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Research Article

Hypolipidemic and Antioxidant Activity of Camel Milk on Poloxamer-Induced Hyperlipidemia in Rats

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Keywords:
Antioxidant, Camel milk, Hyperlipidemia, Poloxamer, Atorvastatin

ABSTRACT

Background: Hyperlipidemia has been implicated as the major risk factor of cardiovascular diseases. The current hypothesis suggests oxidative stress as an underlying mechanism through which hyperlipidemia provoke degenerative diseases. The aim of this study is to investigate the ameliorative and antioxidant effect of camel milk on poloxamer 407 (P407) induced hyperlipidemia in albino rats. **Methods:** Thirty male wistar rats were subdivided into six groups (Group 1-6) with each containing five animals (n=5). Group 1 served as normal control, while Groups 2-6 were induced with Poloxamer 407 intra peritoneally twice a week for three weeks. Group 2 served as hyperlipidemic untreated, group 3 was co-administered with atorvastatin tablet 20mg/kg orally and groups 4, 5 and 6 were co-administered with camel milk at a dose of 250mg/kg, 500mg/kg and 1000mg/kg respectively via oral route. After three weeks, blood samples determination of Total cholesterol (TC), Triglyceride(TG), High Density Lipoprotein (LDL), Low Density Lipoprotein(LDL), Malondialdhyde (MDA), Catalase(CAT) Superoxide Dismutase(SOD) and Gluthatione Peroxidase(GPx) were carried out. **Results:** Total cholesterol was significantly ($p< 0.05$) decreased in group treated with camel milk at 1000mg/kg (174.68 ±46.92 mg/dl), treatment with camel milk doses 250mg/kg(63.57±6.34mg/dl), 500mg/kg (45.07±3.13mg/dl), 1000mg/kg (91.38±5.52mg/dl) significantly ($p<0.05$) reduced high triglyceride level induced by P407. Camel milk treated group at dose 250mg/kg showed significant increase in HDL (208.72±7.88 mg/dl), while camel milk treated groups 250mg/kg and 1000mg/kg showed significant decrease in LDL; (214.15±21.72mg/dl) and (114.75±42.83mg/dl) respectively. Camel milk significantly ($p<0.05$) increase in the level of SOD at 250mg/kg and 500mg/kg (9.25±0.51 U/ml and 11.04± 1.14 U/ml) respectively, however, there was no significant ($p>0.05$) effect on CAT. There was also no significant difference in MDA between all camel milk treated groups and the normal control group. **Conclusion:** These findings highlight the ameliorative potentials of camel milk in P407 induced hyperlipidemia and oxidative stress of albino rats.

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death for both men and women among all racial and ethnic groups (Smith, 2004). It accounts for nearly 50% of all deaths in the developed world (Thomas and Rich, 2007) and have also been predicted to affect approximately 23.6 million people globally by 2030 (Ooi and Liong, 2010). Hyperlipidemia is a global pandemic and a major risk factor for cardiovascular diseases such as artherosclerosis, stroke, myocardial infarction and pancreatitis (Olorunnisola *et al.*, 2012; Harikumar *et al.*, 2013). The burden of this condition is very high in terms of morbidity, mortality and medical costs (Oguejiofor *et al.*, 2012). Hyperlipidemia may result from hereditary factors or acquired from underlying diseases such as; type 2 diabetes mellitus, liver cholestasis, alcohol, nephrotic syndrome, chronic renal failure, hypothyroidism, cigarette smoking, drugs, hormone disturbances and obesity (Olorunnisola *et al.*, 2012; Harikumar *et al.*, 2013; Onwe *et al.*, 2015). Common features of hyperlipidemia include elevation

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of serum total cholesterol, triglyceride, low density lipoprotein, very low density lipoprotein, and reduced high density lipoprotein (Olorunnisola *et al.,* 2012). Oxidative stress has been implicated as an underlying mechanism through which hyperlipidemia induce tissue damage with several studies paying attention to the oxidative modification of Low Density Lipoprotein(ox-LDL), protein glycation, glucose auto-oxidation and lipid peroxidation (Bansal and Jaswal 2009; Olorunnisola *et al.,* 2012; Adekunle *et al.,* 2013; Ngoc 2015). Poloxamer 407 (P407) is a ubiquitous manmade surfactant and non-ionic detergent. Structurally, P407 is a copolymer of ethylene oxide and propylene oxide with a molecular weight of 12,600. P407 has unusual thermoreversible properties. It is a liquid at room temperature, while at body temperature it reassembles into micelles that aggregate into a gel. These temperature-dependent micellization and gelation properties have led to the widespread use of P407 in personal care products such as mouthwashes, deodorants, and skin care products and also as an excipient in a variety of pharmaceutical preparations (Dumortier *et al.,* 2006). P407 has a major adverse effect, which hyperlipidemia is observed in experimental animals after parenteral administration (Johnston and Palmer 1993; Johnston 2004).

There are several allopathic hypolipidemic drugs currently available; however, some of these drugs do not fulfill the conditions for patients' compliance (Davidson and Tooth, 2004). Consumption of such drugs have been reported to have adverse effect such as hyperuricemia, diarrhea, nausea, myositis, gastric irritation, flushing, dry skin and abnormal liver function (Dhaliya *et al.,* 2013). The search for potential cardiovascular protective agents from natural sources had been gaining universal acceptance; many studies are paying attention to natural products as candidates of hypolipidemics which are also antioxidant but have no side effects. These candidates are supposed to improve quality of life which can be impaired by conventional hypolipidemic agents (Bansa and Jaswal 2009; Sefi *et al.,* 2010; Olorunnisola *et al.,* 2012). Camel milk has been utilized since ancient times due to its therapeutic benefit. It is used in countries such India and Egypt in the treatment of wide range of diseases, some of which include; edema, jaundice, asthma, splenic disorders, anemia, hemorrhoids, diabetes and fatigue (Redwan *et al*., 2003; Chakrapany and Chandan, 2014). In ancient Soviet Republic, camel milk was used in sanitoria for the treatment of tuberculosis (Guakhar and Bernand, 2004). The main component of the milk which has a major impact on its nutritional value and technological suitability is protein and vitamins (Gizachew *et al*., 2014).However, it does not contain β-lacto globulin and can be easily digested by lactose-intolerant individuals (Gizachew *et al*., 2014).Camel milk does not form coagulum in acidic environment (Hassan and Bayoumi, 2010) and is reported to have insulin encapsulated in nano particles (lipid vesicles) which make its absorption through the gastrointestinal tract and entry into circulation possible (Ajamaluddin *et al.,* 2012).It also contains vitamin and disease fighting immunoglobulins which are small in size, allowing penetration of antigens and boosting the effectiveness of the immune system (Gizachew *et al.,*2014). Recent researches have shown that camel milk possess hypoglycemic and anti hyperlipidemic properties in diabetes models (Agrawwal *et al.,* 2002; Al Numair, 2010,Isa *et al.,* 2013), antioxidant and hepatoprotective effect in autistic children (Al Ayadhi and El Amin 2013), $AlCl_3$, Acetaminophen and CCL_4 intoxication (Al Hashem, 2009; Al Humaid, 2010; Alfartosi 2012; Ibrahim *et al.,* 2017).

To the best of our knowledge, the ameliorative effect camel milk on poloxamer 407-induced hyperlipidemia in albino rats has not been examined. Hence, the aim of this study is to determine the effect of camel milk on lipid profile and oxidative stress markers of poloxamer 407-induced hyperlipidemia in albino rats.

MATERIALS AND METHODS

Experimental animals

Thirty adult male wistar rats weighing 150-200g were obtained from the Animal House, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria, Nigeria. All the rats were kept in well ventilated steel wire cages (5 rats per cage) with normal photoperiod and fed the same type of food elements (Vital Feeds) with access to water *ad libitum*. The rats were allowed to acclimatize under laboratory conditions for two weeks before commencement of the experiment.

Collection of Camel Milk

Milk collection was done every day from camel herds *(Camelus dromedaries)* in Kaura Namoda Farms, Zamfara State. It was stored in screwed bottles and stored in ice-cold boxes. The milk was transferred and refrigerated 3-5ºC (37-41ºF) at the Department of Pharmacology Laboratory, Ahmadu Bello University, Zaria.

Proximate Analysis of Camel Milk

Proximate analysis of the milk was carried out at National Animal Production Research Institute (NAPRI) and National Research Institute for Chemical Technology (NARICT) all in Zaria prior to commencement of administration. Determination of all constituents was based on the guidelines outlined by the Association of Analytical Chemist (AOAC), (2005).

Induction of Hyperlipidemia
Poloxamer407 (Lutrol F127; BASF,Ludwigshafen, Germany) was utilized to induce Hyperlipidemia. Prior to the administration, it was dissolved in distilled water and refrigerated overnight to facilitate its dissolution. It was administered at a dose of 500mg/kg intraperitoneally twice a week for 3 weeks (Woo *et al.,* 2010). Needles and syringes used for administration were cooled to prevent gelation within the syringe during injection as described by Johnston and Palmer (1993).

Acute Toxicity Studies of Camel Milk
Determination of Median Lethal Dose (LD_{50}) of camel milk was conducted using the method of Lorke (1983). The median lethal dose was found to be greater than 5000mg/kg via oral route.

Preparation of stock concentration of camel milk
A beaker was placed on the gallen metter balance.10mls of the milk was weighed and was equivalent 10g. Hence, 1ml of the milk was equivalent to 1g after weighing. Stock concentration of 1000mg/kg is equivalent to 1000mg/ml.

Preparation of Standard Drug
Atorvastatin was purchased in tablet form at strength 20mg (Strovas Tablet 20mg/kg, Ranbaxy Laboratory Ltd, Paonta Sahib Distribution, Sirmour H.P. 173025, India). Tablets were dissolved in distilled water and administered via oral route once daily (Victor *et al.,* 2014).

Animal Groupings
Group 1: Normal Control animals fed with a standard diet and orally administered 1 ml/kg distilled water for 21 days. **Group II**: Hyperlipidemic Control was induced with 500mg/kg of poloxamer 407 intra peritoneally twice a week without treatment for 3 weeks Group **III**: Induced with 500mg/kg of Poloxamer 407 intra peritoneally twice a week and treated with Atorvastatin tablet (ATV) orally at 20mg/kg body weight/day for 21 days. Groups **IV**: Induced with 500mg/kg of Poloxamer 407 intra peritoneally twice a week and co administered with 250mg/kg of camel milk orally once daily for 21 days. Group **V**: Induced with 500mg/kg of Poloxamer 407 intra peritoneally twice a week and co administered with 500mg/kg of camel milk orally once daily for 21 days. Group **VI**: Induced with 500mg/kg of Poloxamer 407 intra peritoneally twice a week and co-administered with 1000mg/kg of camel milk orally once daily for 21 days.

Collection of Blood Samples
At the end of the 21-day experimental period, animals were fasted overnight and sacrificed by cervical dislocation. Blood was collected via cardiac puncture into anticoagulant free bottles and centrifuged at 3000 rpm for 15 minutes with the resultant sera harvested into plain sample bottles.

Biochemical Parameters
Serum Total Cholesterol (TC), Triglyceride (TG) and High Density Lipoprotein (HDL) were determined using Agappe Diagnostics Reagents (Agappe Diagnostics, Switzerland, GmbH). Low Density Lipoprotein (LDL) was calculated according to Friedewald *et al*., (1972).

Table 1: Composition of camel milk as determined from proximate analysis

S/N	COMPOUND	COMPOSITION (%, mg/dl)
01	Total Solid	12.30 %
02	Moisture	87.70 %
03	Ash	0.61 %
04	Carbohydrate	3.91 %
05	Crude Protein	4.08 %
06	Fat	3.71 %
07	Solid Non Fat	8.60 %
08	Lactic Acid	0.30 %
09	Nitrogen	0.64 %
10	Flavanoids	Negative
11	Cardiac Glycosides	Positive
12	Saponin	Negative
13	Free Fatty Acids	3.230 mg/dl
14	Vitamin A	1.167 mg/dl
15	Vitamin B2	6.942 mg/dl
16	Vitamin C	0.329 mg/dl
17	Vitamin E	6.075 mg/dl

Lipid Peroxidation and Antioxidant Enzyme Assays
Malondialdehyde (MDA) was assayed in the form of Thiobarbituric Acid Reacting Substances (TBARS) according to Fraga *et al.,* (1988). Glutathione peroxidase (GPx) was measured using the method of Rotruck *et al.,* (1973). Superoxide dismutase (SOD) was measured as described by Martin *et al.,* (1987), while Catalase (CAT) enzyme activity was measured according to the method of Aebi (1984).

Statistical Analysis
Data obtained was expressed as mean (±SEM). The result was analysed using one way analysis of Variance(ANOVA), followed by Tukey's Post hoc Test to compare the level of significance between groups using Statcato software version 0.9.12. Values of $p < 0.05$ were considered significant.

RESULTS
Constituents of camel milk
The camel milk constituents as determined from proximate analysis are shown in table 1. Camel milk revealed the following constituents; ash, carbohydrates,

fats, fatty acids, lactic acid, nitrogen, moisture and tested positive to glycoside. Camel milk also proved the presence of vitamins A, B2, C and E at various wavelengths.

Effect of Camel Milk on Total Cholesterol (TC) and Triglyceride (TG) of P407 Induced Hyperlipidemic wistar Rats

Total Cholesterol (TC)

The total cholesterol level in rats within the normal control group is (74.28 ±5.70 mg/dl) as shown in figure 1. After induction with P407, cholesterol level in the hyperlipidemic untreated group was significantly ($p<0.05$) higher (727.24 ±126.59 mg/dl) than the normal control group. Treatment with camel milk at 1000 mg/kg orally resulted in significant($p<0.05$) reduction in cholesterol level (174.68 ±46.92 mg/dl) more than when atorvastatin 20 mg/kg (215.39 ±32.68 mg/dl) is given.

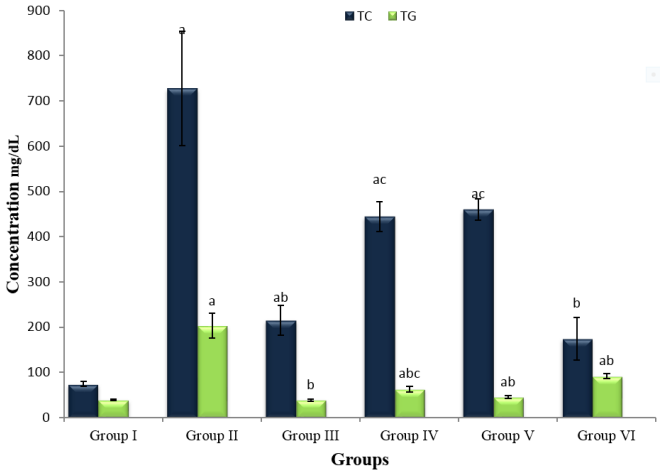

Fig. 1: Effect of Camel Milk on Total Cholesterol and Triglyceride on P407 Induced Hyperlipidemic Wistar Rats. Results are expressed as mean ± standard error of mean, n = 5. Group I: Normal control Group II : P407(500mg/kg) Group III P407(500mg/kg) + AT(20mg/kg), Group IV: P407(500mg/kg) + CM(1000mg/kg),Group V: P407(500mg/kg) +CM500mg/kg, Group VI: P407(500mg/k) + CM (250mg/kg).Values with superscripts are statistically significant ($p<0.05$); a = when compared to Group I, b = when compared to Group II, c = when compared to Group III.

Triglyceride (TG)

There was significant increase ($p < 0.05$) in triglyceride of the hyperlipidemic untreated group (203.16 ± 27.64mg/dl) when compared to the normal control group (38.97±1.51mg/dl). Treatment with atorvastatin at a dose of 20mg/kg (38.74±2.97mg/dl) and at all camel milk doses 250mg/kg (63.57±6.34mg/dl), 500mg/kg(45.07±3.13mg/dl), 1000mg/kg (91.38 ±5.52mg/dl) significantly ($p<0.05$) reduced high triglyceride level induced by P407.

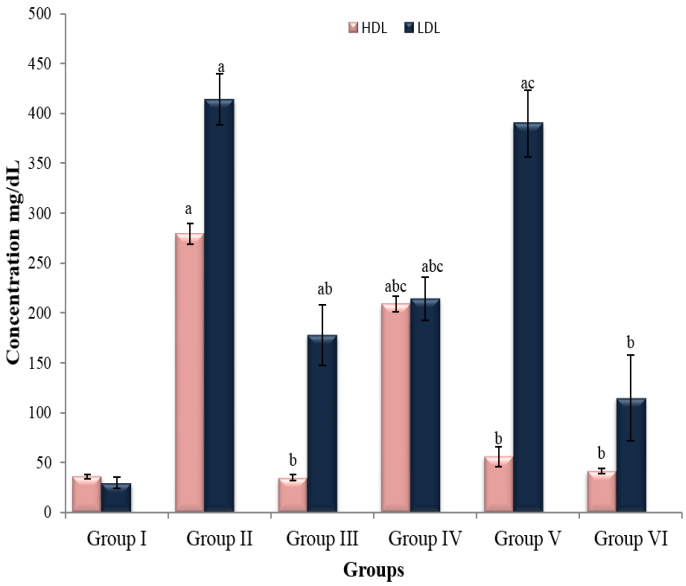

Fig. 2: Effect of Camel Milk on High Density Lipoprotein and Low Density Lipoprotein on P407 Induced Hyperlipidemic Wistar Rats. Results are expressed as mean ± standard error of mean, n = 5. Group I: Normal control Group II: P407(500mg/kg) Group III P407(500mg/kg) + AT (20mg/kg), Group IV: P407(500mg/kg) + CM(1000mg/kg), Group V: P407(500mg/kg) +CM500mg/kg, Group VI: P407(500mg/k) + CM (250mg/kg).Values with superscripts are statistically significant ($P<0.05$); a = when compared to Group I, b = when compared to Group II, c= when compared to Group III.

Effect of Camel Milk on High Density Lipoporotei n(HDL) and Low Density Lipoporotein (LDL) of P407 Induced Hyperlipidemic wistar Rats:

High Density Lipoporotein (HDL)

The HDL level in the normal control group is 35.97 ± 2.43mg/dl as shown in figure 2. After induction, the hyperlipidemic untreated group showed significant ($p< 0.05$) increase (279.45± 10.33mg/dl) compared to the normal control group. There was significant ($p< 0.05$) increase between the camel milk treatment group 250mg/kg (208.72±7.88 mg/dl) and the normal control group.

Low Density Lipoprotein (LDL)

The LDL level in rats within the hyperlipidemic untreated group showed significant increase ($p<0.05$) (414.09±25.96mg/dl) compared with the normal control group (29.74±5.85mg/dl). There was significant ($p< 0.05$) difference between camel milk treated group 250mg/kg (214.15±21.72mg/dl), 1000mg/kg (114.75±42.83mg/dl) and atorvastatin treated group (177.59±30.36mg/dl) compared to the hyperlipidemic untreated group.

Table 2: Effect of Camel Milk on Oxidative Stress Biomarkers of Poloxamer 407 Induced Hyperlipidemic Wistar Rats

Group (n=5)	CAT (U/ml)	SOD (U/ml)	GPx (U/ml)	MDA(nMols/ml)
Group I	7.25 ± 0.69	11.23 ± 0.97	31.97 ± 3.70	119.23±20.70
Group II	3.26 ± 0.47[a]	3.25 ± 1.05[a]	25.32 ±0.60	180.18±18.66[a]
Group III	5.59 ± 1.64	5.68 ± 0.65[a]	31.03 ± 6.00	173.27±14.07[a]
Group IV	3.04 ± 0.36[a]	9.25 ± 0.51[bc]	32.81 ± 5.18	130.00 ± 9.05[c]
Group V	3.62 ± 0.72[a]	11.04 ± 1.14[bc]	47.60 ± 5.60	125.82 ± 9.77[c]
Group VI	3.88 ± 0.33[a]	7.58 ± 1.70	36.82 ± 3.85	165.82 ±16.72

Effect of Camel Milk on Serum Oxidative Stress Biomarkers of P407 Induced Hyperlipidemic wistar Rats

Catalase (CAT)

The effect of P407 on catalase activity showed a significant ($p<0.05$) decrease in the hyperlipidemic untreated group when compared to the normal control group as shown in table 2. The mean value of the hyperlipidemic untreated group (3.26 ± 0.47 U/ml) is lower normal when compared to the normal control group (7.25 ± 0.69U/ml). The mean values of all camel milk treated groups (250mg/kg, 500mg/kg and 1000mg/kg) (3.04 ± 0.363U/ml 3.62 ± 0.72U/ml and 3.88 ±0.33U/ml) are lower when compared to normal control group ($p<0.05$).

Superoxide Dismutase (SOD)

There was a significant ($p<0.05$) decrease in superoxide dismutase of the hyperlipidemic untreated group when compared to normal control group as shown in Table 2. Camel milk treated groups 250mg/kg and 500mg/kg (9.25±0.51 U/ml and 11.04± 1.14 U/ml) showed significant increase ($p<0.05$) when compared to hyperlipidemic untreated and atorvastatin treated groups respectively. There was no significant difference ($P>0.05$) between the normal control group and all camel milk treatment groups (9.25±0.51 U/ml, 11.04± 1.14 U/ml and 7.58±1.70 U/ml).

Gluthathione Peroxidase (GPx)

There was no significant ($p>0.05$) difference between all the groups as shown in Table 2.

Malondialdehyde (MDA)

Serum Malondialdehyde level showed significant ($p<0.05$) increase in the hyperlipidemic untreated group (180.18±18.66nMols/ml) compared to normal control group (119.23±0.97 nMols/ml) (Table 2). Camel milk treated groups 250mg/kg, 500mg/kg and 1000mg/kg (130.00±9.05nMols/ml 125.82±9.77nMols/ml and165.82 ±16.72nMols/ml) respectively had no significant ($p>0.05$) difference when compared to the normal control group.

DISCUSSION

Hyperlipidemia progresses with alteration in the serum lipids profile making it important risk factor in many degenerative diseases (Kolawole *et al.,* 2012; Sodipio *et al.,* 2012). Lipid abnormality can be qualitative or quantitative (Oguejiofor *et al.,* 2012). Quantitatively, it is due to elevated Total Cholesterol (TC), elevated Low Density Lipoprotein Cholesterol (LDL-C) elevated Triglyceride (TG) and reduced High Density Lipoprotein Cholesterol (HDL-C) levels occurring singly or in combinations. Qualitatively it implies changes in composition of LDL-C which includes small dense LDL-C increased TG content or increased electronegativity of LDL-C (Oguejiofor *et al.,* 2012). Poloxamer 407 induced hyperlipidemia is associated with alterations in the activities of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, lecithin cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein (CETP), hepatic lipase (HL) and lipoprotein lipase (LPL) (Johnston and Plamer, 1993). P-407 directly inhibits heparin releasable fraction of LPL and HL with indirect increase in the biological activities of CETP and LCAT (Johnston and Plamer, 1993). In the present study, rats treated with P-407 were characterized by higher serum lipid profiles after repeated administration for 3 weeks. The increase in the level of TC, TG, HDL and LDL in the hyperlipidemic untreated group is consistent with the works of Korolenko *et al.,* (2012), Korolenko *et al.,* (2013) and Mithun *et al.,* (2011). However, camel milk lowered serum TC, TG, LDL and increased HDL which is in agreement with the works of Al Hashem, (2009), Al Numair, (2010), Abd el aziz *et al.,* (2012), Isa *et al.,* (2013) and Ibrahim *et al.,* (2017). Camel milk contains vitamins C and E (table 1), both of which have been reported to lower TC TG and LDL (Badr *et al.,* 2011). The hypolipidemic activity of the camel milk in the p407 model may be due to inhibition of HMG-CoA reductase, stimulation of Cholesterol-7-alpha-

hydroxylase which converts cholesterol into bile acids, or inhibition of cholesterol absorption from the intestine due to formation of complexes with compounds such as glycosides (table 1) (James *et al.,* 2010). Ibrahim *et al.,* (2017) proposed that the reduction in TC and LDL cholesterol by camel milk could as well be due to the increase in inhibitory activity on lecithin cholesterol acyl transferase enzyme, increase binding of LDL to LDL receptor and/or through an indirect effect on thyroid hormones. Al Numair (2010) and Abd el aziz *et al.,* (2012) concluded from their findings that significant decrease in TG by camel milk is due to the presence of insulin like protein and high amount of zinc (Al Numair, 2010). Insulin attenuates lipoprotein lipase activity which in turn decreases the level of TG (Arkilla *et al.,* 2001). Moreover, it was previously shown that zinc supplementation facilitates insulin secretory activity in pancreatic islets of the ob/ob mouse (Begin-Heick*et et al.,* 1985). Extracellular ATP and zinc activate multiple P2X purinergic receptor channels expressed by islet beta-cells to potentiate insulin secretion (Richards *et al.,* 2008). On the other hand, an elevated level of HDL is probably the result of attenuation of hepatic lipase by camel milk. Elevated level of HDL exerts an anti-atherogenic effect by counteracting LDL oxidation and facilitating the translocation of cholesterol from peripheral tissue such as arterial walls to the liver for catabolism (Yoon *et al.,* 2008). HDL also transports cholesterol and cholesterol esters from the peripheral tissues and cells back to the liver, where cholesterol is metabolized into bile acids. This pathway plays a very important role in reducing the level of cholesterol in the blood and peripheral tissues and in inhibiting the formation of atherosclerotic plaque in the aorta (Kim *et al.,* 2008; Imafidon 2010). This significant hypolipidemic effect of camel milk shows its potential ability to reduce atherosclerosis risk.

Measurement of thiobarbituric acid (TBARS) has been used as indicators to determine lipid peroxidation and oxidative stress in vitro and in vivo (Fraga *et al.,* 1988; Beltowski *et al.,* 2000). Lipid peroxidation is initiated by peroxidative decomposition of membrane polyunsaturated fatty acids by free radicals, leading to their transformation and fragmentation to alkanes and reactive aldehyde compounds such as MDA and 4 hydoxy-2,3- nonenals (HNE) (Olorunnisola *et al.,* 2012; Ngoc 2015). Evaluation of the effect of poloxamer 407 in experimental rats showed a significant increase in MDA levels in serum. The observed increase in lipid peroxidation is consistent with several experimental studies which have shown that hyperlipidemia leads to increase lipid peroxidation (Dutta and Bishayi, 2009; Olorunnisola *et al.,* 2012 Woo *et al.,* 2012; Ngoc 2015). Co-adminstration of poloxamer 407 induced hyperlipidemic rats with camel milk at doses of 250mg/kg, 500mg/kg significantly reduced MDA concentration when compared to atorvastatin. The result of our findings agrees with the work of Al Hashem (2009) and Al Fartosi *et al.,* (2012). The ability of camel milk to inhibit the process of lipid peroxidation in vivo may be due to the free radical scavenging properties of its vitamins and zinc as reported by al Ibrahim *et al.,* (2017). In addition to vitamins C and E, camel milk from our proximate analysis also contains vitamins A and B2 (table 1); all of which possess antioxidant properties (Al Hashem, 2009; Al Humaid 2010, Badr *et al.,* 2011; Dawud *et al.,* 2012; Ibrahim *et al.,* 2017). Vitamins C and E work synergistically to quench the activities of free radicals and also regenerates the reduced form of vitamin E (Chuong *et al.,* 2008). Vitamin E also inhibits the process of lipid peroxidation through its radical chain-breaking antioxidant properties (Bjelakovic *et al*., 2007). Vitamin C is a scavenger of free oxygen radicals which are toxic by product of many metabolic processes. The presence of zinc in camel milk may have induced the production of metallothionein, an effective scavenger of hydroxyl radicals (Sahin and Kucuk, 2003). Serum antioxidant enzymes (SOD and CAT) activities were significantly decreased in rats induced with P407 compared to normal control group. The decrease in the activities of these enzymes, could be attributed to their exhaustive utilization in quenching the free radicals generated due to the hyperlipidemia (Ma *et al.,* 2011) as manifested by the high level of lipid peroxidation. Co-administration of camel milk to P407 induced hyperlipidemic rats at doses 250mg/kg, and 500 mg/kg significantly increased the level of SOD which is consistent with the findings of Al Hashem (2009) and El Said *et al.,* (2010) but differs with respect to reduced catalase activity. This difference may be attributed to the percentage composition of each elements and geographical location where the milk is found. Camel milk showed tendencies to increase in GPx activity possibly due its magnesium content (Kamal *et al.,* 2007; Al Hashem, 2009; Ibrahim *et al.,* 2017). Magnesium in addition to glycine, γ-glutamyl cysteine and ATP are required for the biosynthesis of glutathione synthetase and thus glutathione (Virginia *et al*., 1971). Our results indicate that camel milk had a free radical scavenging activity which probably protects organs protection from hyperlipidemia.

CONCLUSION

Poloxamer 407 had adverse hyperlipidemic effect in on male Wistar rats. Our results demonstrated that poloxamer 407 is capable of inducing marked

alterations in biochemical parameters and oxidative damage, and inhibiting the function of antioxidant enzymes. Consequently, attention should be paid to the use of poloxamer in gels, mouth washes and drugs excipient. Camel milk administration during poloxamer 407 induced hyperlipidemia minimized P407-associated hazards in male albino rats. Therefore, drinking camel milk could be beneficial in alleviating some health hazards associated with hyperlipidemia.

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Conflict of interest statement

Authors have declared that no competing interests exist.

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