma mg/dl	Tissue mg/g T		
NORMAL RATS GROUP 1 (n=6)	39.68 ± 3.40	4.50 ± 0.39	128.2 ± 2.83	16.64 ± 2.15	4.26 ± 1.26	0.94 ± 0.11
ALLOXAN DIABETIC RATS GROUP 2 (n=6)	95.0*** ± 18.10	5.7*** ± 0.48	176.4*** ± 2.0	26.8*** ± 1.6	13.84*** ± 1.40	0.81* ± 0.06
DADPDS TREATED ALLOXAN DIABETIC RATS GROUP 3 (n=6)						

Figure 5: Table 1 :

.1 Global Journal of Medical Research Volume XII Issue V Version I

[Biochem. Int] , *Biochem. Int* 15 p. .

[Henry et al. ()] , Richard J Henry , Donald C Connan , W James , Winkalman . *Clinical Chemistry -Principles and Practice* 1974. 1974. Harper Row Publishers. p. . (2 nd Edn)

[Gilbert and Stewart ()] , H F Gilbert , M L Stewart . *J. Biol Chem* 1981. 256 p. .

[Fenwick and Hanley ()] , G Fenwick , A Hanley . *CRC Critical Reviews in Food Science and Nutrition* 1985. 23 p. .

[Kashinath and Joseph (2009)] 'A Study On Garlic Toxicity'. R T Kashinath , P K Joseph . *Journal of Advance Researches in Biological Sciences* Dec.2009. 1 (2) p. .

[Imada ()] *Abst. I world Congress on health significance of garlic & garlic constituents*, Osama Imada . 1990. Washington.

[Sharma et al. ()] 'Antihyperglycemic, Antihyperlipidemic and Antioxidative potential of prosopis cineraria Bark'. Nidhi Sharma , Veena Garg , Arpita Paul . *Ind Jclin .Biochem* 2010. 25 (2) p. .

[Yu-Yanyeh and Liu ()] 'Cholesterol Lowering Effect of Garlic Extracts and Organosulfur copounds: Human and Animal studies'. Lijuan Yu-Yanyeh , Liu . *Journal of nutrition* 2001. p. .

[Arky and Kozak ()] 'Clinical correlates of metabolic derrangements of diabetes mellitus'. R A ; G P Arky , Kozak . *Complications of diabetes mellitus*, (Philadelphia) 1982. W B Saunders. p. .

[Henry (ed.) ()] *Clinical diagnosis and management by laboratory methods*, J Henry . saunders WB (ed.) 1984. 17 p. 1433.

[Varley et al. ()] 'Determination of Blood Cholesterol'. H Varley , . A Gowenloch , M Bell . *Practical Clinical Biochemistry* 1991. 1 p. . (5 th edn)

[Gebhardlt and Beck ()] 'Differential inhibitory effects of garlic -derived organosulfur compounds on cholesterol biosynthesis in primary rat hepatocytes cultures'. R & Gebhardlt , H Beck . *Lipids* 1996. 31 p. .

[Umesh et al. (2004)] 'Effects Of Sodium-orthovanadate and Trigonella foenum-graecum seeds on hepatic and renal lipogenic enzymes and lipid profile during alloxan diabetes??? in'. C S Umesh , K Yadav , Moorthy , Z Najma , Baquer . *J. Bio sci* March 2004. 29.

[Kashinath ()] *Hypolipidemic effects of disulphides in rats fed high lipid diet and or ethanol*, R Kashinath . 1993. Bangalore university. (Ph.D thesis)

[Qureshi ()] 'Influence of minor plant constituents on porcine hepatic lipid metabolism: impact on serum lipid'. A Qureshi . *Atherosclerosis* 1987. 64 p. .

[Qureshi ()] 'Inhibition of cholesterol and fatty acid biosynthesis in liver enzymes and chicken hepatocytes by polar fractions of garlic'. A Qureshi . *Lipids* 1983a. 18 p. .

[Colowick ()] 'Joslin's Diabetes Mellitus'. Kaplan Colowick . *Enzymes in Lipid Metabolism in*, 19. 2005. 1957 p. . (14 th Edn B. I Publications)

[Nadiger et al. ()] 'Malonyldialdehyde levels in different organs of rat subjected to acute alcohol toxicity'. H A Nadiger , S R Marcus , M Chandrakala , D D Kulkarni . *Ind J clin.Biochem* 1986. 1 p. .

[Ashok and Chougale ()] 'Optimization of Alloxan Dose is Essential to Induce Stable Diabetes for prolonged period'. D Ashok , Chougale . *Asian Journal of Biochem* 2007. 296 p. .

[Sochor et al. ()] *Regulation of enzymes of glucose metabolism and lipogenesis in diabetic rat liver by thyroid hormones*, S Sochor , N Z Baquer , M R Ball , P Mclean . 1987.

[Reynolds ()] E F Reynolds . *Martindale The Extra Pharmacopeia. Acrolein. 12322a, 13 th Edition*, (London) 1993. Pp 1331. The Pharmaceutical Press.

[Ziegler ()] 'Role of reversible oxidationreduction of enzyme thiols-disulfides in metabolic regulation'. . D Ziegler . *Ann. Rev .Biochem* 1985. 54 p. 314.

[Qureshi ()] 'Suppression of avian hepatic lipid metabolism by solvent extracts of garlic: impact on serum lipids'. A A Qureshi . *J. Nutr* 1983b. 113 p. .

[Szkudelski ()] 'The Mechanism of Alloxan and Streptozotocin Action in B cells of the Rat pancreas'. Szkudelski . *physiol .Res* 2001. 50 p. .

[Altan ()] 'The pharmacology of diabetic complications'. V M Altan . *Current Medicinal Chemistry* 2003. 10 p. .

[Yeh and Yeh ()] Yu- , Yan Yeh , Shaw-Mei Yeh . *Garlic Reduces Plasma Lipids by Inhibiting Hepatic Cholesterol and Triacylglycerol synthesis*, 1994. 29 p. .