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Research Article
Camel Milk plus Atorvastatin Influence Lipid Profile and Body Weight in Hyperlipidemic Rats

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Abstract

Background and Objective: Camel milk is a common ethnopharmacological remedy as well as a nutritional substance used in Northern Nigeria either alone or in combination with some orthodox drugs used in treating obesity and hyperlipidemia. This study was carried out to investigate the influence of concurrent administration of fresh camel milk with atorvastatin in high fat diet-induced hyperlipidemic rats. **Materials and Methods:** Synergistic activity between atorvastatin-camel milk combination was also assessed using internationally accepted synergy analysis models (Loewe additivity, Bliss independent and highest single agent). Eleven groups of Wistar rats (n = 6) were used for the study, of which ten were rendered hyperlipidemic by feeding with a high-fat diet and one left as control. Six groups were administered with either the camel milk or the atorvastatin at three different doses each (0.5, 1 and 1.5 mL kg^{-1} for the camel milk and 2, 7 and 20 mg kg^{-1} for atorvastatin), while another 3 groups were co-administered with the camel milk and atorvastatin at 3 different ratios each (0.5 mL kg^{-1}: 2 mg kg^{-1}, 1 mL kg^{-1}: 7 mg kg^{-1} and 1.5 mL kg^{-1}: 20 mg kg^{-1}). Lipid profile and body mass index were determined at day 21 of treatment. **Results:** The results revealed a synergistic activity of the camel milk and atorvastatin combination in reducing total cholesterol (based on Loewe and HSA models) and LDL (based on HSA model). **Conclusion:** In conclusion, it is shown that the combination of camel milk and atorvastatin was synergistic in reducing hyperlipidemia and obesity.

Key words: Hyperlipidemia, obesity, camel milk, atorvastatin, high fat diet, co-administration, hypertriglyceridemia

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Non-communicable chronic diseases including diabetes, obesity, dyslipidemia, cancer and coronary heart diseases are responsible for an increasing burden of the already existing burden of communicable diseases in developing countries of Sub-Saharan Africa[1,2]. Hyperlipidemia, defined as the presence of abnormal blood concentrations of one or more of the following: Total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides, can be categorised into isolated hypercholesterolemia, hypertriglyceridemia or a combination of both[3]. It is a component of metabolic syndrome and an important modifiable risk factor for arteriosclerosis, stroke, pancreatitis, coronary heart disease[4,5]. The increased prevalence of dyslipidemia has become a worldwide public health issue[6]. Dyslipidaemia is prevalent among the general adult population in Africa, particularly among patients with coexisting risk factors[7].

Statins are the drugs of choice for LDL-C and TC reduction and are most commonly used to reduce the risk of CVD and death for both primary and secondary prevention of coronary artery disease[8]. For high LDL-C levels patients, the initial treatment goal is to lower the LDL-C to the target level first with statin therapy. In mixed dyslipidemia ezetimibe, fibrate or niacin can be added as ad-on to Statins[9]. Atorvastatin is one of the most prescribed statins which act by inhibiting the enzyme (3-hydroxy methyl glutaryl coenzyme A) responsible for the conversion of HMG-CoA to mevalonate which is a cholesterol precursor. A decrease in intracellular cholesterol levels promotes an expression of LDL receptors on the hepatocyte surface, resulting in increased clearance of LDL from the blood[10]. It also inhibits their synthesis and promotes their catabolism. It has a much longer plasma t½ of 18-24 hrs than other statins and has additional antioxidant property[11].

Obesity, a disorder involving excessive body fat, is classified by Body Mass Index (BMI), which is calculated as body weight in kilograms divided by the height in meters squared (kg/m^2). The prevalence of obesity worldwide has been exponentially growing with doubling rates for adult and childhood obesity (6-11 years) and tripling rates of adolescent obesity (12-19 years)[12]. Non-pharmacologic management includes lifestyle modification (healthy diet and increase of physical activity)[13]. Pharmacotherapy should be considered when diet, exercise and behaviour modification do not produce sufficient weight loss[13].

About 80% of the world's population practice the use of herbal medicine[14]. In some parts of the world, such as China, India, there is a practice of integration of other forms of healthcare with the modern system of healthcare in the treatment of diseases[15]. The practice is underway in Nigeria as policies are currently being put in place to integrate traditional medicine with the orthodox system of health care[16], thus the need for search and standardization of available traditional drugs. Herbal medicines are well patronized for persons across the world, with some patrons using both traditional and orthodox forms of medicines concurrently without knowing whether unwanted effects may occur as a result of the combination[17].

Drug combination therapy is a form of treatment approach employed in treating the most dreadful diseases, such as cancer, tuberculosis and AIDS, to achieve a synergistic therapeutic effect, reduction of toxicity and minimization of induction of resistance[18]. Drug-drug interactions could be favourable or detrimental, generally, drug interactions happen when a patient's response to a drug is altered by food, nutritional supplements, formulation excipient, environmental factors, other drugs or disease[19]. Clinically relevant food-drug interactions are caused by food-induced changes in the bioavailability of the drug. Such interactions are often produced by chelation with constituents in food. Again, the physiological response to food intake, especially gastric acid secretion, may affect the bioavailability of certain drugs[20].

In many communities in Nigeria, especially in the northern part of the country, the use of camel milk is becoming more popular due to the folklore stories and scientific reports supporting its therapeutic potential against a wide range of diseases. Camel milk and its products have nutritional and medical properties. Camel milk commonly ingested fresh by pastoralists is used in the management of several ailments in several parts of Africa and Asia including gastrointestinal disorders, sugar diseases, food allergy, psoriasis, hepatitis C and B, autism and tuberculosis[21]. It has been found scientifically to have hypolipidemic[10,22,23], antidiabetic[24,25], antihypertensive[26], anticancer[27], hepatoprotective[28] and antioxidant activity[22].

Several studies have investigated the hypolipidemic effect of the use of camel milk alone in rats and humans[10,22,23,32,33], however, to the best of our knowledge, no study investigated whether when camel milk, a common ethnopharmacological remedy used in northern Nigeria is used in combination with atorvastatin, the hypolipidemic effect of the drug. Therefore, this study aimed to determine the effect of concurrent use of camel milk and atorvastatin on lipid profile and obesity markers of high fat diet-induced hyperlipidemia in Wistar rats and determine the possible synergistic effect of the combination using Combenefit software.

MATERIALS AND METHODS

Study area: This study was carried out at the Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, College of Health Sciences, Usmanu Danfodiyo University Sokoto, Nigeria from October, 2020 to March, 2021.

Experimental animals: A total number of 81 Albino Wistar rats (*Rattus norvegicus*) of mixed gender in 1:1 ratio weighing 160-200 g were used in this study. The rats were obtained from Institute for Advanced Medical Research and Training, UCH, Ibadan. The rats were then housed 6 per cage in a temperature and humidity controlled environment and were given food and water *ad libitum*. The rats were acclimatized for two weeks before the experiment.

Preparation of stock concentration of camel milk: About 9 mL of the camel milk was weighed using an electronic weighing scale (SHIMADZU weighing balance, TXB422L, Max 420 g, Min 0.2 g, e = 0.1 g, d = 0.01 g) and was found to be equivalent to 10 g. Hence, 0.9 mL was equivalent to 1 g. Stock concentration of 1000 mg kg^{-1} is equivalent to 1000 mg/0.9 mL[22].

Determination of the chemical composition of camel milk: The chemical composition of the milk was determined by proximate analysis to determine the nutritional values with regards to protein, carbohydrate, moisture, ash contents, crude fibre and crude fat contents using standard method[29].

Acute toxicity study: The Median Lethal Dose (LD_{50}) of camel milk was determined using Lorke's method[30]. The median lethal dose was found to be greater than 5000 mg kg^{-1} via the oral route.

Induction of hyperlipidemia: All the rats used in the study for hyperlipidemia, except for the control group, were rendered hyperlipidemic by feeding with a high-fat diet [fat 46% (animal fats), carbohydrates 24% (maize), protein 20.3% (soya beans), fibre 5% and salt mixture 3.7% and vitamin mixture 1%] for 4 weeks[10,31].

Preparation of stock concentration of atorvastatin: Atorvastatin tablet with the strength of 20 mg was dissolved in distilled water and administered via oral route once.

Experimental design: A total of 66 rats were employed for the study. The rats were randomly assigned to 11 groups using computer-generated numbers, with each group containing 6 rats:

- **Group 1:** Normal control rats were placed on normal feeds and water throughout the experiment
- **Group 2:** High fat diet rats (HFD) served as positive hyperlipidemic control
- **Group 3, 4 and 5:** High fat diet rats (HFD) received oral camel milk at 3 graded doses of 0.5, 1 and 1.5 mL/kg/day, respectively for 3 weeks
- **Group 6, 7 and 8:** High fat diet rats (HFD) received oral Atorvastatin (ATO) graded doses, 2, 7 and 20 mg/kg/day, respectively for 3 weeks
- **Group 9, 10 and 11:** High fat diet rats (HFD) received orally camel milk and atorvastatin graded dose × 3 weeks, respectively, CM: 0.5 mL/kg/day+ATO = 2 mg/kg/day, CM: 1 mL/kg/day, ATO: 7 mg/kg/day, CM: 1.5 mL/kg/day and ATO: 20 mg/kg/day

Determination of bodyweight: Animal weights were measured in grams (g) using an electronic weighing scale (SHIMADZU weighing balance, TXB422L, maximum 420 g, minimum 0.2 g, e = 0.1 g, d = 0.01 g) on Day 0, 28 and 49[32].

Body Mass Index (BMI): BMI of the rats was determined by using the formula advanced by Wilmore and Costill (2004)[32]:

$$\text{BMI} = \frac{\text{Weight (kg)}}{\text{Height (m}^2\text{)}}$$

Determination of height: Animal heights were measured in meters using the measuring tape, taking measurements from the head to the tail[32].

Blood sample collection: About 24 hrs after the last dose, the animals were anaesthetized with chloroform and blood samples were collected by cardiac puncture in well labelled sterile bottles. They were allowed to clot and centrifuged at 4000 g for 10 min. The sera obtained were then pipetted into labelled test tubes for biochemical analysis.

Biochemical analysis/lipid profile: Total cholesterol assay[33], triglyceride assay[34], HDL-cholesterol assay[35], LDL-cholesterol assay were also determined[36].

Interpretation of the combination study results: Synergistic activity between atorvastatin-camel milk combination was

also assessed using internationally accepted synergy analysis Models (Loewe additivity, Bliss independent and highest single agent).

RESULTS AND DISCUSSION

Chemical composition of camel milk: Proximate analysis of camel milk reveal, a high concentration of carbohydrate (8.08%), followed by lipid (2.2%) (Table 1).

Acute toxicity study: Acute toxicity studies revealed the non-toxic nature of camel milk. The behaviour of the treated rats also appeared normal. There was no lethality or toxic reaction at any selected dose in both phases of the study. The median lethal dose was found to be greater than 5000 mg kg^{-1} via the oral route (Table 2).

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

Compounds	Composition (%)
Moisture	86.93
Ash	1.00
Carbohydrate	8.08
Crude protein	1.78
Lipid	2.20
Nitrogen	0.29

Table 2: Result of oral acute toxicity studies of fresh camel milk on normal rats

Dose (mg kg^{-1}) PO	Number of animals dead/used	Mortality (%)
Phase 1		
10	0/3	0
100	0/3	0
1000	0/3	0
Phase 2		
1000	0/1	0
1600	0/1	0
2900	0/1	0
5000	0/1	0

Effect of co-administration of camel milk and atorvastatin on TC, TG, HDL and LDL in the high-fat diet-induced hyperlipidemic rat at day 21 of treatment: Treatment with either camel milk or atorvastatin (at three escalating doses each), alone or in combination, resulted in a significant reduction ($p<0.05$) in total cholesterol in all the treatment groups when compared to vehicle-treated hyperlipidemic rats (418.7±20.59 mg dL^{-1}). There was also significant reduction in TC ($p<0.05$) in the groups that received ATO 20mg kg^{-1} (99.83±2.242 mg dL^{-1}), CM 1 mL kg^{-1}+ATO 7 mg kg^{-1} (98.33±5.308 mg dL^{-1}) and CM 1.5 mL kg^{-1}+ATO 20 mg kg^{-1} (74.67±7.260) when compared to other treatment groups Fig. 1a.

Treatment with either camel milk or atorvastatin (at three escalating doses each), alone or in combination, resulted in a significant reduction ($p<0.05$) in triglyceride when compared to vehicle-treated hyperlipidemic rats (194.0±5.859 mg dL^{-1}). There was also significant reduction in triglyceride ($p<0.05$) in the groups that received ATO 2 mg kg^{-1} (65.50±2.849 mg dL^{-1}), ATO 7 mg kg^{-1} (49.67±3.712 mg dL^{-1}), ATO 20 mg kg^{-1} (40.50±0.5627) and CM 1.5 mL kg^{-1}+ATO 20 mg kg^{-1} (41.67±3.018 mg dL^{-1}) when compared to other treatment groups (Fig. 1b).

Treatment with either camel milk or atorvastatin (at three escalating doses each), alone or in combination resulted in no significant reduction ($p>0.05$) in HDL cholesterol level in groups treated with CM 1 mL kg^{-1} (43.67±4.169 mg dL^{-1}), CM 1.5 mL kg^{-1} (50.33±2.108), ATO 7 mg kg^{-1} (44.67±1.308 mg dL^{-1}), ATO 20 mg kg^{-1} (45.67±1.838), CM 1 mL kg^{-1}+ATO 7 mg kg^{-1} (50.00±2.633 mg dL^{-1}) CM 1.5 mL kg^{-1}+ATO 20 mg kg^{-1} (50.17±2.072 mg dL^{-1}) when compared to vehicle-treated hyperlipidemic rats (56.83±5.062 mg dL^{-1}). There was however significant reduction in HDL ($p<0.05$) in the groups that received CM 0.5 mL kg^{-1} (40.50±2.232 mg dL^{-1}), ATO 2 mg kg^{-1} (41.50±0.9220 mg dL^{-1}) and CM 0.5 mL kg^{-1}+ATO 2 mg kg^{-1} (42.83±0.4773) when compared to other treatment groups (Fig. 1c).

Treatment with either camel milk or atorvastatin (at three escalating doses each), alone or in combination, resulted in a significant reduction ($p<0.05$) in LDL cholesterol level in all treatment groups when compared to vehicle-treated hyperlipidemic rats (148.8±6.524 mg dL^{-1}). There was also significant reduction in LDL ($p<0.05$) in the groups that received CM 1.5 mL kg^{-1} (35.17±4.983), ATO 20 mg kg^{-1} (28.33±3.801) and CM 1.5 mL kg^{-1}+ATO 20 mg kg^{-1} (22.00±2.490) when compared to other treatment groups (Fig. 1d).

The mechanism of hypolipidemic activity of camel milk might be due to inhibition of HMG-CoA reductase stimulation of cholesterol-7-alpha-responsible for conversion of cholesterol to bile acid, decrease intestinal absorption of cholesterol, increase in expression of LDL receptors on the hepatocyte surface, resulting in increased clearance of LDL from the blood[16]. A previous study by Zuberu *et al.*[22] found the mechanism of CM hypolipidemic effect due to the presence of vitamins C and E both of which were reported to have a hypolipidemic effect.

Increased HDL level may be due to a decrease in plasma level of LDL in circulation. The HDL is cardio-protective cholesterol (good cholesterol) that transports cholesterol from the peripheral circulation and tissue to the liver, where it is

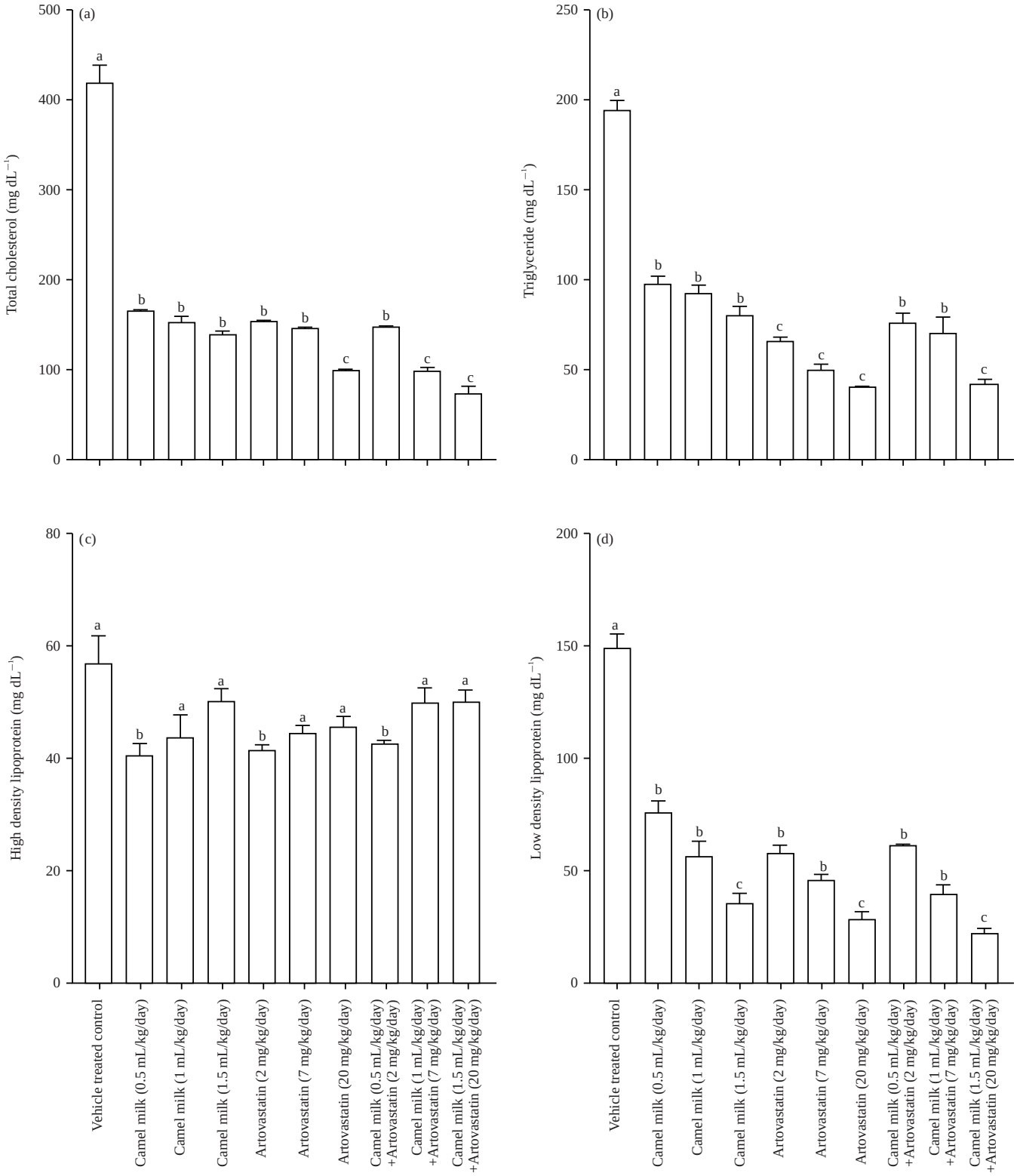

Fig. 1(a-d): Effect of co-administration of camel milk and atorvastatin on (a) Total blood cholesterol, (b) Triglyceride, (c) HDL and (d) LDL in high fat diet-induced hyperlipidemic rats at day 21 of treatment

Data are presented as Mean±SEM, [b,c]Signify $p<0.05$ when compared with the vehicle-treated hyperlipidemia group, n = 6, one way ANOVA and Tukey Krammer multiple comparison *post hoc* tests were used to arrive at the p-value

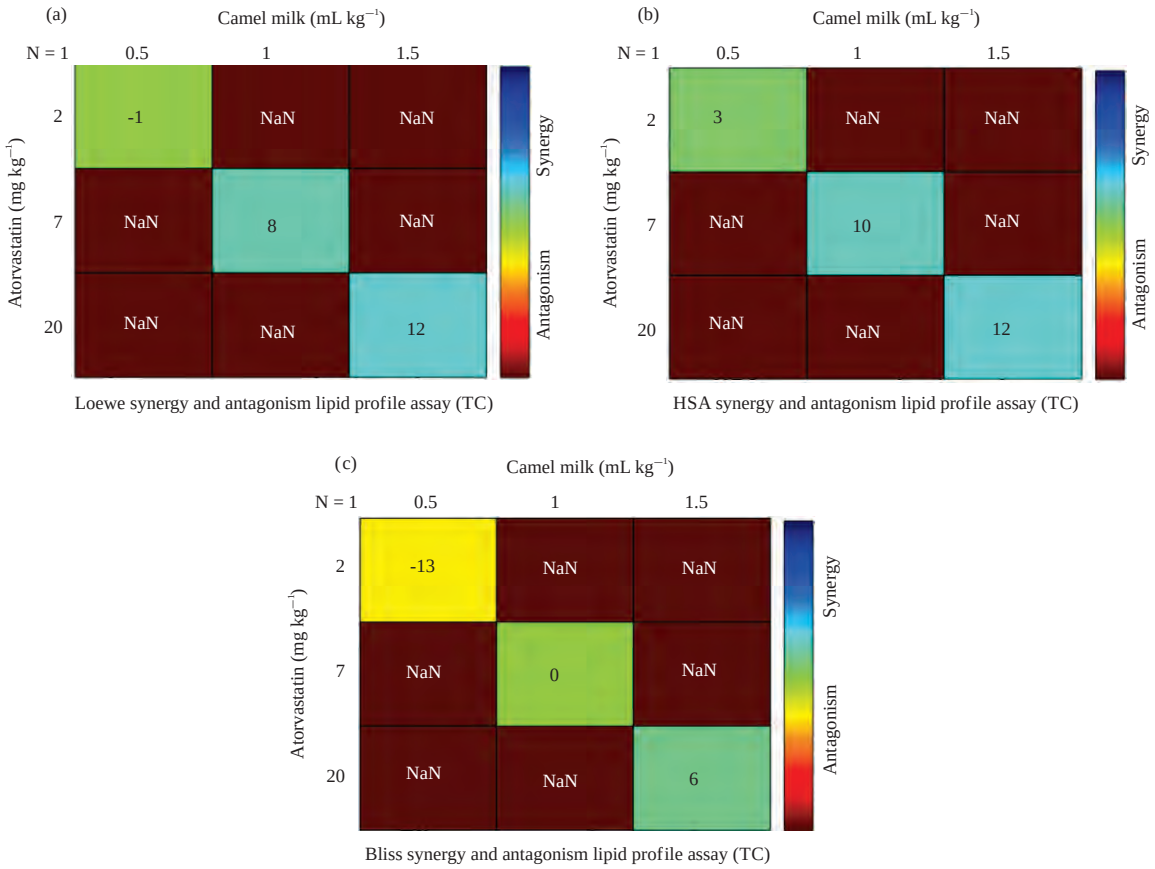

Fig. 2(a-c): Synergy and antagonism matrix of the change in total cholesterol following 21 days concurrent treatment of fresh camel milk and atorvastatin in high fat diet-induced hyperlipidemic rats, (a) Loewe, (b) HSA and (c) Bliss
Values > or < 0 indicate synergism or antagonism, respectively

catabolized into bile acid. This hypolipidemic effect signifies that camel milk has a significant role in preventing cardiovascular diseases.

Co-administration of CM escalating doses of CM and escalating doses of ATO to hyperlipidemic rats reduces TC, TG and LDL much lower at higher dose group (CM 1.5 mL kg^{-1}+ATO 20 mg kg^{-1}) compared to those treated with CM alone. This shows that combination therapy with CM and ATO enhances the hypolipidemic activity of CM, which, to the best of our knowledge, is the first finding of its kind. This finding resembles the finding of Mohamed *et al.*[31] using a different plant extract co-administered with ATO[37]. HDL level is, however, not much affected in the treatment groups when compared to vehicle-treated hyperlipidemic groups this may suggest that mechanism of hypolipidemic action of CM involving HDL may be antagonistic.

Loewe, HSA and bliss synergy and antagonism metrics: Using the Loewe model, the value of the sum of synergy and antagonism of the change in total cholesterol with escalating doses of camel milk and atorvastatin when co-administered in high fat diet-induced hyperlipidemic rats for 21 days was 1.158312663. The values of the maximum synergism and antagonism were 11.59701473 and -5.144005226, respectively (Fig. 2a). Using the HSA model, the value of the sum of synergy and antagonism was 1.517520663. The values of the maximum synergism and antagonism were 12.06755498 and -5.144005226, respectively (Fig. 2b). Using the Bliss model, the value of the sum of synergy and antagonism was -0.436099415. The values of the maximum synergism and antagonism were 5.954649559 and 12.98533667, respectively (Fig. 2c).

Using the loewe model, the value of the sum of synergy and antagonism of the change in triglyceride with escalating doses of camel milk and atorvastatin when co-administered in high fat diet-induced hyperlipidemic rats for 21 days was -1.975365313. The values of the maximum synergism and antagonism were 5.866680241 and -14.42873177, respectively

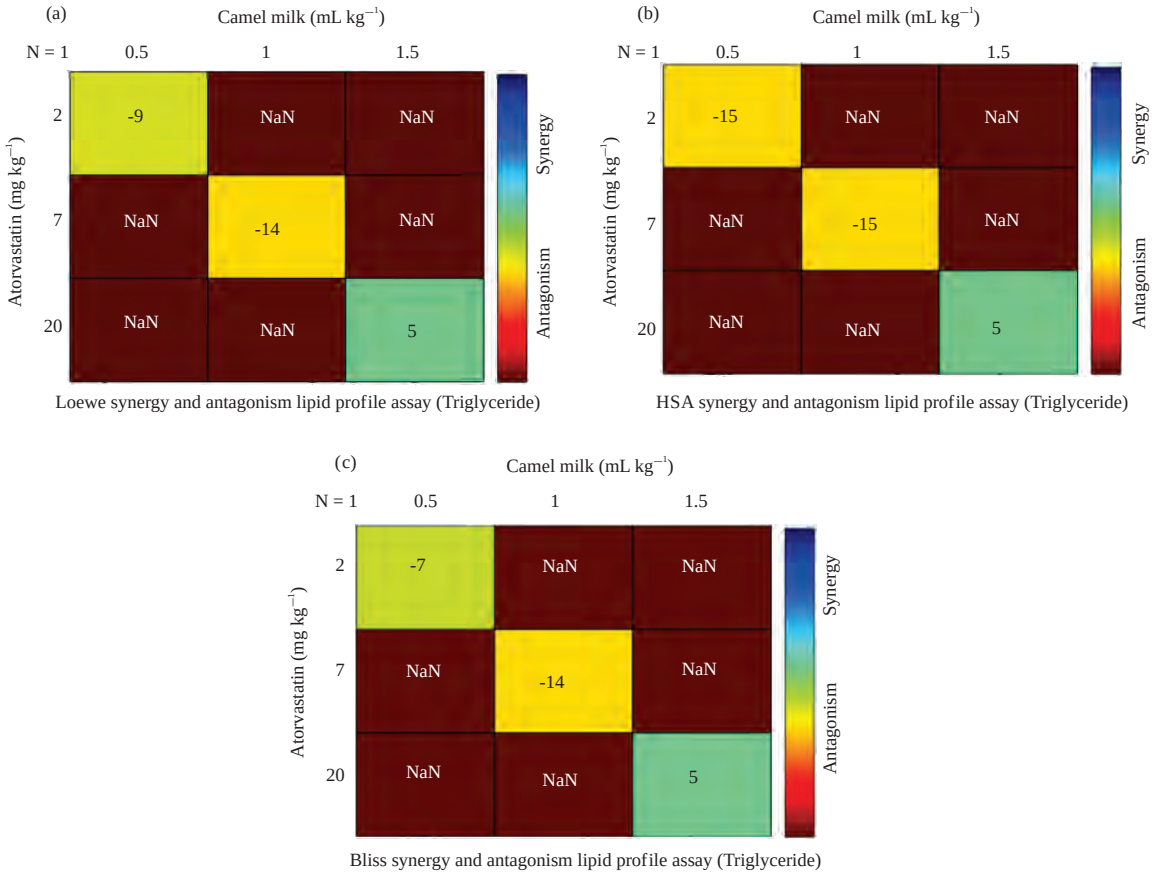

Fig. 3(a-c): Synergy and antagonism matrix of the change in triglyceride following 21 days concurrent treatment of fresh camel milk and atorvastatin in high fat diet-induced hyperlipidemic rats, (a) Loewe, (b) HSA and (c) Bliss
Values > or < 0 indicate synergism or antagonism, respectively

(Fig. 3a). Using the HSA model, the value of the sum of synergy and antagonism was -1.915912904. The values of the maximum synergism and antagonism were 5.866680241 and -14.4287196, respectively (Fig. 3b). Using the bliss model, the value of the sum of synergy and antagonism was -2.235888964. The values of the maximum synergism and antagonism were 5.866680241 and -14.68884261, respectively (Fig. 3c).

Using the LOEWE model, the value of the sum of synergy and antagonism of the change in high-density lipoprotein cholesterol (HDL-C) with escalating doses of camel milk and atorvastatin when co-administered in high fat diet-induced hyperlipidemic rats for 21 days was 43.19495553. The values of the maximum synergism and antagonism were 883.7349398 and 0, respectively (Fig. 4a). Using the HSA model, the value of the sum of synergy and antagonism was 73.63253211. The values of the maximum synergism and antagonism were 883.7349398 and 0, respectively (Fig. 4b). Using the bliss model, the value of the sum of synergy and antagonism was 73.63253211. The values of the maximum synergism and antagonism were 883.7349398 and 0, respectively (Fig. 4c).

Using the LOEWE model, the value of the sum of synergy and antagonism of the change in low-density Lipoprotein cholesterol (LDL-C) with escalating doses of camel milk and atorvastatin when co-administered in high fat diet-induced hyperlipidemic rats for 21 days was -0.739125766. The values of the maximum synergism and antagonism were 4.707320707 and -9.236144018, respectively (Fig. 5a). Using the HSA model, the value of the sum of synergy and antagonism was 0.279049237. The values of the maximum synergism and antagonism were 7.781126729 and -4.111520043, respectively (Fig. 5b). Using the BLISS model, the value of the sum of synergy and antagonism was -2.131608892. The values of the maximum synergism and antagonism were 3.587180584 and -18.58899027, respectively (Fig. 5c).

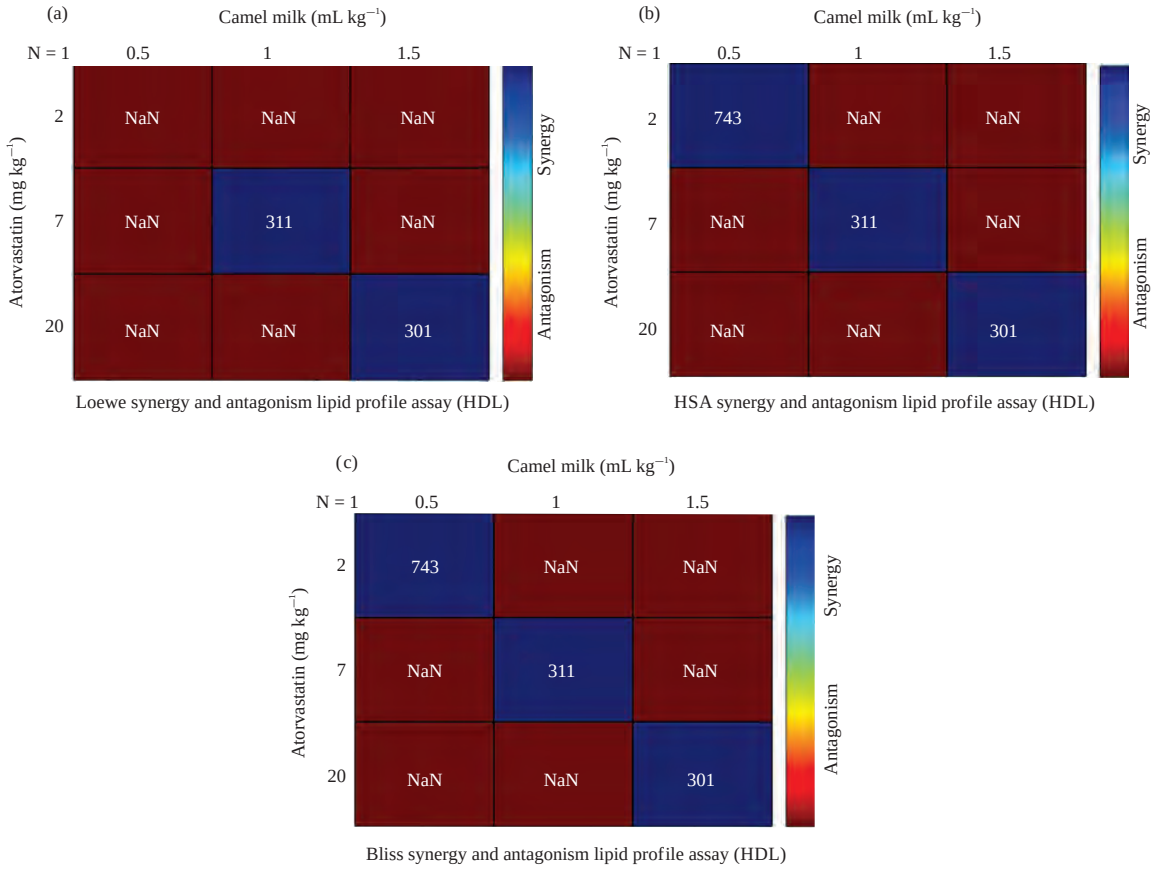

Fig. 4(a-c): Synergy and antagonism matrix of the change in HDL-C following 21 days concurrent treatment of fresh camel milk and atorvastatin in high fat diet-induced hyperlipidemic rats, (a) Loewe, (b) HSA and (c) Bliss
Values > or < 0 indicate synergism or antagonism, respectively

Using Loewe and HSA models of synergism assessment, this study found out that, CM has synergistic activity with ATO in reducing TC, also using the HSA model only, it showed synergistic action in reducing LDL-C as observed by the sum of synergism and antagonism to be greater than zero. To the best of our knowledge, this is the first study to report the synergistic effect of combining camel milk and atorvastatin in reducing hyperlipidemia.

Effect of co-administration of camel milk and atorvastatin on body weight and BMI of high-fat diet-induced hyperlipidemia rat at day 21 of treatment: Treatment with either camel milk or atorvastatin (at three escalating doses each), alone or in combination resulted in a significant reduction ($p<0.05$) in mean body weight of rats in the groups that received ATO 20 mg kg^{-1}, CM 1 mL kg^{-1}+ATO 7 mg kg^{-1} and CM 1.5 mL kg^{-1}+ATO 20 mg kg^{-1} when compared to the vehicle-treated hyperlipidemic group after 21 days of treatment. Twenty eight days feeding with HFD results in a significant increase ($p<0.05$) in body weight of all groups when compared to the normal control group (Table 3). Also, treatment with either camel milk or atorvastatin (at three escalating doses each), alone or in combination resulted in a significant reduction ($p<0.05$) in BMI of rats in the groups that received ATO 20 mg kg^{-1}, CM 1 mL kg^{-1}+ATO 7 mg kg^{-1} and CM 1.5 mL kg^{-1}+ATO 20 mg kg^{-1} when compared to the vehicle-treated hyperlipidemic group after 21 days of treatment. 28 days feeding with HFD results in a significant increase ($p<0.05$) in BMI of all groups when compared to the normal control group (Table 4).

On the changes in body weight and BMI, here, a significant loss in body weight and BMI was observed following coadministration of CM with ATO when compared with control. This showed that obesity has been alleviated in the combination therapy group when compared to camel milk only and untreated hyperlipidemic groups. To the best of my knowledge, this is the first reported finding of the ability of CM to enhance the antiobesity effect of ATO in obese rats.

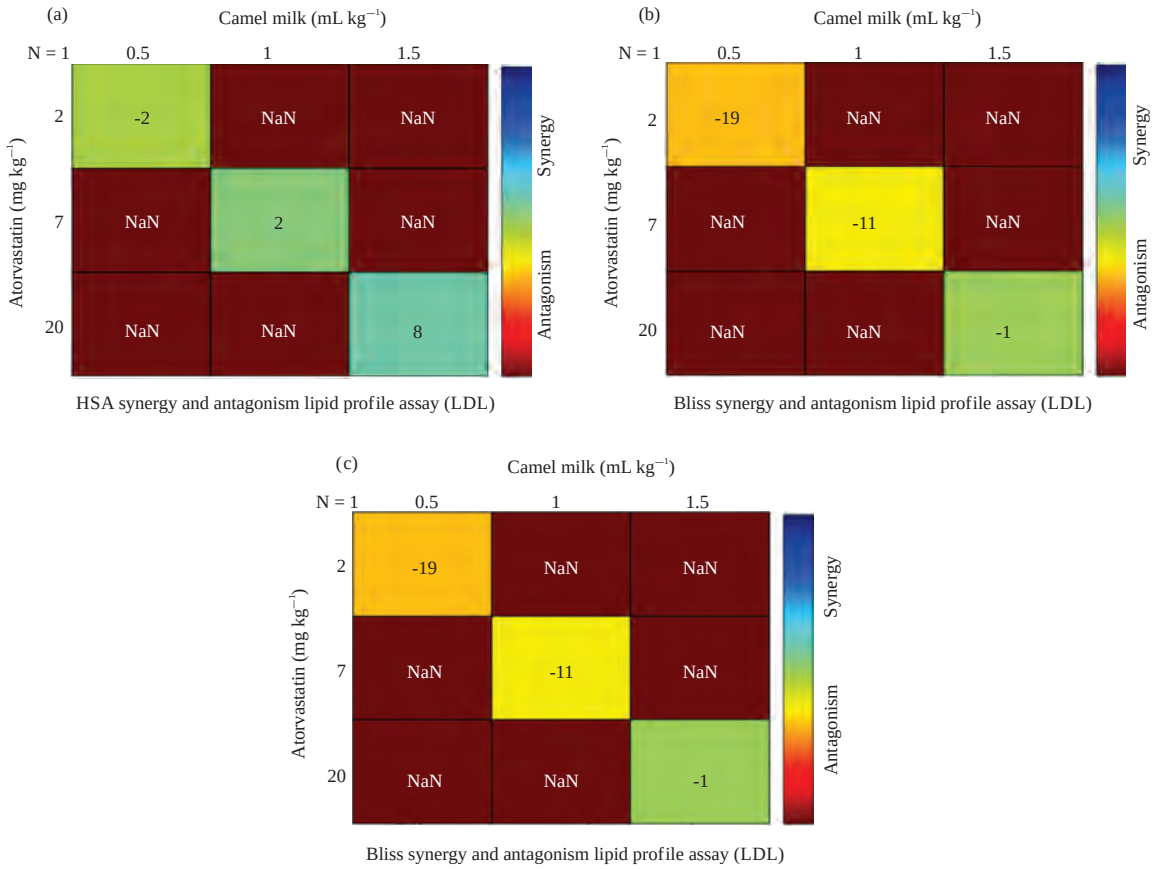

Fig. 5(a-c): Synergy and antagonism matrix of the change in LDL-C following 21 days concurrent treatment of fresh camel milk and atorvastatin in high fat diet-induced hyperlipidemic rats, (a) Loewe, (b) HSA and (c) Bliss
Values > or < 0 indicate synergism or antagonism, respectively

Table 3: Effect of co-administration of camel milk and atorvastatin on body weight of high-fat diet-induced hyperlipidemic rats at day 21 of treatment

	Body weight of the rats		
Treatment groups	Day 0	Day 28	Day 49
Normal control	121.8±2.18	164.7±4.08^{a}	168.2±6.65
Negative control	164.0±1.46	253.3±1.20^{b}	277.5±4.27^{c}
HFD+CM 0.5 (mL kg^{-1})	180.7±2.64	257.8±3.32^{b}	234.2±2.10^{c}
HFD+CM 1 (mL kg^{-1})	154.2±2.30	256.0±2.84^{b}	235.7±2.11^{c}
HFD+CM 1.5 (mL kg^{-1})	173.8±0.87	265.7±4.84^{b}	226.2±1.49^{c}
HFD+ATO 2 (mg kg^{-1})	165.7±0.92	235.8±15.91^{b}	219.3±0.61^{c}
HFD+ATO 7 (mg kg^{-1})	184.8±0.95	244.3±2.79^{b}	231.0±10.47^{c}
HFD+ATO 20 (mg kg^{-1})	171.5±3.58	238.7±3.25^{b}	215.8±2.55^{d}
HFD (CM 0.5 (mL kg^{-1})+ATO 2 (mg kg^{-1}))	176.8±3.79	237.3±2.82^{b}	189.8±19.15^{c}
HFD (CM 1 (mL kg^{-1})+ATO 7 (mg kg^{-1}))	133.7±10.15	237.3±3.52^{b}	171.2±12.40^{d}
HFD (CM 1.5 (mL kg^{-1})+ATO 20 (mg kg^{-1}))	147.2±4.25	242.2±5.41^{b}	148.3±5.30^{d}

Before induction of hyperlipidemia (Day 0), after induction (Day 28) and after treatment (Day 49) of Wistar rats. HFD: Hyperlipidemic group, CM: Camel milk, ATO: Atorvastatin, ^{a,b,c,d}Represent the level of significance, different alphabets across columns signify differences in the level of significance. Results are expressed as Mean±Standard error of the mean, n = 6. One way ANOVA with Tukey's multiple comparison post hoc tests was used to arrive at the p-value

However, studies by Fallah *et al.*[38] and Korish[39] report the antiobesity effect of camel milk given alone in obese rats.

It, therefore, implies that the findings in this study can be applied in terms of the use of camel milk either alone or in combination with atorvastatin in the management of obesity and hyperlipidemia. The limitation of this study is its pre-clinical nature and animal studies, further advanced studies to isolate the possible compound in the camel

Table 4: Effect of co-administration of camel milk and atorvastatin on body mass index of high-fat diet-induced hyperlipidemic rats at day 21 of treatment

	Body mass index (kg/m^2)		
Treatment groups	Day 0	Day 28	Day 49
Normal control	4.28±0.28	5.05±0.14^a	5.17±0.15
Vehicle treated control	4.55±0.27	5.77±0.16^b	7.12±0.38^a
HFD+CM 0.5 (mL kg^{-1})	4.80±0.38	6.90±0.14^b	6.18±0.42^a
HFD+CM 1 (mL kg^{-1})	4.70±0.50	6.20±0.09^b	6.75±0.64^a
HFD+CM 1.5 (mL kg^{-1})	4.88±0.37	6.65±0.15^b	6.13±0.54^a
HFD+ATO 2 (mg kg^{-1})	4.63±0.39	5.73±0.45^b	5.98±0.43^a
HFD+ATO 7 (mg kg^{-1})	4.80±0.27	6.07±0.15^b	6.08±0.44^a
HFD+ATO 20 (mg kg^{-1})	4.28±0.35	6.83±0.56^b	4.88±0.13^b
HFD (CM 0.5 (mL kg^{-1})+ATO 2 (mg kg^{-1}))	5.35±0.39	6.67±0.50^b	5.35±0.49^a
HFD (CM 1 (mL kg^{-1})+ATO 7 (mg kg^{-1}))	3.43±0.26	7.32±0.53^b	4.40±0.38^b
(HFD (CM 1.5 (mL kg^{-1})+ATO 20 (mg kg^{-1}))	3.43±0.75	6.12±0.33^b	4.03±0.37^b

Before induction of hyperlipidemia (Day 0), after induction (Day 28) and after treatment (Day 49) of Wistar rats, HFD: Hyperlipidemic group, CM: Camel milk, ATO: Atorvastatin, ^{a,b}Represent the level of significance, different alphabets across columns signify differences in the level of significance. Results are expressed as Mean±Standard error of the mean, n = 6. One way ANOVA with Tukey's multiple comparison post hoc tests was used to arrive at the p-value

milk responsible for the synergistic action and probable mechanism of action is recommended.

CONCLUSION

It can now be therefore concluded from this study that, combination therapy of camel milk and atorvastatin was synergistic in reducing hyperlipidemia with obesity. It also showed synergistic action of camel milk with atorvastatin in reducing hyperlipidemia and obesity in high-fat diet-induced hyperlipidemic rats.

SIGNIFICANCE STATEMENT

This study discovers the possible synergistic effect of camel milk and atorvastatin combination that can be beneficial for hyperlipidemic and obese rats. This study will help to uncover the critical area in the management of metabolic syndrome using camel milk that many researchers have not explored. Thus, a new theory on camel milk combination and possibly other combinations, may be arrived at.

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