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ORIGINAL ARTICLE

Development and Assessment of Polyherbal Syrup for Hyperlipidemia Management in Animal Model Rabbit

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ABSTRACT

Background: Hyperlipidemia is known as one of major factor causing heart attack and stroke. It is described by an increase in blood cholesterol, low-density Lipoprotein (LDL), and decrease in high-density lipoprotein (HDL) levels. In hypercholesterolemia, elevated cholesterol levels can disrupt neurotransmitter balance, contributing to increased oxidative stress and inflammation in the brain. Certain neurotransmitters, such as serotonin and dopamine, may have antioxidant and anti-inflammatory effects, helping to mitigate these effects.

Objective: Formulation and evaluation of herbal syrup for physicochemical, toxicological and efficacy study in hyperlipidemic rabbit model

Methodology: In this study polyherbal syrup containing *Trigonella foenum-graecum* seeds, *Allium sativum* buds and *Aloe vera* gel is formulated and further evaluated for its acute oral toxicity and efficacy studies in maleWistar rats and Triton induced hyperlipidemia in rabbits respectively.

Results: Polyherbal syrup was developed at laboratory scale further assessed for its physicochemical characteristics like pH, viscosity, density, stability and organoleptic properties. During these studies this formulation was found stable and further used for acute oral toxicity and efficacy studies in albino rats and rabbits. Acute oral toxicity study was conducted in albino wistar female rats as per OECD guidelines 423. Based on clinical findings, it is inferred that the LD50 dose for the herbal syrup exceeds 5,000 mg/kg. For efficacy study, hyperlipidemic rabbit model was prepared by injecting Triton WR-1339 (200 mg/kg i.p.).15 days pretreatment of polyherbal syrup clearly indicates that the cholesterol level was significantly lower in test group (39.2±7.46 mg/dl) and standard group (34.2±3.19 mg/dl) compared with that of control group (119±9.61mg/dl). The triglyceride level was also significantly decreased in test group (68.2±7.64mg/dl) and standard group (74±19.73mg/dl) groups as compared to control group (185.6±13.9 mg/dl).The low-density Lipoprotein (LDL) level was also significantly decreased in test (24.6±6.91mg/dl) and standard groups(43.4±9.36 mg/dl) as compared to control group (127±13.5mg/dl).The high-density lipoprotein (HDL) level was increased in test (27.2±6.30 mg/dl) and standard groups (32.7±7.07 mg/dl) as compared to control group (17.8±3.96 mg/dl).

Conclusion: The results achieved from this study indicate that regular use of this polyherbal syrup may be helpful in managing hyperlipidemia and viable replacement to synthetic medicines.

Keywords: Polyherbal syrup, Triton WR-1339, acute oral toxicity, Hyperlipidemia

INTRODUCTION

Hyperlipidemia is a medical condition that is defined as an increase in concentration of lipids, or fat, in the blood. Depending of the lipid involved, it can be further divided into hypertriglyceridemia and hypercholesterolemia. This condition may be caused by abnormality in fat metabolism which results in overproduction of lipoproteins or their proper degradation cannot occur at any of the steps [1]. Hyperlipidemia is diagnosed by the determination of blood lipid profiles such as; high density lipoprotein cholesterol (HDL), low density lipoprotein (LDL), total cholesterol, and triglycerides [2]. In clinical practice, the widely accepted Frederickson's classification identifies six types of hyperlipidemia: I, II, IIa, IIb, III, IV, V. [3]. In terms of its etiopathogenesis they can be said to be; idiopathic, primary, genetic or familial, and secondary or acquired hyperlipidaemia. Secondary hyperlipidemia has been described with metabolic conditions such as type 2 diabetes mellitus and alcohol intake, drugs used for various ailments [1]. There are the sources of elevated hyperlipidemia including smoking, high intake of fatty foods, lack of regular bodily activities and thus central obesity [4-5].

People with hyperlipidemia are at risk for coronary heart disease (CHD) and extra-coronary atherosclerosis, both of which can be potentially fatal [6]. Reducing the probability of getting CHD requires employing proper nutrition and lifestyle practices which does not involve engaging in the use of tobacco and or its products, moderate use of alcohol, avoiding foods rich in simple carbohydrates and cutting down on excess use of table salt. These measures form the basic approach that is taken to cater for hyperlipidemia.

Among all the medications used for the management of hyperlipidemia, statins and fibrates are considered the most effective [2]. Despite their use for more than forty years, these therapies which include statins have various side effects among them are the induction of diabetes, statin induced myalgia and possibility of hepatotoxicity, nephrotoxicity and neurotoxicity [7]. In addition, one must differentiate between individual therapies, while some patients were intolerant to statin therapy; this was manifest in a third of the patients. This is the case because the primary complication of statin therapy to date remains its toxicological considerations. Since there are several consequences of hyperlipidemia and the adverse effects associated with the pharmacological management, a large number of hyperlipidemic patients seek for herbal products either as an option or adjuvant to the conventional regimen. The public approve herbs as natural foods with little negative repercussions and are preferred due to their relative cheapness and because they are environmentally sound [8]. With regard to this; medicinal herbs in different combination are being look over as an impending alternative approach for formulation of polyherbal syrup that may be used for antihyperlipidemia. It is also recognized that plant extracts in different combination are supercilious to individual plant extract, and exert improved curative effects as compare to single plant/herb [9-10].

The present study is proposed with the aim to formulate polyherbal syrup containing *Trigonella foenum-graecum* seeds, *Allium sativum b*uds and *Aloe vera* gel and investigating its physicochemical characteristics followed by acute oral toxicity in male Wistar rats and effectiveness in male rabbits. Many other studies further noted that detailed toxicological assessment must be conducted by employing the most appropriate model of animals to offer the proper‘safety dosage’ of the compound for human use.

Trigonella foenum-graecum in common language is called as methi or fenugreek used in human food for flavor. Various ailments of day to day life have been treated using this product as described in literature. Some of the chronic health conditions are; cardiovascular diseases, high cholesterol levels, high blood sugars, liver disorders, and hormonal problems such as hypogonadism [11]. *Trigonella foenum-graecum* is viewed as a heavy source of dietary fiber and essential nutrients for the growth and development process. It is a rich source of phytonutrient, alkaloids, carbohydrates, triterpene glycosides, amino-acids, and minerals used for nutritional and medicinal purpose [12].

Allium sativum (garlic) has been used throughout the world for the treatment of bronchial inflammation, high blood pressure, pulmonary tuberculosis, liver dysfunction, diarrhea, abdominal discomfort, intestinal worms, arthritis, diabetes mellitus and fever. These medicinal properties of garlic are due to its phytochemical constituents such as organosulfur and bioactive compounds which demonstrate diverse biological activities [13]. It is also documented that garlic has an impact like atorvastatin in regards to the

protection of lipemic-oxidative disorder in hypercholesterolemic rats [14].

Aloe vera gel is described by its pro Prism contents: it is primarily constituted by water (> 98%) and contains a number of putative active ingredients. Some of the bioactive compound groups found of interest are; vitamins, minerals, enzymes, polysaccharides, phenolic compounds, organic acids, amino acids, sterols and fatty acids [15]. Research studies show that there are many research studies linked to *Aloe vera* including; antioxidant, hypoglycemic and antihyperlipidemic [16-18].

METHODOLOGY

Trigonella foenum-graecum seeds, *Allium sativum* buds and *Aloe vera* were obtained from local market. All three plants were validated by botanist (Herbarium identification numbers are TF-164, AS-165 and AV-166 respectively). A herbal syrup containing extracts of *Trigonella foenum-graecum* seeds *Allium sativum* and *Aloe vera* gel is prepared.

Preparation of Syrup

Step I

Preparation of extract

The 500g fenugreek seeds were washed thoroughly and dried in shade then grinded in coarse powder. The powder material was soaked in n- hexane to remove lipids then filtered and dried again at room temperature for three days. Dried material was again poured in ethanol for five days with irregular mixing. The material was filtered through muslin cloth to separate organic debris from liquid part. This filtrate again filtered through whatman's filter paper of grade 1.The excess solvent was consequently evaporated on a rotary evaporator at 40ºC to achieve semisolid material which was kept in refrigerator at 4ºC.

For garlic extract, fresh garlic buds were purchased from local market washed thoroughly and dried in oven at 40ºC for two to three hours. After drying grinded in coarse powder and soaked 500g material in ethanol for five days. Material was filtered and evaporated on rotary evaporator at 40ºC under reduced pressure. Thick semisolid material was obtained and kept in refrigerator.

For *Aloe vera* gel preparation, fresh leaves of *Aloe vera* were obtained from PCSIR premises then washed and further proceeded for gel collection. The colorless gel was separated from the thick outer green cuticle. After grinding and filtration stored at 4^{o}C refrigerator.

Step II

Formulation

- Water and thickening agent were added in a sterilized container and heated to boil;
- Sorbitol was added with continuous mixing;
- Then one-by-one extracts were added to the above mixture with continuous mixing;
- Sodium Benzoate as a preservative initially dissolved in lukewarm water then added to the above mixture with regular mixing;
- Polysorbate as emulsifier was added
- The syrup was then cooled by using chilled water circulation;
- A flavoring agent was then added to mask the smell of herbal extracts.

Physicochemical Properties

This formulation was further evaluated for physicochemical parameters and organoleptic properties.

Determination of pH

pH of syrup was determined by using a calibrated digital pH meter in the right manner recommended by its manufacturer. Before employing the pH meter to measure the solution's pH, it was first standardized with buffer solutions with pH of 4, 7 and 9. Then, 1 ml of syrup was diluted with 100 ml deionized water, and the pH of the obtained solution was measured after immersing the electrodes into it.

Determination of density

Thus, in order to determine density of material, one has to know volume and weight of the certain substance. Specific gravity measuring bottle was rinsed properly with chromic acid then washed with distilled water two to three times. Mass of the empty bottle as well as the mass of the capillary tube stopper without the sample was recorded. Liquid to be tested was added into the bottle, and stopper was plugged tightly. Any droplet sticking on the exterior part of the bottle was cleaned by tissue paper. The most accurate method of measuring the volume was used; therefore, take the mass of the bottle and the liquid together using an analytical balance. Find the weight of the unknown liquid in grams. The density on the other hand can be found through combining the weight of the substance

with the volume to give a figure usually measured in gm/ml.

Formula for density:

Density of liquid under test (syrup) = weight of liquid under test /volume of liquid under test

Measurement of Specific Gravity

To calculate the specific gravity of a substance, weight of water and weight of test substance must be known. The specific gravity bottle was washed with chromic acid and rinsed with distilled water two to three times. The empty bottle was weighed with the capillary tube stopper. Then bottle with capillary tube stopper was weighed with water and liquid to be tested separately

Formula for specific gravity:

Specific gravity of liquid under test (syrup) = weight of liquid under test /weight of water

Measurement of Viscosity

Oswald viscometer is generally used to measure viscosity of a liquid with that of water for its determination. First, the viscosity of water is determined, by filling the Oswald viscometer with water up to the desired level (A), and noting the time taken for the water to rise from mark A to mark B. The same process is done on the liquid to be tested (syrup). Common salt solution is used as the standard to which the viscosities of other liquids are compared to. The viscosity of the liquid can be determined using a formula having the observed time multiplied by the viscosity of the water.

Formula for viscosity = Density of test liquid x Time required to flow test liquid x Viscosity of water

Density of water x Time required to flow water

Organoleptic Properties

a) Color examination:Five ml syrup was taken into watch glasses and kept against white back ground in white tube light. Then observed with naked eye for its color.

b) Odour examination: Two ml of syrup was smelled. 2 minutes time interval was kept among two smelling to abolish the effect of previous smelling.

***c) Taste examination*:** Few drops of syrup was taken and placed on taste buds of the tongue.

Stability testing

The stability of the prepared herbal syrup was checked by exposing sample to different temperature conditions. The syrup was dispensed into test tubes and place at 4°C, room temperature, and 47°C. Physicochemical parameters, turbidity, and homogeneity for any alterations were assessed at 24-hour, 36-hour, and 72-hour intervals. Results are mentioned in Table **2**

In vivo studies

Animal selection

The albino rats are commonly used for toxicity studies suggested by the international guidelines (OECD 423)[19]. Healthy nulliparous and non-pregnant female Wistar Albino rats having body weight of 160-180 g and age between 8–12 weeks were selected for acute oral toxicity study. These rats were kept individually in polypropylene boxes with food and water ad libitum., with a room temperature 22±2°C, 50±5% humidity under 12/12-hour light/dark cycle; For anti-hyperlipidemic activity,rabbits were selected. Approval for animal studies was taken from the Institutional Animal Ethical Committee (Approval No. IEC/AS-03)

Acute Oral Toxicity Study (Limit test at 5,000 mg/kg b. wt.)

As per OECD guidelines 423Limit test at 5,000 mg/kg was performed for a period of 14 days. Animals were arranged into two groups of three animals each (n=3): control and test group. Prior to dosing, animals were kept overnight in fasting. Following the period of fasting, body weight of each animal was noted and according to body weight dose was calculated. The polyherbal syrup was administered orally in a single dose volume 2 ml/100 gm body weight. After dose administration, food was withheld for a period of 3-4 hours. In control group only 2 ml distilled water was administered. After intake of herbal syrup, the rats were kept under observation for 24, 48, 72 hours.

Clinical observation and body weight

All animals were observed twice daily for behavioral responses morbidity and mortality throughout the experimental period for a total of 15 days. Observations were including changes in skin, fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activities. Bodyweight of all animals was noted on first day of experiment then weekly. All

the animals were found normal and healthy during the study period as shown in table:**4**

Gross Pathology

After 14 days of observation period, all animals were euthanized and gross macroscopic examination of visceral organs was conducted.

Anti-hyperlipidemic activity

Three groups of rabbits (1.5-2kg) were arranged having 05 rabbits in each group. Group 1 is control group administered orally distill water (3 ml/animal) once daily for 15 days. Group-II: is test group administered herbal syrup (3 ml/animal) once daily for 15 days. Group-III: served as standard group received atorvastatin (0.5 mg/kg body weight p.o.) once daily for 15 days. Doses were administered to each group of animals respectively for 15 days. On 15th day before dosing, blood samples were collected from the marginal ear vein of all rabbits. Triton WR-1339 (200 mg/kg) of Sigma-Aldrich in normal saline was injected intraperitoneally to all animals of each group immediately after the last dose of herbal syrup. Blood samples were again drawn from the marginal ear vein of all animals. 24 hours after Triton injection and analyzed for total cholesterol (TC), triglycerides (TG), HDL cholesterol and LDL cholesterol.

Statistical Analysis

All numerical data were calculated for the mean ± SD values and statistically analyzed by student t test. The p values at <0.05 were considered significant (*) when compare with respective controls.

RESULTS

Physicochemical analysis

Appearance of formulated syrup regarding color, odor and taste is acceptable. The pH of the syrup is suitable for oral use. The viscosity is also fine for storage and use.

Stability Study

The prepared herbal syrup formulation was clear having no particulates. Stability assessments were conducted for 24, 36, and 72 hours at 4°C, 47°C and at room temperature [20].Throughout the study, no alterations were noted in its physical characteristics (color, odour, taste) or pH. Notably, it remained clear and free from turbidity even at the lower temperature of 4°C. Similarly, at the elevated temperature of 47°C, it maintained its homogeneous clarity. Therefore, it can be affirmed that the herbal syrup achieved a desirable state of stability following its development.

Table 1. Physicochemical Parameters of syrup formulation.

Sr.#	Parameters	Observation/Value
1	pH	6.1
2	Viscosity	88.8 cps
3	Density	1.13064
4	Specific Gravity	1.18
5	Organoleptic Properties: Color Odour Taste	• Yellow • Aromatic • Bitter

Table 2. Stability Study

Time period (in hour)	Temperature (°C)	Physicochemical parameters				
		Color	Odour	Taste	pH	Turbidity
24	04◦C	No change	No change	No change	6.1	No Turbidity
	Room Temp	-do-	-do-	-do-	6.1	-do-
	47◦C	-do-	-do-	-do-	6.1	-do-
36	04◦C	-do-	-do-	-do-	6.1	-do-
	Room Temp	-do-	-do-	-do-	6.1	-do-
	47◦C	-do-	-do-	-do-	6.1	-do-
72	04◦C	-do-	-do-	-do-	6.1	-do-
	Room Temp	-do-	-do-	-do-	6.1	-do-
	47◦C	-do-	-do-	-do-	6.1	-do-

Table 3. Behavioral observations of Test Group for the limit test at 5,000 mg/kg b. wt.

Responses	30 min	4 hr	24 hr	48 hr	One wk	Two wk
Skin & Fur	Normal	Normal	Normal	Normal	Normal	Normal
Alertness	Active	Active	Active	Active	Active	Active
Eyes	Normal	Normal	Normal	Normal	Normal	Normal
Mucous Membrane	Normal	Normal	Normal	Normal	Normal	Normal
Salivation	Nil	Nil	Nil	Nil	Nil	Nil
Behavior	Normal	Normal	Normal	Normal	Normal	Normal
Tremor	Nil	Nil	Nil	Nil	Nil	Nil
Convulsion	Nil	Nil	Nil	Nil	Nil	Nil
Diarrhea	Nil	Nil	Nil	Nil	Nil	Nil
Lethargy	Nil	Nil	Nil	Nil	Nil	Nil
Sleep	Normal	Normal	Normal	Normal	Normal	
Coma	Nil	Nil	Nil	Nil	Nil	Nil

Acute oral toxicity Study (Maximum Limit test at 5,000 mg/kg body weight)

The acute oral toxicity study of polyherbal syrup containing *Aloe vera* gel, *Allium sativum*, and *Trigonella foenum-graecum* in female Wistar rats was conducted at different dose levels. Revealed no negative effects on the rats' reported mortalities and behavioral responses over a 14-day period. Examining the rats physically revealed no abnormalities in their eyes, skin, fur, mucous membranes, behavior patterns, tremors, salivation, or diarrhea. No animal showed, any changes in body weight as showed in table **3**; however, on days 7 and 14, there were noticeable weight increases relative to baseline (day 1) body weight. At 15th day, all albino rats were euthanized and necropsy was done. During necropsy detailed observations of individual gross pathological findings were conducted: no gross pathological lesions were found all visceral organs. Based on these findings, it is inferred that the LD50 dose for the herbal syrup exceeds 5,000 mg/kg. Consequently, the herbal syrup demonstrated practically non toxic according to Hodge and Sterner toxicity scale and can be classified in Category 5 of Globally Harmonized Classification System (GHS). Essentially, the method doesn't aim to calculate an exact LD50; it does facilitate identifying specific exposure ranges likely to result in lethality. The higher dose limit test, such as 5,000 mg/kg b. wt., is primarily utilized when there's prior indication that the test material is probably non-toxic.

Efficacy Study of Polyherbal Syrup Formulation

The results indicated that intraperitoneal injection of Triton WR-1339 produced hyperlipidemia in all animals of three groups but Total Lipid Profile of control group was significantly higher than the Total Lipid Profile of standard and test group. 24 hours after Intraperitoneal injection of Triton WR-1339 in rabbits total cholesterol raised from 27.6 to 119 mg/dl, triglyceride increased from 60.2 to 185.6 mg/dl and LDL level was also increased from 19.8 to 127 mg/dl in control group as compared to test and standard groups (Table **4**).

Table 4. Effect of pre& post intraperitoneal injection of Tritonon lipid profile of rabbits

Parameters (mg/dL)	Control Group		Test Group		Standard Group	
	Pre I.P injection	Post I.P injection	Pre I.P injection	Post I.P injection	Pre I.P injection	Post I.P injection
TC	27.6±6.02	119±9.61	29.66±8.16	39.2±7.46	28.16±5.73	34.2±3.19
TG	60.2±4.81	185.6±13.9	65.8±5.11	68.2±7.64	72.6±16.36	74±19.73
LDL	19.8±3.7	127±13.5	21.2±5.26	24.6±6.91	23.08±4.65	26.6±4.4
HDL	35.6±7.02	17.8±3.96	30.6±7.53	27.2±6.30	39.3±8.57	32.7±7.07

All data were statistically analyzed by student t test. The p values at <0.05 were considered significant.(*)

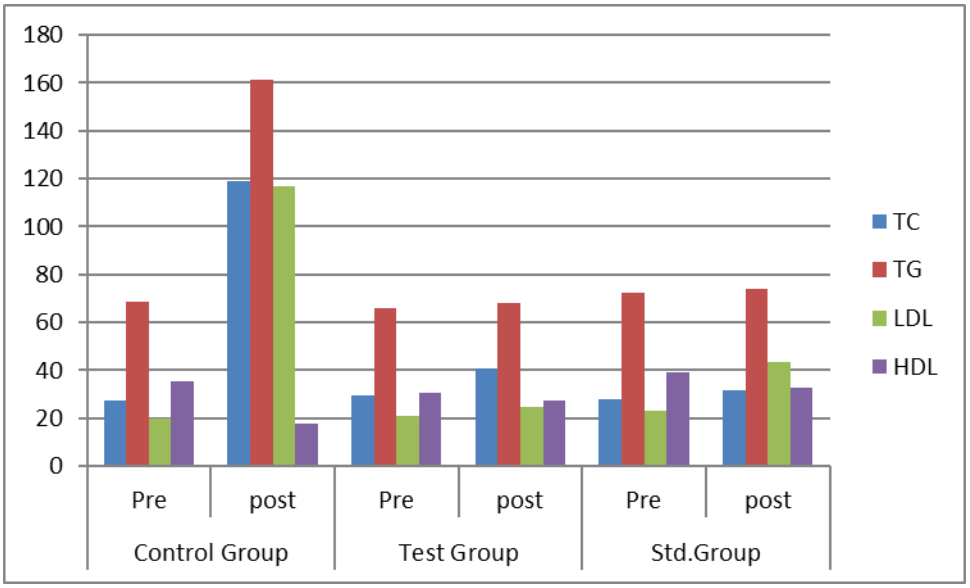

Figure 1. Efficacy study of Polyherbal Syrup in Rabbit Model

The herbal syrup formulation showed remarkable results by improving the lipid profile in test group as compare to control group. The total cholesterol concentration was significantly lower in test group (39.2±7.46 mg/dl) and standard group (34.2±3.19 mg/dl) compared with that of control group (119±9.61mg/dl). The triglyceride concentration was also significantly decreased in test group (68.2±7.64mg/dl) and standard group (74±19.73mg/dl) groups as compared to control group (185.6±13.9 mg/dl).The level of LDL was also significantly lower in test (24.6±6.91mg/dl) and standard (43.4±9.36 mg/dl) groups as compared to control group (127±13.5mg/dl).The HDL concentration was significantly increased in test (27.2±6.30 mg/dl) and standard (32.7±7.07 mg/dl) groups as compared to control group (17.8±3.96 mg/dl) asshowed in Tab. **4**.

DISCUSSION

This study aims to development and evaluation of polyherbal syrup for its physico-chemical properties, acute oral toxicity, and anti-hyperlipidemic activity.

Acute oral toxicity of polyherbal syrup in Wistar Albino rats is evaluated at limit dose 5000mg/kg followed by a 14-days observation period according to OECD Guideline 423. Our results demonstrate that the polyherbal formulation does not find acutely toxic to female Wistar rats at maximum dose limit (5000mg/kg) according to the Globally Harmonized System (GHS) for chemical classification (OECD Guideline 423) as mentioned in table **3**.

For efficacy study of polyherbal syrup against hyperlipidemia, Triton WR-1339 was used to develop hyperlipidemia in rabbits. Triton WR-1339 is commonly used to produce acute hyperlipidemia in animal models for the screening of herbal and synthetic drugs. This chemical inhibits lipase activity and prevents the uptake of lipoproteins from the bloodstream, leading to increase in lipids circulating in blood, a main risk factor for various heart problems [21].

In current study, 24 hours after Intraperitoneal injection of Triton WR-1339 in rabbits , we observed a 4.3 times increase in total cholesterol, a 5.91 times increase in LDL cholesterol, and a 2.35 times increase in triglycerides in control group. Instead of this in test and standard groups increase in total cholesterol, triglycerides and LDL cholesterol comparative to control group is less Additionally, HDL cholesterol levels were 2.5 times lower than those in the control group. These results are in accordance with those reported by other researchers [22].

These findings indicate that polyherbal syrup significantly decreased total cholesterol (TC), triglycerides (TG) and LDL cholesterol level in the test group as compare to the lipid profile of control group. Results are in accord with the findings of previous studies that showed improvements in TC and LDL cholesterol concentration after intake of fenugreek seeds and garlic in combination and alone [23-24].

Another study of 12 weeks was conducted in animal model for lipid profile assessment by feeding *Allium Sativum* only and by combining with atorvastatin reported a remarkable decrease in TC, TG, LDL and VLDL, and an increase HDL after 12 weeks of drug administration [25]. Few more studies conducted in rat model by feeding raw garlic with 2% cholesterol in diet showed significant improvement in lipid profile [26-27].Different studies conducted on *Aloe vera* indicate that it improves the immune system, raises HDL, lowers LDL, lowers blood sugar, and lowers blood sugar, reduction in high cholesterol with *Aloe vera* in take [28].The anti-hyperlipidemic effect of polyherbal syrup used in this study depend on various factors, notably their phytochemical constituents present in *Allium sativum*, Fenugreek seeds and *Aloe vera*. These constituents inhibit biosynthesis of cholesterol, impeding its absorption, and modulating the activity of lipogenic and lipolytic enzymes, thus reducing lipid metabolism. *Allium sativum* (garlic) is recognized for its disease-preventive phytochemicals, particularly water-soluble sulfur compounds that transform into allicin, an active ingredient with inhibitory effects on cholesterol biosynthesis enzymes like HMG-CoA reductase [29]. It also contains various other compounds such as saponins, alkaloids, tannins, steroids, flavonoids, and terpenoids, ketones and phlobutanin contributing to its anti-hyperlipidemic properties [30-32].

Trigonella foenum-graecum (Fenugreek seeds) a key component of the polyherbal formulation, is rich in important phytochemicals, including carbohydrates, proteins, lipids, alkaloids,steroids, flavonoids, fibres, steroidal saponins, vitamins, minerals and nitrogen compounds. GII compound identified from fenugreek seeds as capable of reducing total cholesterol levels and increasing HDL cholesterol, indicative of its positive impact on lipid profiles [33-34]. Steroids, for instance, decrease cholesterol absorption, promoting its excretion through feces, while saponins bind with cholesterol in the intestinal lumen, inhibiting its absorption into the bloodstream [35]. 45.4% dietary fiber is present in *Trigonella foenum-graecum* seeds by which 32% insoluble and 13.3% is soluble. The gummy part is composed of galactose and mannose which are important in reducing glycemia and cholesterolemia [36].

Aloe vera, another ingredient in the formulation, boasts glucomannan, anthraquinone, folic acid, and vitamins B3 and C, among others, which collectively aid in combating hyperlipidemia. Its diverse array of compounds including polysaccharides, flavonoids, and phytosterols further enhance its therapeutic potential in managing lipid levels [37]. Incorporating *Aloe vera* extract into the formulation was based on its demonstrated benefits in the treatment of hyperlipidemia, complementing the synergistic effects of other herbal constituents to address this condition effectively.

CONCLUSION

On the basis of above mentioned results it can be assumed that the Polyherbal syrup based on *Aloe vera* gel, *Allium sativum* buds, and *Trigonella foenum-graecum* seeds was found effective as that of standard in terms of managing Total Cholesterol, Triglyceride,LDL and HDL level without having any toxic effects.

REFERENCES

1. Nirosha K, Divya M, Vamsi S, and Sadiq M. A review on hyperlipidemia. International Journal of Novel Trends in Pharmaceutical Sciences.2014; 4:81–92.
2. Fischer S, Schatz U, Julius U. Practical recommendations for the man¬agement of hyperlipidemia. Atherosclerosis Supplements. 2015;18:194–198.
3. Jain KS, Kathiravan MK, Somani RS, ShishooCJ.The biology and chemistry of hyperlipidemia. Bioorganic & Medicinal Chemistry.2017; 15:4674–4699.
4. Karr S. Epidemiology and Management of Hyperlipidemia. The American Journal of Managed Care.2017; 23:S139-S148.
5. Alkushi, AG.Alternative Natural Management of Dyslipidemia. In: McFarlane, S.I. (Eds), Dyslipidemia (IntechOpen). 2019;Doi: 10.5772/intechopen.82430
6. Micallef MA, Garg ML.Beyond blood lipids: phytosterols, statins and omega-3 polyunsaturated fatty acid therapy for hyperlipidemia. The Journal of Nutritional Biochemistry.2009; 20:927–939.
7. Sirtori CR. The pharmacology of statins. Pharmacological Research.2014; 88:3–11.
8. Tiwari S. Plants: A rich source of herbal medicine. Journal of Natural Products.2008; 1:27–35.
9. Aparna P, Desu BSR. Assessment of Anti-Hyperlipidemic activity of a Polyherbal Formulation Ba019. Inter J Modern Pharm Res. 2020;4:37–39.

10. Kaur P, Robin, Mehta RG, Singh B, Arora S. Development of aqueous-based multiherbal combination using principal component analysis and its functional significance in HepG2 cells. BMC Comp Alternative Med. 2019;19(18):3–17.
11. Bahmani M, Shirzad H, Mirhosseini M, Mesripour A, Rafieian-Kopaei M. A review on ethnobotanical and therapeutic uses of fenugreek (Trigonella foenumgraceum L). J Evid Based Complementary Altern Med. 2016;21(1):53-62 doi: 10.1177/2156587215583405.
12. Shreya J, Swati P, Jyothi G, Vijay D. Preliminary Phytochemical and Pharmacognostic Studies on a Well Known Medicinal Plant Trigonella foenum-graecum. Int J Pharmacogn Chinese Med. 2019; 3(4): 1–7. DOI: 10.23880/ipcm-16000192
13. Vandana S, Kumar R. Study of Phytochemical Analysis and Antioxidant Activity of Allium sativum of Bundelkhand Region. International Journal of Life-Sciences Scientific Research.2017;3(6):1451–1458.
14. Jafari S, Farokhi F, Sadeghi A. Comparative effects of garlic (Allium sativum) powder and atorvastatin in female reproductive system of hypercholesterolemic rats: A histological and biochemical evaluation. Journal of Shahrekord University of Medical Sciences. 2021; 23(3):131–138. doi: 10.34172/jsums.2021.22
15. Maharjan H, Radha, Nampoothiri P, Laxmipriya. Evaluation of biological properties and clinical effectiveness of Aloe vera: A systematic review Journal of Traditional and Complementary Medicine. 2015; 5:21-26. doi: 10.1016/j.jtcme.2014.10.006
16. Hossen MM, Hossain ML, Mitra K , Hossain B , Bithi UH , Nazim Uddin M. Phytochemicals and in-vitro antioxidant activity analysis of Aloe vera by-products (skin) in different solvent extract. Journal of Agriculture and Food Research.2022;10:1-9.DOI:10.1016/j.jafr.2022.100460
17. Riyanto and Wariyah, Ch. Hypoglycemic effect of instant aloe vera on the diabetic rats. Food Research.2018; 2(1): 46 – 50. DOI: https://doi.org/10.26656/fr.2017.2(1).119
18. Atik N, Berbudi A, Kusumarini D, Zahra TA, Nur Shifa SS, Avriyanti E, Kartiwa RA. The Protective Effect of Aloe vera L. on Lipid Profile in Rat after being Chronic Exposed to Cigarette Smoke. International Medical Journal.2020;25(02):749-756
19. Organization for Economic Cooperation and Development (OECD) guidelines for acute toxicity of chemicals. No. 423.
20. Shakeel S, Zeeshan AS , Syed FZ and Khan UG. Development and evaluation of polyherbal Entoban syrup. Spatula DD. 2015; 5(2):97-102. DOI 10.5455/spatula.20151001032308
21. Sikarwar MS, Patil MB, Antihyperlipidemic activity of Salacia chinensis root extracts in Triton-induced and atherogenic diet-inducedhyperlipidemic rats. Indian Journal of Pharmacology.2012.;44: 88–92. doi: 10.4103/0253-7613.91875
22. Deora N, Venkatraman K. Aloe vera in diabetic dyslipidemia: Improving blood glucose and lipoprotein levels in pre-clinical and clinical studies. Journal of Ayurveda and Integrative Medicine.2022;3(4): vol. 13,100675. doi: 10.1016/j.jaim.2022.100675
23. Mukthamba P, Srinivasan K. Protective effect of dietary fenugreek (Trigonella foenum-graecum) seeds and garlic (Allium sativum) on induced oxidation of low-density lipoprotein in rats. Journal of Basic and Clinical Physiology. 2016; 27(1):39–47. doi: 10.1515/jbcpp-2015-0037.
24. Mukthamba P, Srinivasan K. Hypolipidemic influence of dietary fenugreek (Trigonella foenum-graecum) seeds and garlic (Allium sativum) in experimental myocardial infarction. Food Function. 2015;6(9):3117–25. DOI: 10.1039/c5fo00240k
25. Sil S, Roy UK, Biswas S, Mandal P, Pal K. A Study To Compare Hypolipidemic Effects Of Allium Sativum (Garlic) alone and in combination with Atorvastatin Or Ezetimibe in experimental model. Serbian Journal of Experimental and Clinical Research. 2020; 22(1):11–19. DOI: https://doi.org/10.2478/sjecr-2020-0058
26. Elmahdi B, Khalil MM, AbulgasimAI.The effect of fresh crushed garlic bulbs on plasma lipids in hypercholestermicrats.Journal of Veterinary and Animal Sciences.2008;3:15-19
27. Asgharpour M, Khavandegar A, Balaei P, Enayati N, Mardi P, Alirezaei A, Bakhtiyari M. Efficacy of Oral Administration of Allium sativum Powder “Garlic Extract” on Lipid Profile, Inflammation, and Cardiovascular Indices among Hemodialysis Patients. Evidence-Based Complementary and Alternative medicine. 2021;17:6667453.DOI: 10.1155/2021/6667453
28. Haghani MR, Arabnezhad S, Mohammadi, Ghaffarian-Bahraman A. Aloe vera and Streptozotocin-Induced Diabetes Mellitus. Revista Brasileira de Farmacognosia.2022; 32(2):174–187. DOI: 10.1007/s43450-022-00231-3

29. Yeh YY, Liu L. Cholesterol-lowering effect of gar-lic extracts and organosulfur compounds: human and animal studies. Journal of nutrients. 2001;131(3):989–93. doi: 10.1093/jn/131.3.989S.
30. Nazir I, Chauhan RS. Qualitative phytochemical analysis of Allium sativum (Garlic) and Curcuma longa (Turmeric). Journal of Entomology and Zoology Studies.2019;7(1):545–547.
31. Kiprop K, MuthangyaM.Phytochemical Screening and Antimicrobial Properties of Allium sativumAgainstLactobacillus.International Journal of Sciences:Basic and applied Research. 2021; 60(1):172–180.
32. Vandana S, Ramesh K. Study of Phytochemical Analysis and Antioxidant Activity of Allium sativum of Bundelkhand Region. International Journal of Life-Sciences Scientific Research. 2017;3(6):1451–1458
33. Kumari S, Rao NB, Gajula RG. Phytochemical analysis and anti-microbial activity of Trigonella foenumgracum (Methi seeds). Journal of medicinal plants studies. 2016; 4(4):278–281.
34. Mahmooda MN, Yahya IK. Nutrient and Phytochemical of Fenugreek (Trigonella Foenum graecum) Seeds. International Journal of Sciences: Basic andApplied Research. 2017; 36(3):203–213.
35. Muraki E, Hayashi Y, Chiba H, Tsunoda N, Kasono K. Dose-dependent effects, safety and tolerability of fenugreek in diet-induced metabolic disorders in rats. Lipids in Health and Disease. 2011;21(1):240. doi: 10.1186/1476-511X-10-240
36. Roberts KT. The potential of fenugreek (Trigonella foenumgraecum) as a functional food and nutraceutical and its effects on glycemia and lipidemia. Journal of Medicinal Food. 2011;14(12): 1485-9. doi: 10.1089/jmf.2011.0002.
37. Henni G, Hendy M, Horas R. Test of the effectiveness of giving Aloe vera extract In reducing cholesterol in Male Wistar Rats (Rattus Norvegicus) with hypercholesterolemia. International Journal of Health and Pharmaceutical.2023;3(4):928-935