academicJournals

Vol. 11(11), pp. 226-231, 17 March, 2017
DOI: 10.5897/JMPR2014.5378
Article Number: D23718E63316
ISSN 1996-0875

http://www.academicjournals.org/JMPR

Journal of Medicinal Plants Research

Full Length Research Paper

Effects of *Commiphora swynnertonii* on weight and plasma cholesterol levels in *Rattus rattus*

Mdegela, R. H.[1]*, Bakari, G. G.[1], Simon, S.[1] and Mosha, T. E. C.[2]

[1]Department of Veterinary Medicine and Public Health, Sokoine University of Agriculture, P. O. Box 3021, Morogoro, Tanzania.
[2]Departments of Food Science and Technology; Sokoine University of Agriculture, P. O. Box 3600, Morogoro, Tanzania.

Received 23 January, 2014; Accepted 26 September, 2016

Experimental studies that aimed to determine the effects of crude aqueous resin extracts of the *Commiphora swynnertonii* on plasma cholesterol levels and weight changes were carried out in rats (*Rattus rattus).* A total of 24 experimental rats divided into four groups with equal sample size (n=6) were used. Group one (G1) served as negative control that received 0.5ml of distilled water (0 mg/kg) orally. Groups 2 (G2), 3 (G3) and 4 (G4) received 50, 100, and 200 mg/kg body weight orally on daily basis for 21 days respectively. Results revealed a significant decrease ($P < 0.05$) in the body weight and on cholestrol levels between the treated and the control groups in a dose dependent manner ($R^2 = 0.89$). *Commiphora swynnertonii* resin lowered cholesterol level by 54, 76 and 79% and weight changes by 18, 31 and 23% for the exposed rats at concentrations of 50, 100 and 200 mg/kg BW respectively. The rats were able to tolerate resin at concentrations lower than 100 mg/kg BW. At higher (>100 mg/kg) doses, few rats showed signs of illness including diarrhoea and finally death. Based on these results, *C. swynnertonii* has a potential to serve as an anti-cholesterol agent with body weight lowering properties.

Key words: Oltemwai, Cardiovascular diseases, rats, Tanzania, blood chemistry.

INTRODUCTION

Cardiovascular diseases associated with increased levels of blood cholesterol particularly the low density lipoprotein cholesterol are increasingly becoming a worldwide health challenges that lead to human deaths. Such disorders are treated, controlled and prevented using different methods including medicinal plants and herbs (Kochhar et al., 2006). Several *Commiphora* species have been studied to assess their activities as anti-lipidemic, anti-cholesterolaemic and anti-atherosclerotic, thus reducing serum cholesterol concentrations without causing any detrimental side effects (Adebayo et al., 2006). In various studies *C. mukul* has been claimed to decrease atherosclerosis and to lower serum cholesterol by 27% and triglycerides by 31% (Singh et al., 1994). Guggulipid, a product from *C. mukul*, increased the high density lipoprotein cholesterol (HDL) (Singh et al., 1994). It exerts its activity by lowering the level of cholesterol by reducing total cholesterol, low density lipoprotein cholesterol (LDL-c), and very low density lipoprotein (VLDL-c) cholesterol at the same time

*Corresponding author. E-mail: rmdegela@yahoo.com. Tel: +255 754 371 628.

elevating the high density lipoprotein cholesterol (HDL-c) (Adebayo et al., 2006). *Commiphora mukul* contains guggulsterone, a compound that act by antagonizing the effect of the nuclear farnesoid × receptor (F×R) (Huang et al., 2003; Adebayo et al*.,* 2006). This receptor is identified as a bile acid receptor and biological sensor for the regulation of bile acid biosynthesis (Huang et al., 2003). Farnesoid × receptor regulates cholesterol metabolism in two ways: (i) chenodeoxycholic acid (CDCA), a primary bile acid, binds directly to and activates F×R, which then mediates the feedback suppression by bile acids of cholesterol 7 alpha-hydroxylase (CYP7A1), the rate-limiting enzyme in bile acid biosynthesis from cholesterol. (ii) Farnesoid × receptor participates in the activation of intestinal bile acid binding protein (IBABP), which is involved in the enterohepatic circulation of bile acids. Thus F×R constitutes a potential therapeutic target that can be modulated to enhance the removal of cholesterol from the body (Tu et al*.,* 2000). The other mechanism reported by Wang et al. (2004), is through the presence of ketosteroid , an active compound of *C. mukul* which acts by stimulating the thyroid gland and has also found to reverse the decrease of catecholamine and dopamine – p- decarboxylase activity that is involved with anticholesterolaemia (Wang et al*.,* 2004). This is done by improving the liver's ability to process, metabolize and excrete cholesterol and improving thyroid function by increasing T_3 and T_4 conversion (Wang et al*.,* 2004). Ethanolic leaf extract of *C. africana* and *C. myrrha* were also shown to exhibit hypolipidaemic activity in experimental rats (Adebayo et al*.,* 2006). Though several studies reported anti-cholesteremic effect of several *Commiphora* spp, relatively little has been investigated in clinical trials on the effect of *C. swynnertonii*. Therefore, this study aimed at evaluating the effect of *C. swynnertonii* on the weight gain and plasma cholesterol levels using rat's model.

MATERIALS AND METHODS

Plant materials

Commiphora swynnertonii plant materials were collected from Simanjiro district in Manyara Region. The plant was identified by a botanist as *Commiphora Swynnertonii* from the family Burseraceae. A voucher specimen (reference number CK 6489) was prepared and preserved at Tanzania National Herbarium, in Arusha (Kayombo, 2009 Personal communication). Tanzania and transferred to Sokoine University of Agriculture (SUA) for processing and use in the experiments. One hundred grams (100 g) of the resin was brewed in 750 ml distilled water and thereafter allowed to stand for 30 minutes. The mixture was filtered using filter paper No 3 and stored in a clean bottle before administered to rats. Twenty mls aliquots of the decoction were evaporated to dryness using an electric heater at 60 to 70°C. The residues were used to determine the concentrations of C. *swynnertonii* extracts which were administered to different groups of experimental rats (Edem et al., 2009).

Sample size determination for experiment animals

The sample size for the experimental animals was determined according to Kirkwood and Sterne (2003).

Experimental design

Twenty four white albino rats (*Rattus rattus*) of seven months old of both sexes weighing 125.7 to 180 g were used in this study. The rats were obtained from the small animal unit at Sokoine University of Agriculture Faculty of Veterinary Medicine. Once in the experimental house, all rats were assessed for signs of diseases. They were caged and maintained on grower mash and drinking water *ad libitum*. The rats were left for three weeks to acclimatize with experimental environment. Following acclimatization, they were weighed, tagged and randomly assigned into four experimental groups of six rats each.

Treatment allocation

The animals were randomly assigned into four groups of six rats (n=6) each. All rats were housed in well-ventilated cages. Groups; G2 - G4 rats were given different doses of aqueous resin extract orally for 21 days consecutive days. G1 remained as negative control that received distilled water only. Blood samples were collected for evaluation of haematological and biochemical parameters.

Preparation of plasma and analysis

At baseline, the body weights of the rats were recorded. About 3 mls of blood samples for plasma preparation were collected from the tail artery using sterile syringes and blood samples were stored in EDTA sterile vacutainer tubes. The blood samples were thereafter centrifuged at 1300 × g for 5 minutes using a bench top centrifuge model to obtain the plasma. The plasma was stored in a refrigerator for analysis of biochemical parameters.

Cholesterol analysis

Total plasma cholesterol level was determined according to Erba Mannheim protocol (Trinders, 1969; Erba, 2010). All analyses on plasma were completed within 24 h after blood collection as recommended (Goji et al., 2009).

Statistical analysis

The data obtained were compiled, coded and analysed using Microsoft excel statistical package (2007) and SAS (Statistical Analysis System) program (Version 8.3) for Window^R. Results from experimental Tests for differences between the means were done and compared by Duncan's Multiple Range Test (DMRTS) at ($p < 0.05$).

RESULTS

Signs of toxicity

Animals used in the study in the negative control group

Table 1. Grouping and treatment allocation

Group (n =6)	Treatment given	Dose
GI	Distilled water	0.5 ml
G2	Resin	50 mg/kg
G3	Resin	100 mg/kg
G4	Resin	200 mg/kg

Table 2. Weight (g) changes following resin administration in rats during the study

Time (weeks)	Dose rate in mg/kg body weight			
	0	50	100	200
0	159.53±6.76[b]	137.13±6.76[b]	169.75±6.76[b]	152.23±6.76[ab]
1	163.63±7.50[b]	114.50±7.50[a]	129.07±7.50[a]	117.70±7.50[a]
2	164.67±6.27[b]	115.65±6.27[a]	118.63±7.14[a]	119.54±8.17[a]
3	165.88±6.36[b]	112.18±6.36[a]	117.08±7.24[a]	117.70±8.29[a]
Percentage (%) change	+4	-18	-31	-23

[a] Means ± SEM based on Weight, [abc] Means in row wise with different superscript are significance different at p< 0.05. *Percentage change refer to positive (+) increase and negative (-) decrease in cholesterol levels.

were apparently in good health condition, as they remained alert, consumed food (growers mash) and water freely and exhibited normal weight increase over time. Depression and diarrhoea were observed in all groups treated with resin extract. The symptoms of toxicity observed with extract administration were dose dependent. Three to seven days after administration of extract all rats in the various groups were very weak. Signs observed before death included loss of appetite, diarrhoea, blindness and coma.

Mortality rate

Mortality was observed in one rat from G3 and two rats from G4 by day eight following an oral administration of resin extract. The rats treated in G2 and G3, were depressed and less active compared to the rats in the other groups during the day.

Changes in body weight

Animals in control group (G1) maintained their weight gain throughout the experimental period (Table 1). The body weights of rats receiving the oral dose of *C. swynnertonii* extract decreased significantly in a time and dose dependent manner. Rats receiving 50 mg/kg (G2) body weight lost about 16.5% of their average body weight during the first week, 15.7% during the 2nd and 18.2% during the 3rd week. Rats receiving 100 mg (G3) of *C. swynnertonii* extract the weight losses were 24.0% (week 1), 30.0% (week 2) and 31.0% (week 3). Likewise, for rats receiving 200 mg of *C. swynnertonii* extract, weight losses were 23.0% (week 1), 21.5% (week 2) and 23.0% (week 3). Overall, animals receiving the *C. swynnertonii* extract lost weight in the range 18 to 31% (Figures 1 and 2).

Changes in the levels of plasma cholesterol

The plasma cholesterol levels of rats before and after administration of *C. swynnertonii* extract at three different doses are shown in Table 2. There was a significant ($P < 0.05$) decrease in plasma cholesterol levels in all rats in the treated groups in a dose dependent manner (R^2-0.89: P=0.03). The body weight for rats in G2, decreased significantly ($P < 0.05$) from week 2 of treatment with resin extract. The plasma cholesterol levels for rats in G2, decreased by 54 % while in G3 and G4, the decrease was by 76 and 79 % respectively. There was a significant positive correlation between weight and cholesterol at different concentrations of *C. swynnertonii* (Figure 3). The correlations were r = 0.432 and P=0.035 for control group, and for exposed groups, the values were r = 0.432 and P=0.009; r = 0.712 and P=0.000 and r = 0.487 and P =0.282; for G1, G2 and G3 treated rats, respectively.

DISCUSSION

The present study has demonstrated the effect of aqueous crude resin extracts from *C. swynnertonii* on plasma total cholesterol in rats. Results revealed that rats in a negative control group were clinically healthy and

Table 3. Changes in the cholesterol level (mmol/L) following administration of resin orally.

Time (weeks)	Dose rate in mg/kg body weight			
	0	50	100	200
0	5.65 ± 0.46[a]	5.29 ± 0.46 [a]	4.30 ± 0.46 [a]	5.49 ± 0.46 [a]
1	5.71 ± 0.37[b]	3.94 ± 0.37[a]	3.19 ± 0.37[a]	3.89 ± 0.37[a]
2	5.50 ± 0.42[d]	3.25 ± 0.42[bc]	1.77 ± 0.48[b]	2.20 ± 0.54[ab]
3	5.78 ± 0.41[c]	2.42 ± 0.41[b]	1.03 ± 0.47[b]	1.13 ± 0.54[ab]
Percentage (%) change	+2.3	-54	-76	-79

*abc Means in row with different superscript are significance different at p< 0.05. *Percentage change refer to positive (+) increase and negative (-) decrease in cholesterol levels.

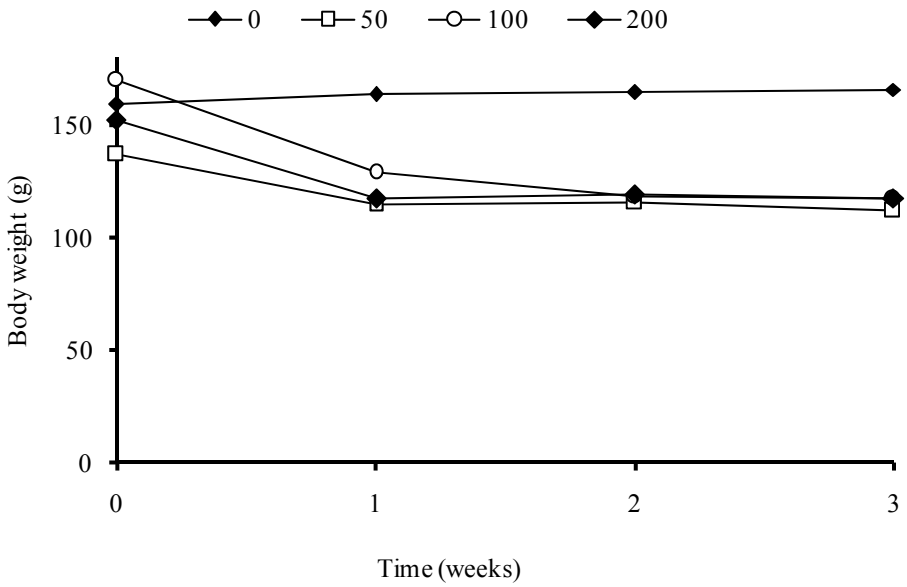

Figure 1. Weight changes over time following oral administration of resin extract in the rats.

their body weights increased significantly all along the study period. Diarrhoea and deaths observed in few treated rats implies that prolong administration of resin extract could be lethal and toxic to the rats. Similar observations were reported in previous studies (Ruitang, 2007) in which extracts from *C. mukul* lead to gastrointestinal discomfort such as loose faeces, mild nausea, and hiccup. The reduced weight gain in a dose dependent manner could be due to reduced feed consumption since the animals were depressed, inactive and with lost appetite. Studies done by Bakari et al. (2012a,b) and Scott, (2005) reported the association between the reduction in weight and the plasma cholesterol and glucose levels through stimulation of thyroid hormone (T3 and T4) function thus interfering with basal metabolic rate leading to loss of body weight (Scott, 2005). Thyroid hormones (T3), stimulates the production of RNA polymerase I and II and, therefore, increases the rate of protein synthesis, potentiates the effects of the β-adrenergic receptors on the metabolism of glucose (Guyton and John, 2006). Therefore, it increases the rate of glycogen breakdown and glucose synthesis in gluconeogenesis. Also stimulates the breakdown of cholesterol and increases the number of LDL receptors, thereby increasing the rate of lipolysis (Guyton and John, 2006).

In the current study, administration of resin from *C. swynnertonii* significantly lowered blood cholesterol. This finding is significant in managing conditions such as coronary heart and atherosclerosis. This was also demonstrated by Helal et al. (2005 and 2006); Ojha et al. (2008); Goji et al. (2009) whereby the application of extracts from *C. myrrha, C. africana* and *C. mukul* using rats lowered the blood cholesterol and glucose while maintaining the myocardial membrane integrity thus preventing myocardial impairment. The effect of *C. swynnertonii* may also base on its ability to bind bile acids in the intestinal lumen and to interrupt the entero-hepatic

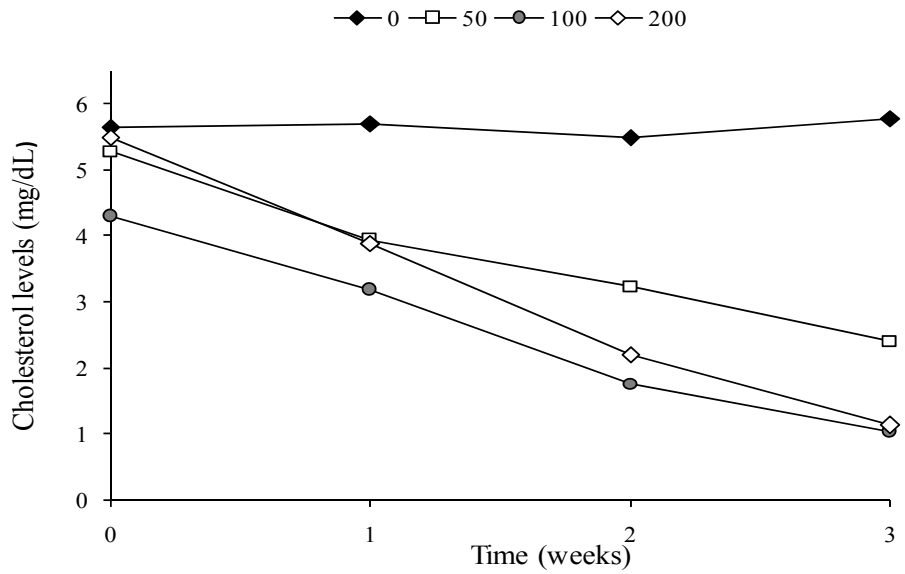

Figure 2. Cholesterol level changes over time following oral administration of resin extract in the rats.

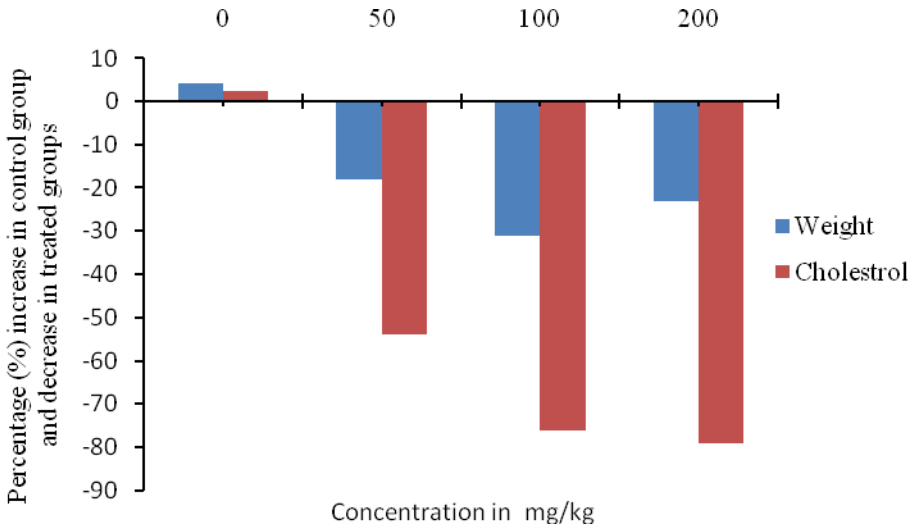

Figure 3. Percentage change in weight and cholesterol in the rats during the experiment

circulation of bile acids, leading to increased excretion of steroids (Singh et al., 1994). Depletion of the hepatic sterol pool may cause compensatory increases in cholesterol biosynthesis, which may cause increased catabolism of LDL particles from plasma (Singh et al., 1994). *Commiphora mukul* contains guggulsterone, a compound which act by antagonizing the effect of the nuclear farnesoid X receptor (FXR) (Huang et al., 2003; Adebayo et al., 2006). This receptor is identified as a bile acid receptor and biological sensor for the regulation of bile acid biosynthesis (Huang et al., 2003). Thus, according to Tu et al. (2000), FXR constitutes a potential therapeutic target that can be modulated to enhance the removal of cholesterol from the body. Another possible mechanism is through the presence of ketosteroid, an active compound of *C. mukul* which acts by stimulating the thyroid gland and has also found to increase the activity of catecholamine and dopamine –p-decarboxylase that are involved in lowering plasma cholesterol (Wang et al., 2004). Some secondary plant metabolites such as coumarin, flavonoid, terpenoid, arginine and glutamic acids have been shown to confer

cholesterol lowering effects in various experimental animal models (Akah and Okafor, 1992; Marles and Farnsworth, 1995). The significant anticholesterol observed in the current study can therefore be explained by the fact that *C. swynnertonii* contain remarkable amounts of saponins terpenoids and flavanoids. Saponins are glycoside components often referred to as "natural detergent" because of their foamy nature (Edeoga et al., 2005) and are reported to posses health benefits such as cholesterol lowering activity (Edeoga et al., 2005). The observed reduction in body weight of resin-treated rats is well connected with the observed levels of plasma cholesterol. High carbohydrate (glucose) and cholesterol intake are known to increase body fats, hence increased body weight and eventually obesity (Scott, 2005).

In conclusion, this study has demonstrated that rats were able to tolerate oral administration of *C. swynnertonii* resin at doses lower than 100 mg/kg bodyweight. Administration of higher doses had negative effects thus causing diarrhoea and genera body weakness in rats. The observed anti-cholesteremic and body weight lowering effect warrants further studies on potentials of this plant.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

ACKNOWLEDGMENTS

The study has been funded by the Carnergie Rise - AFNNET Program. The authors wish to thank the many people who assisted at various stages of the work including botanists and laboratory technicians at the Faculty of Veterinary Medicine.

REFERENCES

Adebayo AH, Aliyu R, Gatsing D, Garba IH (2006). The Effects of Ethanolic Leaf Extract of *Commiphora africana* (Burseraceae) on Lipid Profile in Rats. Int. J. Pharm. 2:618-622.

Akah PA, Okafor CL (1992). Blood sugar lowering effect of *Veronia amygdalina* (Del) in an experimental rabbit model. Phytother. Res. 6:171-173.

Bakari GG, Max RA, Mdegela RH, Phiri ECJ, Mtambo MMA (2012a). Antiviral activity of crude extracts from *Commiphora swynnertonii* (Burrt) against Newcastle disease virus *in ovo.* Tropic. Anim. Health Prod. 44(7):1389-93.

Bakari GG, Max RA, Mdegela RH, Phiri ECJ, Mtambo MMA (2012b). Effect of crude extracts from *Commiphora swynnertonii* (Burrt) against selected microbes of animal health importance. J. Med. Plants Res. 6(9):1795-1799.

Edem DO, Usoh IF (2009). Biochemical changes in wistar rats on oral doses of mistletoe (*Loranthus micranthus*). Am. J. Pharma. Toxicol. 4(3):94-97.

Edeoga HO, Okwu DE, Mbaebi BO (2005). Phytochemical constituents of some Nigerian plants. Afr. J. Biotech. 4(7):685-688.

Goji ADT, Dikko AAU, Bakari AG, Mohammed A, Tanko Y (2009). Evaluation of the Effect of Aqueous-ethanolic Stem Bark Extract of *Commiphora africana* on Blood Glucose Levels of Alloxan Induced Diabetic Wistar Rats. Asian J. Med. Sci. 1:18-21.

Guyton AC, John E (2006). Textbook of Medical Physiology (11th ed.). Philadelphia: Elsevier Inc. ISBN 0-7216-0240.

Helal EGE, Mahmoud A, El-Badawy EE, Kahwash AA (2006). Effect of *Commiphora myrrha* extract on some physiological parameters and histological changes in diabetic albino rats. Egyptian J. Hosp. Med. 148-162.

Huang CJ, Zhao L, Lew A, Yu JL, Sahoo J, Meinke S, Royo PT, Pelaez I, Wright F (2003). Guggulsterone is an FXR antagonist in co activator association assays but acts to enhance transcription of bile salt export pump. J. Biol. Chem. 1-3.

Kirkwood BR, Sterne JAC. (2003). Essential Medical Statistics. Blackwell, Cornwall, United Kingdom. 146p.

Marles RJ, Farnsworth NR (1995). Antidiabetic plants and their active constituents. Phytomedicine 2:137-187.

Ojha SK, Nandave M, Arora S, Mehra RD, Joshi S, Naran R, Arya DS, (2008). Effect of *Commiphora mukul* extract on cardiac dysfunction and ventricular function in isoproterenol-induced myocardial infarction. Indian J. Exp. Biol. 46:646-652.

Ruitang D (2007). Therapeutic effects of guggul and its constituent guggulsterone: cardiovascular benefits. J. Cardiovasc. Drug Rev. 25(4):375-390.

Scott AM (2005). Gum Guggul and Some of Its Steroidal Constituents. Review of Toxicological Literature Prepared for National Toxicology Program (NTP) and National Institute of Environmental Health Sciences (NIEHS). National Institutes of Health U.S Department of Health and Human Services. Research Triangle Park, North Carolina. pp. 18-21.

Trinders P (1969). Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Ann. Clin. Biochem. 6:24.

Tu H, Okamoto AY, Shan B (2000). FXR a bile acid receptor and biological sensor. Trends Cardiovasc. Med. 10(1):30-5.

Wang XJ, Greiberger G, Ledinski G, Kager B, Paigenand GJ (2004). The hypolipidemic natural product, *Commiphora mukul* and its component guggulsterone inhibit oxidative modification of LDL. Atherosclerosis 172:239-249.