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(54) **NATURAL PRODUCT COMPOSITIONS FOR MANAGEMENT OF CHOLESTEROL LEVELS**

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None

See application file for complete search history.

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(57) **ABSTRACT**

A composition includes *Commiphora mukul* extract, *Camellia sinensis* extract, and *Trigonella foenum*-graecum extract. The composition may further include *Allium sativum* extract, *Zingiber officinale* extract, and *Cinnamomum verum* extract. The composition may include *Commiphora mukul* extract at about 24%-36% by weight of the total composition, the *Allium sativum* extract at about 20%-30% by weight of the total composition, the *Camellia sinensis* extract at about 12%-18% by weight of the total composition, the *Trigonella foenum*-graecum extract at about 12%-18% by weight of the total composition, the *Zingiber officinale* extract at about 8%-12% by weight of the total composition, and the *Cinnamomum verum* extract at about 4%-6% by weight of the total composition. The disclosure further provides methods of treating hyperlipidemia using the disclosed compositions.

17 Claims, No Drawings

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NATURAL PRODUCT COMPOSITIONS FOR MANAGEMENT OF CHOLESTEROL LEVELS

BACKGROUND

Technical Field

This disclosure relates to compositions for hyperlipidemia, including cholesterol management in a mammal.

Description of Related Art

Most individuals with high cholesterol must currently take synthetic medications or pharmaceuticals that have significant short term and long-term side effects. Cholesterol management is a long-term chronic challenge, so patients often must take these medications over a long period of time for example, even many decades. Side effects, however, tend to get progressively worse over time.

Natural products, for example herbal extracts, offer potential long-term solutions since they tend to have fewer and less severe side effects. However, very few natural products for cholesterol management have been tested and proven for safety and efficacy. Many natural products are sold on the basis of traditional historical usage, but generally do not have rigorous modern-day science and testing to support their claims of efficacy.

Currently, there are medications available for managing cholesterol, however, the side-effects and costs associated with these medications are significant. The primary Adverse Events (AE) with statins, which were originally derived from fungi, are the statin-induced myopathies. AE for the fibrates, another class of drugs used to treat hyperlipidemia, include nausea, pain, cholelithiasis, cholecystitis, hepatic disorders, and clotting disorders. A natural product alternative to the available medications could provide a low-cost option with fewer and milder side-effects. Currently, there is no supplement proven to be safe and effective in treating hyperlipidemia.

Accordingly, there is a need for natural product compositions that provide proven safe and effective long-term solutions for cholesterol management that have fewer side effects compared to existing pharmaceuticals.

SUMMARY DISCLOSURE OF THE INVENTION

A composition for the treatment of hyperlipidemia in a mammal includes *Commiphora mukul* extract, *Camellia sinensis* extract, and *Trigonella foenum*-graecum extract. The composition may further include *Allium sativum* extract, *Zingiber officinale* extract, and *Cinnamomum verum* extract. The composition may include *Commiphora mukul* extract at about 24%-36% by weight of the total composition, the *Allium sativum* extract at about 20%-30% by weight of the total composition, the *Camellia sinensis* extract at about 12%-18% by weight of the total composition, the *Trigonella foenum*-graecum extract at about 12%-18% by weight of the total composition, the *Zingiber officinale* extract at about 8%-12% by weight of the total composition, and the *Cinnamomum verum* extract at about 4%-6% by weight of the total composition.

Methods of treating hyperlipidemia in a mammal are further disclosed which include administering a composition including *Commiphora mukul* extract, *Camellia sinensis* extract, and *Trigonella foenum*-graecum extract to a mammal in need thereof. The composition may further include *Allium sativum* extract, *Zingiber officinale* extract, and *Cinnamomum verum* extract.

Other features and aspects will be apparent from the following detailed description and the claims.

DETAILED DISCLOSURE OF THE INVENTION

The following detailed description is provided to assist the reader in gaining a comprehensive understanding of the methods, products, and/or systems, described herein. However, various changes, modifications, and equivalents of the methods, products, and/or systems described herein will be apparent to an ordinary skilled artisan.

Modes for Carrying Out the Invention

The present invention includes a unique herbal extract blend that supports cholesterol management. In embodiments, the invention is an herbal extract blend consisting of up to six herbal extracts standardized to specific active marker compounds. These extracts work synergistically together to provide strong results as demonstrated in a human clinical trial.

The extract may include a blend in powder form. In addition, the blend may include excipients; sometimes in small amounts. Extraction solvents to obtain the extracts may include water and alcohol. The extracts may be included in tablets/capsules/pills, food/beverages, and/or skin care products as nonlimiting examples.

A significant feature is the selection of a unique blend of herbal extracts that act synergistically with each other to provide strong results seen in human clinical trials as disclosed below. The blend may include a specific ratio of ingredients and the blend may include specific amounts of active compounds.

In embodiments, the disclosed compositions include *Commiphora mukul* extract, *Camellia sinensis* extract, and *Trigonella foenum*-graecum extract. In embodiments, the disclosed compositions may consist of or consist essentially of *Commiphora mukul* extract, *Camellia sinensis* extract, and *Trigonella foenum*-graecum extract. In embodiments, the disclosed compositions may include *Commiphora mukul* extract, *Camellia sinensis* extract, *Trigonella foenum*-graecum extract, *Allium sativum* extract, *Zingiber officinale* extract, and *Cinnamomum verum* extract. In embodiments, the disclosed compositions may consist of or consist essentially of *Commiphora mukul* extract, *Camellia sinensis* extract, *Trigonella foenum*-graecum extract, *Allium sativum* extract, *Zingiber officinale* extract, and *Cinnamomum verum* extract. In this case the composition can include the active ingredients stated above as well as other inactive ingredients, excipients, fillers, additives, vehicles, etc.

In embodiments, the disclosed compositions include *Commiphora mukul* extract at about 30% by weight, *Allium sativum* extract at about 25% by weight, *Camellia sinensis* extract at about 15% by weight, *Trigonella foenum*-graecum extract at about 15% by weight, *Zingiber officinale* extract at about 10% by weight, and *Cinnamomum verum* extract at about 5% by weight.

In embodiments, other herbal extracts can also be added to the composition and may provide an even more enhanced benefit. For example, Turmeric extract, Coriander extract, *Capsicum* annum extract, Horse chestnut extract, Rosehip extract, Radish extract, and/or *Citrus sinensis* extract. Other extracts known and commonly used in the herbal medicine art may also be added.

The amounts of extracts used in the disclosed compositions may vary in amounts ranging from about 1% to about 20% by weight and continue to provide compositions with a comparable level of efficacy.

Accordingly, a composition may include *Commiphora mukul* extract at about 24%-36% by weight of the total composition, the *Allium sativum* extract at about 20%-30% by weight of the total composition, the *Camellia sinensis* extract at about 12%-18% by weight of the total composition, the *Trigonella foenum*-graecum extract at about 12%-18% by weight of the total composition, the *Zingiber officinale* extract at about 8%-12% by weight of the total composition, and the *Cinnamomum verum* extract at about 4%-6% by weight of the total composition.

In embodiments, the product may be a blend of six herbal extracts. In one embodiment, each extract may be prepared individually and then the extracts combined in particular amounts to make a final product. For example, the *Commiphora mukul* extract may be prepared to include about 2.5% active substance Commiphytes by weight; the *Camellia sinensis* extract may be prepared to include about 40% by weight active substance Camitechins; the *Zingiber officinale* may include about 5% active substance Zinzirols by weight. The amounts of active substances(s) in the extracts may be determined by HPLC. As mentioned, the extracts may then be combined in a specific ratio to make a final product.

As one example, the level of active substance Camitechin in the combined blend of extracts may be about 6% by weight. In this case, the *Camellia sinensis* extract is prepared or processed to include about 40% active substance Camitechin. Thus, when combined in the final product with the other extracts, the *Camellia sinensis* extract may be about 15% by weight of the blend as described above. Accordingly, the amount of active substance Camitechin in the blend would be about 6%. The amounts of other active substances may be similarly calculated. The active substance Commiphytes may be about 0.75% of the product blend. The active substance Zinzirols may be about 0.5% of the product blend.

Glossary

Commiphora mukul extract derives from a flowering plant in the family Burseraceae. See e.g., *Commiphora wightii*, Wikipedia, the free encyclopedia, last edited 19 Nov. 2021, herein incorporated by reference. The extract can be obtained through extraction. See Example 1 and "Analysis of Commiphytes in Kara Heart Formula by HPLC method", Green Chem, herein incorporated by reference (IDS). See also, e.g., Extraction (chemistry), Wikipedia, the free encyclopedia, last edited 25 Aug. 2021, herein incorporated by reference; and e.g., Natural Product (isolation and purification), Wikipedia, the free encyclopedia, last edited 8 Dec. 2021, herein incorporated by reference.

Camellia sinensis extract a species of evergreen shrubs or small trees in the flowering plant family Theaceae. See e.g., *Camellia sinensis*, Wikipedia, the free encyclopedia, last edited 30 Nov. 2021, herein incorporated by reference. The extract can be obtained by extraction. See Example 1 and "Analysis of Camitechin in Kara Heart Formula by HPLC method", Green Chem, herein incorporated by reference (IDS). See also, e.g., Extraction (chemistry), Wikipedia, the free encyclopedia, last edited 25 Aug. 2021; and e.g., Natural Product (isolation and purification), Wikipedia, the free encyclopedia, last edited 8 Dec. 2021.

Trigonella foenum-graecum extract derives from a plant in the family Fabaceae. See e.g., Fenugreek, Wikipedia, the free encyclopedia, last edited to December 2021, herein incorporated by reference. The extract can be obtained by extraction. See Example 1. See e.g., Extraction (chemistry), Wikipedia, the free encyclopedia, last edited 25 Aug. 2021; and e.g., Natural Product (isolation and purification), Wikipedia, the free encyclopedia, last edited 8 Dec. 2021.

Allium sativum extract derives from a species of bulbous flowering plant in the genus *Allium*, See e.g., Garlic, Wikipedia, the free encyclopedia, last edited 29 Nov. 2021, herein incorporated by reference. The extract can be obtained by extraction. See Example 1. See also, e.g., Extraction (chemistry), Wikipedia, the free encyclopedia, last edited 25 Aug. 2021; and e.g., Natural Product (isolation and purification), Wikipedia, the free encyclopedia, last edited 8 Dec. 2021.

Zingiber officinale extract derives from a flowering plant in the family Zingiberaceae. See e.g., Ginger, Wikipedia, the free encyclopedia, last edited 25 Nov. 2021, herein incorporated by reference. The extracts can be obtained by extraction procedures. See Example 1 and "Analysis of Zinzirols in Kara Heart Formula by HPLC method", Green Chem, herein incorporated by reference (IDS). See also, e.g., Extraction (chemistry), Wikipedia, the free encyclopedia, last edited 25 Aug. 2021; and e.g., Natural Product (isolation and purification), Wikipedia, the free encyclopedia, last edited 8 Dec. 2021.

Cinnamomum verum extract derives from a small evergreen tree belonging to the family Lauraceae. See *Cinnamomum verum*, Wikipedia, the free encyclopedia, last edited 2 Nov. 2021, herein incorporated by reference. The extract can be obtained by extraction. See Example 1. See also, e.g., Extraction (chemistry), Wikipedia, the free encyclopedia, last edited 25 Aug. 2021; and e.g., Natural Product (isolation and purification), Wikipedia, the free encyclopedia, last edited 8 Dec. 2021.

The term 'hyperlipidemia' is a condition involving elevated levels of lipids in the blood. Hyperlipidemia generally includes elevated cholesterol levels in the blood. Elevated levels of lipids or cholesterol generally refers to amounts that exceed amounts considered normal according to standard medical practice. For example, high cholesterol can be defined as a total cholesterol level above 200 mg/dL. See Hyperlipidemia, Wikipedia, the free encyclopedia, last edited: 4 Oct. 2021, herein incorporated by reference.

Cholesterol is a type of lipid. See Cholesterol, Wikipedia, the free encyclopedia, last edited: 13 Oct. 2021, herein incorporated by reference.

The term 'therapeutically effective amount' refers to an amount of an active ingredient that produces the intended result, i.e., provides some level of treatment, modification, or has an effect on the condition of Hyperlipidemia in a mammal preferably a human. See e.g., Therapy, Wikipedia, the free encyclopedia, last edited 21 Nov. 2021, herein incorporated by reference.

The term 'administration' generally includes oral and intravenous administration as well as any route of administration capable of effectively delivering the composition to the body. Preferred would be pills or tablets. Administration may also be done through a food or beverage or through the skin or other body cavity. See Route of Administration, Wikipedia, the free encyclopedia, last edited 5 Nov. 2021, herein incorporated by reference.

KaraHeart™ is a synergistic herbal formula consisting of herbs including extract of *Commiphora mukul, Allium sativum, Camellia sinensis, Trigonella foenum*-graecum, *Zingiber officinale*, and *Cinnamomum verum.*

Dosage can be from about 100 mg to about 2000 mg per day. Preferred dosage is about 1000 mg per day.

Parameters for total cholesterol management include amounts of high-density lipoprotein (HDL), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and/or TGL (triglycerides) in the bloodstream.

Amounts of high-density lipoprotein (HDL), total cholesterol (TC), low density lipoprotein (LDL), very low density lipoprotein (VLDL), and/or triglycerides (TGL) in a mammal typically refers to measured amounts of these factors in the bloodstream of a mammal or human.

The term mammal as used herein are a group of vertebrate animals constituting the class Mammalia. See Mammal, Wikipedia, the free encyclopedia, last edited 18 Oct. 2021, herein incorporated by reference. Preferably mammal refers to primates and most preferably humans.

The term 'treatment' or 'treating' refers to the attempted remediation of a condition or health problem. Treatment can include providing relief to, preventing, curing, supporting, or maintaining a certain state with respect to a condition or management of a condition. Accordingly, treating hyperlipidemia can include prevention, management, e.g., halting or slowing the condition's development and effects, and relieving the symptoms of, as well as curing or eradicating the condition. See e.g., Therapy, Wikipedia, the free encyclopedia, last edited 21 Nov. 2021, herein incorporated by reference.

An active ingredient or active substance in a composition is an ingredient or substance that is biologically active. In embodiments, the compositions of the disclosure have more than one active ingredient. Excipients are generally biologically inactive ingredients, although need not necessarily be inert. See e.g., Active Ingredient, Wikipedia, the free encyclopedia, last edited 19 Oct. 2021, herein incorporated by reference.

An active ingredient of the *Commiphora mukul* extract comprises Commiphytes or Guggulsterone. See Guggulsterones, Wikipedia, the free encyclopedia, last edited 27 Jan. 2021, herein incorporated by reference.

An active ingredient of the *Camellia sinensis* extract comprises Camitechin or Epigallocatechin gallate. See Epigallocatechin gallate, Wikipedia, the free encyclopedia, last edited 16 Aug. 2021, herein incorporated by reference.

An active ingredient of the *Zingiber officinale* extract comprises Zinzirols or gingerols. See Gingerol, Wikipedia, the free encyclopedia, last edited 4 Oct. 2021, herein incorporated by reference.

A tablet or a pill is an oral dosage form that typically comprises a solid dosage with optional excipients. A tablet or a pill may also include liquids, syrups, elixirs, suspensions, and emulsions as well. See e.g., Tablet (pharmacy), Wikipedia, the free encyclopedia, last edited 21 Nov. 2021, herein incorporated by reference.

Percent amounts of extracts and active substances and other components of the claimed compositions are provided herein by weight.

Example 1

The Composition of KaraHeart™ Formula used in the Examples is as follows: *Commiphora mukul* extract, 30%; *Allium sativum* extract, 25%; *Camellia sinensis* extract, 15%; *Trigonella foenum*-graecum extract 15%; *Zingiber officinale* extract, 10%; *Cinnamomum verum* extract, 5%. All percentages are by weight. Specifications for each component are provided below.

Product name: *Allium sativum* extract; Botanical name: *Allium sativum*; Plant part: Bulbs; Excipients: Nil; Solvents used: Water.

Test parameters	Specification	Testing method
Physical		
Appearance	Light brown to brown powder	Visual
Identification (Identification using the WS of extract prepared using botanically authenticated Allium sativum bulbs)	To comply with working standard	In-house-HPTLC
Particle size	98% min. passes through 20 mesh	USP
Loss on drying	NMT 6%	In-house-IR Moisture balance
Assay of actives		
Saponins	NLT 6%	In-house-Gravimetry
Microbial		
Total plate count	NMT 10000 cfu/g	USP
Yeast and mold	NMT 1000 cfu/g	USP
Coliforms	Absent	USP
Salmonella	Absent	USP
E. coli	Absent	USP
Pseudomonas aeruginosa	Absent	USP
Staphylococcus aureus	Absent	USP
Chemical impurities		
Lead	NMT 5 ppm	USP-ICP-MS
Cadmium	NMT 1 ppm	USP-ICP-MS
Arsenic	NMT 3 ppm	USP-ICP-MS
Mercury	NMT 1 ppm	USP-ICP-MS
Pesticide residues	To comply with USP limits	USP

Product name: *Camellia sinensis* extract Botanical name: *Camellia sinensis*; Plant part: Leaves; Excipients: 5% Dextrin; Solvents used: Ethanol & Water.

Test parameters	Specification	Testing method
Physical		
Appearance	Brown to greenish brown powder	Visual
Identification (Identification using the WS of extract prepared using botanically authenticated Camellia sinensis leaves)	To comply with working standard	In-house-HPTLC
Particle size	100% passes through 20 mesh	USP
Loss on drying	NMT 5%	In-house-IR Moisture balance
Assay of actives		
Camitechin	NLT 40%	Based on USP-HPLC
Microbial		
Total plate count	NMT 10000 cfu/g	USP
Yeast and mold	NMT 1000 cfu/g	USP
Coliforms	Absent	USP
Salmonella	Absent	USP
E. coli	Absent	USP
Pseudomonas aeruginosa	Absent	USP
Staphylococcus aureus	Absent	USP
Chemical impurities		
Lead	NMT 5 ppm	USP-ICP-MS
Cadmium	NMT 1 ppm	USP-ICP-MS
Arsenic	NMT 3 ppm	USP-ICP-MS
Mercury	NMT 1 ppm	USP-ICP-MS
Pesticide residues	To comply with USP limits	USP
Residual solvents	To comply with USP limits	USP

Product name: *Cinnamomum verum* extract; Botanical name: *Cinnamomum verum* Plant part: Barks; Excipients: 5% Dextrin; Solvents used: Water.

Test parameters	Specification	Testing method
Physical		
Appearance	Brown powder with characteristic odour	Visual
Identification (Identification using the WS of extract prepared using botanically authenticated Cinnamomum verum barks)	To comply with working standard	In-house-HPTLC
Particle size	98% min. passes through 20 mesh	USP
Loss on drying	NMT 10%	In-house-IR Moisture balance
Assay of actives		
Polyphenols	NLT 3%	In-house-Titration
Microbial		
Total plate count	NMT 10000 cfu/g	USP
Yeast and mold	NMT 1000 cfu/g	USP
Coliforms	Absent	USP
Salmonella	Absent	USP
E. coli	Absent	USP
Pseudomonas aeruginosa	Absent	USP
Staphylococcus aureus	Absent	USP
Chemical impurities		
Lead	NMT 5 ppm	USP-ICP-MS
Cadmium	NMT 1 ppm	USP-ICP-MS
Arsenic	NMT 3 ppm	USP-ICP-MS
Mercury	NMT 1 ppm	USP-ICP-MS
Pesticide residues	To comply with USP limits	USP

Product name: *Commiphora mukul* extract; Botanical name: *Commiphora mukul* Plant part:

Gum exudates; Excipients: 5% Dextrin; Solvents used: Ethanol & Water.

Test parameters	Specification	Testing method
Physical		
Appearance	Cream colour powder	Visual
Identification (Identification using the WS of extract prepared using botanically authenticated Commiphora mukul gum exudates)	To comply with working standard	In-house-HPTLC
Particle size	98% min. passes through 20 mesh	USP
Loss on drying	NMT 6%	In-house-IR Moisture balance
Assay of actives		
Commiphytes	NLT 2.5%	In-house-HPLC
Microbial		
Total plate count	NMT 1000 cfu/g	USP
Yeast and mold	NMT 100 cfu/g	USP
Coliforms	Absent	USP
Salmonella	Absent	USP
E. coli	Absent	USP
Pseudomonas aeruginosa	Absent	USP
Staphylococcus aureus	Absent	USP
Chemical impurities		
Lead	NMT 5 ppm	USP-ICP-MS
Cadmium	NMT 1 ppm	USP-ICP-MS
Arsenic	NMT 3 ppm	USP-ICP-MS
Mercury	NMT 1 ppm	USP-ICP-MS
Pesticide residues	To comply with USP limits	USP
Residual solvents	To comply with USP limits	USP

Product name: *Trigonella foenum*-graecum extract; Botanical name: *Trigonella foenum*-graecum; Plant part used: Seeds; Solvents used: Water; Excipients: 5% Dextrin.

Test parameters	Specification	Testing method
Physical		
Appearance	Brown to dark brown powder	Visual
Identification (Identification using the WS of extract prepared using botanically authenticated Trigonella (foenum-graecum seeds)	To comply with working standard	In-house-HPTLC
Particle size	100% min. passes through 20 mesh	USP
Loss on drying	NMT 5%	In-house-IR Moisture balance
Assay of actives		
Saponins	NLT 15%	In-house-Gravimetry
Microbial		
Total plate count	NMT 10000 cfu/g	USP
Yeast and mold	NMT 1000 cfu/g	USP
Coliforms	Absent	USP
Salmonella	Absent	USP
E. coli	Absent	USP
Pseudomonas aeruginosa	Absent	USP
Staphylococcus aureus	Absent	USP
Chemical impurities		
Lead	NMT 5 ppm	USP-ICP-MS
Cadmium	NMT 1 ppm	USP-ICP-MS
Arsenic	NMT 3 ppm	USP-ICP-MS
Mercury	NMT 1 ppm	USP-ICP-MS
Pesticide residues	To comply with USP limits	USP

Product name: *Zingiber officinale* extract; Botanical name: *Zingiber officinale*; Plant part: Roots (Rhizomes); Excipients: 5% Dextrin Solvents used: Ethanol & Water.

Test parameters	Specification	Testing method
Physical		
Appearance	Brown to light brown powder	Visual
Identification (Identification using the WS of extract prepared using botanically authenticated Zingiber officinale roots)	To comply with working standard	In-house-HPTLC
Particle size	98% min. passes through 20 mesh	USP
Loss on drying	NMT 10%	In-house-IR Moisture balance
Assay of actives		
Zinzirols	NLT 5%	In-house-HPLC
Microbial		
Total plate count	NMT 10000 cfu/g	USP
Yeast and mold	NMT 1000 cfu/g	USP
Coliforms	Absent	USP
Salmonella	Absent	USP
E. coli	Absent	USP
Pseudomonas aeruginosa	Absent	USP
Staphylococcus aureus	Absent	USP
Chemical impurities		
Lead	NMT 5 ppm	USP-ICP-MS
Cadmium	NMT 1 ppm	USP-ICP-MS
Arsenic	NMT 3 ppm	USP-ICP-MS
Mercury	NMT 1 ppm	USP-ICP-MS
Pesticide residues	To comply with USP limits	USP
Residual solvents	To comply with USP limits	USP

Product name: Kara Heart Formula. Blend of extracts of *Commiphora mukul, Allium sativum, Camellia sinensis, Trigonella foenum* graecum, *Zingiber officinale* and *Cinnamomum verum*.

Test parameters	Specification	Testing method
Physical		
Appearance	Brown to reddish brown powder	Visual
Identification (Identification using the WS of extract prepared using botanically authenticated herbs)	To comply with working standard	In-house-HPTLC
Particle size	100% min. passes through 20 mesh	USP
Loss on drying	NMT 5%	In-house-IR Moisture balance
Assay of actives		
Commiphytes	NLT 0.75%	In-house-HPLC
Camitechin	NLT 6.0%	Based on USP-HPLC
Zinzirols	NLT 0.5%	In-house-HPLC
Microbial		
Total plate count	NMT 1000 cfu/g	USP
Yeast and mold	NMT 100 cfu/g	USP
Coliforms	Absent	USP
Salmonella	Absent	USP
E. coli	Absent	USP
Pseudomonas aeruginosa	Absent	USP
Staphylococcus aureus	Absent	USP
Chemical impurities		
Lead	NMT 5 ppm	USP-ICP-MS
Cadmium	NMT 1 ppm	USP-ICP-MS
Arsenic	NMT 1 ppm	USP-ICP-MS
Mercury	NMT 1 ppm	USP-ICP-MS
Pesticide residues	To comply with USP limits	USP
Residual solvents	To comply with USP limits	USP

Example 2

Hyperlipidemia is a condition involving abnormally high levels of lipids in the blood. Hyperlipidemia is a major risk factor for cardiovascular diseases and refers to either high levels of triglycerides (TGL) or cholesterol. Herbal supplements have been used in the management of cholesterol levels in Ayurveda, a complete medical system originating in India. KaraHeart™ is a multi-herbal extract synergistic blend that may help in the management of healthy cholesterol levels. The current study tested the efficacy, tolerability, and safety of KaraHeart™ versus a placebo in the management of cholesterol levels of patients with mild to moderate hyperlipidemia.

This was a randomized, double-blind, parallel, and placebo-controlled study. A total of 100 patients were divided into two groups. One group was given KaraHeart™ and the other group was given a placebo for 120 days. Treatment results were assessed by checking the lipid profile parameters such as total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and TGL.

The study found that the herbal supplement KaraHeart™ significantly reduced levels of LDL, VLDL, TGL, and total cholesterol, while increasing the levels of HDL in the blood. Additionally, the study concluded that KaraHeart™ was safe to use.

KaraHeart™ was shown to be safe and effective in the management of cholesterol levels.

Hyperlipidemia is a common cause of morbidity worldwide. The most common form of hyperlipidemia is hypercholesterolemia (high cholesterol). High cholesterol is defined as a total cholesterol level above 200 mg/dL. Approximately one third of all ischemic heart diseases (IHDs) in the world are caused by hypercholesterolemia. Globally, as reported by the World Health Organization (WHO), increased cholesterol levels are estimated to cause 2.6 million deaths (4.5% of total) and 29.7 million (2% of total) disability adjusted life years (DALYs). In 2008, the worldwide prevalence of hypercholesterolemia in western countries among adults was 39% in males and 40% in females.

Hyperlipidemia is defined under the umbrella of dyslipidemia, a metabolic abnormality leading to an increase in the plasma concentration of cholesterol and/or triglycerides. These disorders occur due to the elevation of serum cholesterol (total cholesterol/TC), low-density lipoprotein (LDL-C), very-low-density lipoprotein (VLDL), or triglyceride (TGL) concentrations, and a decrease in high-density lipoprotein (HDL-C) cholesterol concentrations. In general, HDL is considered "good cholesterol" while LDL, VLDL and TGL, are considered "bad cholesterol". The ratios of TC/HDL-C and LDL-C/HDL-C are used for predicting the risk of developing ischemic heart disease (IHD).

Typically, the higher the levels of lipids in the blood, the higher the risk of cardiovascular diseases (CVD).

Hyperlipidemia is classified into primary and secondary forms. Primary hyperlipidemia is usually hereditary with a genetic cause, while secondary hyperlipidemia is usually caused by other underlying diseases, dietary factors and/or medications/drugs. Though hyperlipidemia itself does not cause any symptoms, it can lead to symptomatic vascular diseases such as coronary artery disease (CAD), stroke, and peripheral arterial disease (PAD). The impact of cholesterol can be reduced by proper management of hyperlipidemia through lifestyle changes and medications. Concerns about adverse reactions to medications for hyperlipidemia, coupled with high costs, may hinder the long-term use of conventional medicines. Use of alternative treatments and natural supplements may reduce such treatment burden and may help to better and more safely manage hyperlipidemia in the general population.

The following study was conducted to test the efficacy, tolerability, and safety of KaraHeart™ in managing cholesterol levels as compared to a placebo control.

Methods

This was a randomized, double-blind, placebo-controlled study. Reporting of the study was done according to Consolidated Reporting of Randomized Controlled Trials (CONSORT) guidelines.

The study was performed in accordance with the current version of the Declaration of Helsinki. The trial was conducted in agreement with the International Conference on Harmonization (ICH) guidelines on Good Clinical Practice (GCP) and the applicable rules and regulations of India.

The study was performed under strict compliance with the requirements of Indian regulations for carrying out the herbal and Ayurveda clinical trials and Ayurveda, Siddha, and Unani good clinical practices (ASU-GCP). ICH guidelines for Good Clinical Practice (ICH-GCP) issued by the U.S. Department of Health and Human Services were followed wherever applicable. Informed consent was obtained from all participants. The trial was registered with Clinical Trials Registry (CTRI), hosted at the ICMR's National Institute of Medical Statistics as per the mandate of Drugs Controller General of India (DCGI). The trial was also registered with the World Health Organization.

Participants

Sample size was calculated using analysis of covariance (ANCOVA) using the primary objectives. The number of measures pre-randomization and post-randomization were 1 and 4 respectively, assuming an anticipated standard effect size of 0.4 and interclass correlation of 0.5. Estimating a drop-out rate of approximately 25%, a minimum of 47 patients in each arm were needed to be recruited to obtain a power rate of more than 80%. Hence a total of 100 participants, 50 in each arm were recruited in the study.

Inclusion Criteria

Healthy adult men and women between the ages of 20-60 years with a confirmed case of mild to moderate hyperlipidemia

As per ATP III guidelines; baseline LDL ranging >100 mg/dL, TC>200 mg/dL, TGL between

150-199 mg/dL, VLDL-Cholesterol >40 mg/dL, HDL-cholesterol: Men-<40 mg/dL, and women <50 mg/dL

Subjects with at least one or more of the diagnostic criteria mentioned above were selected for the study

Subjects with Normal BMI but Abnormal Lipid Profile

Subjects who were able to understand the risks/benefits of the protocol and were willing to give written informed consent

Exclusion Criteria

Subjects who: were using concurrent lipid-lowering medications like statins or fibrates, or dietary supplements within 30 days prior to screening; had hyperlipidemia due to other medications (e.g. Glucocorticoids); had chronic diseases requiring continuous use of vasoactive diuretics or lipid-lowering drugs; were intractably obese or who had experienced any recent, unexplained weight loss or gain; had a history of major illness or cardiovascular diseases (e.g. Angina pectoris, myocardial infarction, etc.) or a history of a thyroid disorder (TSH-levels of <0.4 or >10 μg/dL), renal disorder, cholelithiasis, polycystic ovary syndrome (PCOS), Type I or II diabetes, abnormal liver or kidney function test

(ALT or AST) two times the upper limit of normal or elevated creatinine (male 125 μmol/L, female 110 μmol/L), a positive HIV test, a history of smoking and/or high alcohol intake (2 standard drinks per day); a history of psychiatric disorders that may impair the ability of subjects to provide written informed consent; females who were pregnant, breast feeding, or planning to become pregnant during the study. Also excluded, were subjects with any other condition that, in the opinion of investigator, would adversely affect the subject's ability to complete the study or its measures.

Finally, subjects with a known allergy to KaraHeart™ constituents or ingredients were also excluded from the study

Intervention

KaraHeart™ is a synergistic herbal formula consisting of herbs, such as extract of *Commiphora mukul, Allium sativum, Camellia sinensis, Trigonella foenum*-graecum, *Zingiber officinale*, and *Cinnamomum verum.*

Both KaraHeart™ and placebo were in the form of 500 mg capsules. Daily dosage for both products was 1000 mg (i.e. 2 capsules/day).

Trial Design

A total of 122 subjects were screened for a final sample size of 100 randomized subjects. Eligible subjects were randomly allocated to either of the study arms in accordance with the randomization code found on the study product containers' label. The same was documented into the randomization record. Identical and sealed packed bottles of KaraHeart™ and placebo capsules were provided to the clinical sites. Investigators prescribed the allocated number of bottles of either KaraHeart™ or placebo in a blinded manner to the subjects on a first come, first served basis.

A total of 100 subjects (50 subjects in each arm) were recruited randomly into the two study arms: Group A—KaraHeart™ and Group B—placebo. Duration of the study was 120 days with 6 scheduled clinical visits (screening visit, baseline, 30 days, 60 days, 90 days, and 120 days). Each visit had a window period of ±3 days (FIG. 1).

Subjects were given assigned medication at visit **2** (day 1) and asked to take 1 capsule orally, twice daily (after breakfast and dinner). Subjects were given supplements to last until the next visit (visit **3**, day 30±3) and asked to record daily consumption in the diaries and compliance cards provided to them. Subjects were also asked to walk for 30 minutes daily and record adverse events, if any. With the exception of the biostatistician, all others (the sponsor's designee, investigator, subjects, and CRO's designee) were kept blinded to the investigational product (IP) provided to each participant. Similarly, all others (the sponsor's designee, investigator, subjects and CRO's designee) were kept blinded about the Investigational Product (IP) provided to each participant. The screening visit included obtaining the informed consent, demographic details of the participants, physical examination, recording of vital signs, collecting medical history from the patients, and laboratory examinations. Height, weight, and BMI of subjects were recorded during the screening visit. Each subject underwent clinical laboratory tests at screening and follow-up visits. Urine for urinalysis and blood for hematology, biochemistry, and serology were collected during screening and at the end of the study visit. For the hematology, biochemistry, and serology laboratory tests, blood samples were collected by direct venipuncture of peripheral veins for clinical laboratory tests at the screening visit (V1), follow-up visits, and the final visit (V6). A total of approximately 40 to 45 ml of blood was collected over the course of this study for clinical laboratory evaluations. Blood and urine samples were collected from each prospective participant to analyze and assess the inclusion criteria for fasting/random blood sugar (FBS/RBS), HbA1C, C-Reactive Protein, ECGs, HIV, liver function tests, kidney/renal function tests and urinalysis were performed during the course of the study. In all female subjects of child-bearing potential, a urine pregnancy test was performed during visits V1-6. Negative results were recorded in the source document to confirm the non-pregnant status of participants in order to confirm eligibility for enrolment and/or continuation in the study.

Each follow-up visit (days 30, 60, 90, and 120±3) involved distribution of the supplement, assessments of lipid parameters, and collection of safety and tolerability information. At no point was the code broken, or un-blinded study product administered to any subject. The investigator had the right to break the blind in special situations such as for treatment of emergent serious adverse events (SAE) or to protect the safety of the patient, but it was not necessary for any participant over the duration of the study.

Compliance and Adverse Events

Any unused or extra medication was returned to the investigators to confirm that the correct number of capsules had been taken. The investigator verified the subjects' daily diary and compliance cards and reconciled the supplement use to subjects. This reconciliation was logged on the IP reconciliation form. Proper care was made to record all adverse events (AEs) in source documents and case report forms (CRF).

AE were recorded for severity and relationship to the consumption of the study supplement. All AEs were followed until they were resolved or stabilized or until they were no longer considered clinically significant by the investigator. All reported AEs were mild to moderate in nature, thus, no additional measurements or evaluations were done to investigate the nature of an AE. There were no severe AEs (SAEs) reported during the study.

Withdrawal and Dropout

Subjects who did not meet inclusion/exclusion criteria were considered screen failures.

Participating subjects could withdraw at any time without the need to justify his/her decision, even after undergoing consenting process (consent withdrawal). No subject was discontinued from the study due to non-compliance with medication, protocol violation, worsening of disease or tolerability, AEs, or SAEs. A total of five subjects (from treatment and placebo groups) dropped out from the study at different intervals due to personal reasons. None of these subjects dropped out due to any AE. Data from these subjects were used to examine safety, but not efficacy. The withdrawal of these subjects was prior to the final outcome assessments; therefore, their data was excluded from the main analysis. In case of statistics on the ITT population, missing values were replaced using the last observation carried forward (LOCF) method and efficacy assessments were completed.

Outcome Measures

Primary outcome measures: Change in the following lipid profile parameters from baseline to end of treatment period at the following time points: Baseline, Day 30 (±3), Day 60 (±3), Day 90 (±3) and Day 120 (±3).

Total Cholesterol (TC): This is a sum of the blood cholesterol content. The average level of TC should be below 200 mg/dL.

High-Density Lipoprotein (HDL): This is called "good" cholesterol because it helps carry away LDL, thus keeping arteries open and blood flowing more freely. The average level of HDL should be above 40 mg/dL.

Low-Density Lipoprotein (LDL): This is called "bad" cholesterol. Too much of it in your blood causes a build-up of fatty deposits (plaques) in the arteries (atherosclerosis), which reduces blood flow. These plaques sometimes rupture and can lead to a heart attack or stroke. The average level of LDL should be less than 100 mg/dL.

Triglycerides (TGL): Triglycerides are a type of fat in the blood. The body converts calories it doesn't need into triglycerides, which are stored in fat cells. High triglyceride levels are associated with being overweight, eating sweets or drinking too much alcohol, smoking, sedentary lifestyle, or diabetes with elevated blood sugar levels. The average levels of triglycerides should be less than 150 mg/dL.

Very-Low-Density Lipoprotein (VLDL): The liver makes VLDL and releases it into the bloodstream. VLDL particles mainly carry triglycerides to the tissues. Elevated levels of VLDL can increase a person's risk of developing heart diseases. Normal VLDL should be less than 30 mg/dL.

Total HDL-Cholesterol Ratio: The ratio of TC/HDL. The optimal ratio is between 3.5 and 1. A higher ratio indicates an increased risk of heart disease.

Secondary Outcome Measures:

Change from Baseline to end of study period (Day 120) in:

Serum Apolipoprotein A1: Apolipoproteins are proteins that bind lipids together to form lipoproteins. Their main function is transportation of lipids (and fat-soluble vitamins) in blood, cerebrospinal fluid, and lymph fluid. The 2 major apolipoproteins responsible for lipid transport are ApoA1 and ApoB. Decreases in the concentration of ApoA1 levels along with increases in the concentration of ApoB are associated with increased risk of cardiac diseases. The ApoA1 is the major protein component of HDL and is associated with fat efflux from tissue to liver for excretion. In patients suffering from CAD, ApoA1 levels serve as a better diagnostic tool than HDL levels as they have higher sensitivity and specificity.

HbA1C: To control and monitor the glycemic index in diabetic patients, the HbA1C test is routinely performed. Factors such as sugar intake, exercise, and adherence to medications can affect the levels of HbA1C. Studies have reported that HbA1c can be utilized as a possible biomarker for predicting dyslipidemia and cardiovascular diseases (CVD). A study published in 2017 found that the ideal HbA1c level for people without diabetes is in the 5.0% to 6.0% range. Beyond 6.0%, the risk of death from CVDs rises significantly.

C-reactive protein (CRP): CRP is an inflammatory marker. Inflammation is a major factor in any atherothrombotic disease. Levels of high-sensitivity C-reactive protein (hs-CRP), a marker of systemic inflammation and a mediator of atherothrombotic disease, are potential risk factors for cardiovascular disease. Currently, CRP is recognized as an indicator of vascular inflammation. CRP may be used as a predictor of cardiovascular conditions secondary to atherosclerosis and is a strong predictor of cardiovascular events when compared with low-density lipoprotein cholesterol (LDL-C). The evaluation of serum CRP together with the lipid pattern can be very useful in the early identification of type 2 diabetic individuals who are at high risk of developing CVD.

Statistical Analysis:

Study data collected was assessed using Statistical Analysis Software (SAS) 9.4 package. Descriptive analysis for baseline summary statistics, including mean, medians, and standard deviation for demographic data and proportion of males and females was performed.

The intention to treat (ITT) efficacy analysis set consisted of subjects who took at least 1 dose of IP and have at least 1 post-baseline assessment. ITT efficacy analysis was provided only for the primary end point. Per protocol set population (PP) analysis set was a subset of the ITT population, consisting of subjects who had no major protocol violations affecting the primary efficacy variables. A total of 95 subjects completed the study and were included in the PP population analysis.

Data are expressed as mean±standard deviation (SD). P values were calculated using paired Students t-tests to compare time points within the same group, ANOVA was performed to compare groups at same time point, or ANCOVA using baseline measurement as a covariant when comparing baseline to V6 across groups. Missing post-baseline observations were imputed using last observation carried forward approach (LOCF). All hypotheses were tested at a significance level of 0.05 and 95% confidence interval.

Results

In total, five subjects discontinued the study: one dropped out in V4 from the placebo group, two subjects dropped out in V5 from the treatment (KaraHeart™) group and two subjects dropped out in V6 from the placebo group; these subjects were included in data analysis as ITT population through LOCF method. However, all efficacy analysis were performed using PP population (Table 1). A summary of baseline demographic data of subjects is summarized in Table 2.

Statistical analysis of Total Cholesterol (TC) (PP Population) revealed that at baseline there were no significant differences in the values between the KaraHeart™ and placebo groups ($P>0.05$). An independent Students t-test was performed (Table 3) and was non-significant ($P=0.8935$) at baseline, confirming that the total cholesterol at baseline between the groups were essentially identical at the beginning of the study and thus, results at the end of study were comparable. ANCOVA was performed to test different effects by eliminating unwanted variance on the outcome variable. ANCOVA analysis did not show a difference at Day 30 between the groups ($P>0.05$). However, TC in KaraHeart™ group was significantly different at Day 30 as compared to baseline ($P<0.0001$), unlike the placebo group. These results suggest that KaraHeart™ helped reduce TC within 30 days of treatment. KaraHeart™ continued to show statistically significant reductions in the level of TC when compared to baseline at Day 60 (5%; ANCOVA $P=0.0022$), Day 90 (7.9%; ANCOVA $P=0.0213$) and Day 120 (10.5%; ANCOVA $P=0.0397$) when compared to the placebo group. By Day 120, the KaraHeart™ group demonstrated approximately twice the reduction in TC compared to that of the placebo group. The placebo group did not show any statistically significant improvement until Day 90, whereas the KaraHeart™ group began showing statistically significant decreases in TC starting at Day 30 (Table 3).

The HDL level was well maintained in the KaraHeart™ group with no statistical difference observed at Day 30 from Baseline. In contrast, the placebo group demonstrated a statistically significant reduction in HDL. At Day 120, the KaraHeart™ group had a statistically significant increase in HDL of 4.7% whereas the placebo group showed a statistically significant decrease in HDL of 5.32%. These data indicate that, without active treatment, the patients' HDL levels were deteriorating (Table 4A). The ANCOVA P values were significant at all time points (Days 30, 60, 90, and 120) indicating that KaraHeart™ increased HDL levels. In a sub-group analysis of high-risk category patients (baseline

HDL below 40 mg/dl), HDL levels in the KaraHeart™ treated group demonstrated an even greater increase than the entire KaraHeart™ group in HDL compared to the placebo group. In this sub-group analysis (Table 4B), a significant increase of HDL (4.67 mg/dl, 13.27%) was observed in the KaraHeart™ group from the baseline to the end of study indicating that KaraHeart™ improved HDL levels. In contrast, there was a decrease of 0.9 mg/dl (2.7%) observed in the placebo group (sub-group analysis) from baseline to the end of study. The ANCOVA P value (0.0089) is significant in the sub-group analysis of HDL levels indicating that KaraHeart™ is effective at increasing HDL, whereas the placebo group experienced deteriorating HDL levels. The paired Students t-test (P=0.004) was significant for KaraHeart™ group, but not for the placebo group (P=0.5355) indicating that that treatment group improved significantly from baseline, but the placebo group did not.

At day 120, the KaraHeart™ group had a tendency toward a decrease in LDL compared to the placebo group, as demonstrated by a nearly 13 mg/dL decrease in mean LDL level compared (10% decrease) to the placebo group (approximately 3 mg/dl increase in mean LDL, a 2.3% increase) ANCOVA P=0.095) (Table 5).

The KaraHeart™ group had a statistically significant reduction in VLDL levels, as compared to baseline, from Day 30 through Day 120. The KaraHeart™ group had statistically significant reductions in mean VLDL of 3 mg/dL (9% reduction) and 7 mg/dL (20% reduction) at Day 30 and Day 120, respectively. In contrast, there was no statistically significant reduction observed in VLDL in the placebo group at any time point compared to baseline. ANCOVA P-values for days 30, 60, 90, and 120 were all less than 0.05 (Table 6A). In a sub-group analysis of high-risk patients (Baseline VLDL above 40 mg/dl), there was a significant decrease (P<0.0001) of 16.3 mg/dl (33.28%) observed indicating a positive effect of KaraHeart™. There was no statistically significant change (P>0.05) observed in the level of VLDL in placebo group from baseline to the end of the study. The ANCOVA p value was significant (p=0.0020), which was due to reduction of VLDL in KaraHeart™ group (Table 6B).

The KaraHeart™ group had a statistically significant reduction of mean TC/HDL-C at Day 30 (5% decrease), Day 60 (8% decrease), Day 90 (11% decrease), and Day 120 (15% decrease) compared to baseline. The placebo group showed no statistically significant decrease during any of the time point.

ANCOVA P-values were less than 0.05 at all measurement times (Table 7).

The KaraHeart™ group had a statistically significant reduction in triglycerides at all time points compared to baseline, whereas the placebo group had no significant reduction at any time point. At Day 30, the KaraHeart™ group had a mean 15.3 mg/dL unit decrease (9% decrease), and by Day 120, the group had nearly a 37 mg/dL decrease (21% decrease) of triglycerides. ANCOVA P-values were less than 0.05 at all measurement times (Table 8A). In a sub-group analysis of high-risk category patients (baseline triglycerides above 160 mg/dl), the KaraHeart™ had an even greater decrease in triglycerides at all time points compared to baseline with a decrease of 81.5 mg/dl (33.2%) in KaraHeart™ group from the baseline to the end of the study period. In contrast, the placebo group did not have a statistically significant change in triglycerides from baseline to end of study in the high-risk sub-group (p=0.0858). ANCOVA P-value (0.0020) and P-value between the two groups (0.0001) were significant indicating that KaraHeart™ was more effective at reducing triglyceride level than the placebo. In the category of patients with baseline TGL values between 160 to 200 mg/dl, a decrease of 38.6 mg/dl.

(22%) was observed in the KaraHeart™ group and a negligible non-statistically significant decrease of

1.9 mg/dl (1.1%) was observed in the placebo group from baseline to the end of the study. The ANCOVA P-value was significant (0.0361) indicating a difference between the groups and supporting a role for KaraHeart™ in decreasing triglycerides in the blood. (Table 8B)

Average HbA1C at baseline in the KaraHeart™ group was 5.37 (SD=0.349) and was 5.42

(SD=0.410) in the placebo group. The mean of two groups was statistically comparable (P=0.536) at Day

0. The level of HbA1C increased 0.17 units from baseline to Day 120 in the KaraHeart™ group (P<0.0001) and it increased by 0.24 units in the placebo group (P<0.0001). ANCOVA P-value was 0.2633 (Table 9A).

Mean C-reactive protein (CRP) in the KaraHeart™ group was 6.54 (SD=1.518) mg/L and mean CRP in the placebo group was 6.22 (SD=1.278) mg/L at the Baseline visit. CRP decreased by 0.59 units at Day 120 from Baseline in KaraHeart™ group (P=0.0463) and decreased by 0.07 units in placebo group (P=0.7717). ANCOVA p-value was 0.4160 (Table 9A).

Serum Apolipoprotein A1 (ApoA1) in the KaraHeart™ group was 136.81 mg/dL (SD=23.237) and in placebo group was 138.81 mg/dL (SD=26.285) at the Baseline visit. In the KaraHeart™ group, ApoA1 increased by 5.37 units at Day 120 compared to Baseline (p=0.0122) and decreased by 1.37 units in the placebo group (P=0.6678). The ANCOVA P-value at Day 120 was 0.0893 (Table 9A). The normal range of ApoA1 for men is 110-180 mg/dL and 250 mg/dL for women. High levels of ApoA1 is considered beneficial for cardiac health and can be considered independently of HDL levels.

KaraHeart™ increased the ApoA1 levels in the present study suggesting that it is beneficial for cardiac health. Table 9B indicates that the subgroup analysis (high, moderate, and low levels of ApoA1) did not reveal any statistically significant differences.

Adverse Events

There were no serious adverse events observed in this study. KaraHeart™ was well tolerated with few mild to moderate side effects which were equally distributed between the KaraHeart™ and placebo groups (3 cases in the KaraHeart™ group, 4 cases in placebo group) (Table 10).

DISCUSSION

The therapeutic goal for treating hyperlipidemia and associated CVD is to manage the level of cholesterol in the blood. Cholesterol is managed by increasing HDL and decreasing LDL, VLDL, and TGL in the blood. In the present study, we show that KaraHeart™ (a supplement with a proprietary herbal composition) is safe and effective in treating hyperlipidemia. Supplementation with KaraHeart™ increased HDL and reduced the levels of LDL, VLDL, TGL and TC in the blood. This study also showed that supplementation with 1000 mg/day of KaraHeart™ was safe, as there were no serious adverse side effects. Thus, KaraHeart™ is shown to be safe and effective in helping patients manage their cholesterol levels.

In conclusion, this study demonstrated that KaraHeart™, a synergistic herbal extract blend, helped manage cholesterol levels by normalizing lipid parameters. KaraHeart™

did not alter the vital signs of the patients and did not cause any serious adverse side effects, making it a safe and effective treatment option for patients with mild to moderate hyperlipidemia.

TABLE 1

Analysis of data sets.

Study Population	n KaraHeart ™	n Placebo
Total number of subjects screened	122	
Total number of subjects enrolled & randomized (V2) (Day 0)	50	50
Drop-out at visit V3 (Day 30 ± 3)	0	0
Drop-out at visit V4 (Day 60 ± 3)	1	0
Drop-out at visit V5 (Day 90 ± 3)	2	0
Drop-out at visit V6 (Day 120 ± 3)	0	2
Intent-to-Treat (ITT) Population	50	50
Safety Population	50	50
Per- Protocol (PP) Population	47	48

TABLE 2

Statistical summary for subjects' demography.

Name	Statistics	KaraHeart ™ (N = 50)	Placebo (N = 50)	P-Value
Gender				
Female	n (%)	26 (52.0%)	24 (48.0%)	
Male	n (%)	24 (48.0%)	26 (52.0%)	
Age (Year)	n	50	50	.3044
	Mean (SD)	40.80 (9.413)	38.84 (9.571)	
	Median	39.5	38.0	
	(Min, Max)	(20.00, 60.00)	(21.00, 60.00)	
Height (m)	n	50	50	.0547
	Mean (SD)	1.61 (0.090)	1.64 (0.077)	
	Median	1.6	1.7	
	(Min, Max)	(1.45, 1.80)	(1.46, 1.82)	
Weight at Day 0 (kg)	n	50	50	.4184
	Mean (SD)	65.89 (9.893)	67.32 (7.660)	
	Median	63.5	67.0	
	(Min, Max)	(43.00, 93.10)	(54.00, 83.00)	
Weight at Day 30 (kg)	n	50	50	
	Mean (SD)	65.65 (9.778)	66.96 (7.783)	
	Median	63.5	66.0	
	(Min, Max)	(43.00, 93.10)	(54.00, 83.00)	
Weight at Day 60 (kg)	n	49	50	
	Mean (SD)	65.66 (9.716)	66.92 (7.793)	
	Median	63.0	66.0	
	(Min, Max)	(43.00, 93.10)	(54.00, 83.00)	
Weight at Day 90 (kg)	n	47	50	
	Mean (SD)	65.22 (9.970)	66.68 (7.686)	
	Median	63.0	65.9	
	(Min, Max)	(43.00, 93.10)	(54.00, 83.00)	
Weight at Day 120 (kg)	n	47	48	
	Mean (SD)	63.96 (9.809)	66.91 (7.586)	
	Median	62.0	66.4	
	(Min, Max)	(43.00, 89.00)	(55.00, 83.00)	
BMI at Day 0 (kg/m^2)	n	50	50	.4112
	Mean (SD)	25.28 (2.490)	24.89 (2.241)	
	Median	25.3	24.6	
	(Min, Max)	(19.11, 30.44)	(20.06, 29.75)	
BMI at Day 30 (kg/m^2)	n	50	50	
	Mean (SD)	25.19 (2.481)	24.75 (2.288)	
	Median	25.3	24.3	
	(Min, Max)	(19.11, 30.44)	(19.75, 29.75)	
BMI at Day 60 (kg/m^2)	n	49	50	
	Mean (SD)	25.17 (2.484)	24.74 (2.338)	
	Median	25.4	24.4	
	(Min, Max)	(19.11, 30.44)	(19.75, 30.12)	
BMI at Day 90 (kg/m^2)	n	47	50	
	Mean (SD)	25.04 (2.577)	24.65 (2.265)	
	Median	25.1	24.4	
	(Min, Max)	(19.11, 30.44)	(19.75, 29.75)	
BMI at Day 120 (kg/m^2)	n	47	48	
	Mean (SD)	24.55 (2.481)	24.68 (2.310)	
	Median	23.9	24.4	
	(Min, Max)	(19.11, 29.69)	(19.75, 29.75)	

Note:
P Value: Two sample t-test

TABLE 3

Statistical analysis for Total Cholesterol (TC) (Per protocol population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
TC at Day 0 (mg/dl)	206.3 (33.026)	207.1 (25.004)	.8935	.1435
TC at Day 30 (mg/dl)	201.1 (31.719)	204.6 (22.979)	.5405	
Mean Difference	−5.26	−2.56		
CI	(−7.434, −3.077)	(−5.882, 0.757)		
P-value[b]	<.0001	.1271		
TC at Day 0 (mg/dl)	206.3 (33.026)	207.1 (25.004)	.8935	.0022
TC at Day 60 (mg/dl)	195.9 (29.829)	206.3 (23.195)	.0617	
Mean Difference	−10.4	−0.85		
CI	(−14.55, −6.260)	(−6.287, 4.579)		
P-value[b]	<.0001	.7532		
TC at Day 0 (mg/dl)	206.3 (33.026)	207.1 (25.004)	.8935	.0213
TC at Day 90 (mg/dl)	190.1 (29.109)	199.9 (25.887)	.0878	
Mean Difference	−16.2	−7.25		
CI	(−22.11, −10.27)	(−13.70, −0.803)		
P-value[b]	<.0001	.0283		
TC at Day 0 (mg/dl)	206.3 (33.026)	207.1 (25.004)	.8935	.0397
TC at Day 120 (mg/dl)	184.7 (30.446)	195.7 (30.743)	.0812	

TABLE 3-continued

Statistical analysis for Total Cholesterol (TC) (Per protocol population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
Mean Difference	−21.7	−11.4		
CI	(−29.50, −13.82)	(−19.25, −3.540)		
P-value[b]	<.0001	.0054		

Note:
P Value[a]: Two sample t-test.
P value[b]: Paired t-test.
P Value[c]: ANCOVA P Value.

TABLE 4A

Statistical Analysis for High Density Lipoprotein-Cholesterol (HDL-C) (Per Protocol Population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
HDL-C at Day 0 (mg/dl)	43.15 (8.715)	43.38 (10.342)	.9086	.0074
HDL-C at Day 30 (mg/dl)	43.81 (7.459)	41.56 (10.683)	.2373	
Mean Difference	0.66	−1.81		
CI	(−0.339, 1.659)	(−3.390, −0.235)		
P-value[b]	.1904	.0252		
HDL-C at Day 0 (mg/dl)	43.15 (8.715)	43.38 (10.342)	.9086	.0001
HDL-C at Day 60 (mg/dl)	44.23 (7.429)	40.92 (10.465)	.0779	
Mean Difference	1.09	−2.46		
CI	(−0.017, 2.187)	(−3.943, −0.974)		
P-value[b]	.0534	.0017		
HDL-C at Day 0 (mg/dl)	43.15 (8.715)	43.38 (10.342)	.9086	.0004
HDL-C at Day 90 (mg/dl)	44.45 (7.762)	40.56 (10.320)	.0412	
Mean Difference	1.30	−2.81		
CI	(−0.054, 2.650)	(−4.755, −0.870)		
P-value[b]	.0596	.0055		
HDL-C at Day 0 (mg/dl)	43.15 (8.715)	43.38 (10.342)	.9086	.0005
HDL-C at Day 120 (mg/dl)	45.17 (7.707)	41.06 (10.873)	.0363	
Mean Difference	2.02	−2.31		
CI	(0.472, 3.571)	(−4.281, −0.344)		
P-value[b]	.0117	.0223		

Note:
P Value[a]: Two sample t-test.
P value[b]: Paired t-test
P Value[c]: ANCOVA P Value.

TABLE 4B

Sub-Group Analysis:

CATEGORY	Variable	KaraHeart ™ Group (N = 47)	Placebo Group (N = 48)	P-Value[a]	ANCOVA P-Value[c]
HDL Above 45	N	15	18		
mg/dl	BASELINE	53.13 (6.435)	53.67 (9.299)	.7115	.3369
	V6	51.80 (8.117)	50.33 (9.804)	.6477	
	Mean Difference	−1.33	−3.33		
	CI	(−3.565, 0.898)	(−7.483, 0.817)		
	P-value[b]	.2208	.1084		
HDL 40 to 45	N	14	11		
mg/dl	BASELINE	42.71 (1.541)	41.91 (1.514)	.3103	.0033
	V6	44.93 (3.731)	38.91 (4.085)	.0015	
	Mean Difference	2.21	−3.00		
	CI	(0.238, 4.191)	(−5.585, −0.415)		
	P-value[b]	.0309	.0271		

TABLE 4B-continued

Sub-Group Analysis:					
CATEGORY	Variable	KaraHeart ™ Group (N = 47)	Placebo Group (N = 48)	P-Value[a]	ANCOVA P-Value[c]
HDL Below 40 mg/dl	N	18	19		
	BASELINE	35.17 (3.746)	34.47 (2.342)	.5018	.0089
	V6	39.83 (5.182)	33.53 (7.741)	.0065	
	Mean Difference	4.67	−0.95		
	CI	(1.698, 7.636)	(−4.098, 2.203)		
	P-value[b]	.0041	.5355		

Note:
P Value[a]: Two sample t-test.
P Value[b]: Paired t-test
P Value[c]: ANCOVA P Value.

TABLE 5

Statistical Analysis for Low Density Lipoprotein-Cholesterol (LDL-C) (Per Protocol Population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
LDL-C at day 0 (mg/dl)	124.8 (28.912)	120.6 (23.005)	.4345	.5277
LDL-C at day 30 (mg/dl)	126.1 (27.902)	125.7 (24.644)	.9414	
Mean Difference	1.27	5.07		
CI	(−5.126, 7.656)	(−0.652, 10.792)		
P-value[b]	.6921	.0811		
LDL-C at day 0 (mg/dl)	124.8 (28.912)	120.6 (23.005)	.4345	.0979
LDL-C at day 60 (mg/dl)	123.5 (26.180)	128.3 (24.723)	.3649	
Mean Difference	1.35	7.61		
CI	(−7.797, 5.102)	(0.370, 14.854)		
P-value[b]	.6760	.0398		
LDL-C at day 0 (mg/dl)	124.8 (28.912)	120.6 (23.005)	.4345	.2221
LDL-C at day 90 (mg/dl)	118.7 (26.606)	122.2 (27.437)	.5378	
Mean Difference	−6.11	1.52		
CI	(−13.00, 0.784)	(−6.395, 9.444)		
P-value[b]	.0810	.7003		
LDL-C at day 0 (mg/dl)	124.8 (28.912)	120.6 (23.005)	.4345	.0095
LDL-C at day 120 (mg/dl)	112.3 (28.107)	123.4 (26.663)	.0504	
Mean Difference	−12.6	2.79		
CI	(−20.00, −5.108)	(−5.751, 11.334)		
P-value[b]	.0014	.5141		

Note:
P Value[a]: Two sample t-test.
P value[b]: Paired t-test
P Value[c]: ANCOVA P Value.

TABLE 6A

Statistical Analysis for Very Low Density Lipoprotein-Cholesterol (VLDL-C) (Per Protocol Population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
VLDL-C at Day 0 (mg/dl)	34.10 (11.488)	39.04 (14.997)	.0752	.0137
VLDL-C at day 30 (mg/dl)	31.15 (9.318)	37.29 (11.541)	.0054	
Mean Difference (mg/dl)	−2.95	−1.75		
CI	(−4.455, −1.443)	(−4.116, 0.624)		
P-value[b]	.0003	.1450		
VLDL-C at Day 0 (mg/dl)	34.10 (11.488)	39.04 (14.997)	.0752	<.0001
VLDL-C at day 60 (mg/dl)	28.19 (7.551)	37.10 (11.587)	<.0001	
Mean Difference	−5.91	−1.93		
CI	(−8.203, −3.619)	(−5.299, 1.432)		
P-value[b]	<.0001	.2536		
VLDL-C at Day 0 (mg/dl)	34.10 (11.488)	39.04 (14.997)	.0752	.0001
VLDL-C at day 90 (mg/dl)	26.95 (7.442)	37.15 (12.835)	<.0001	
Mean Difference	−7.15	−1.89		

TABLE 6A-continued

Statistical Analysis for Very Low Density Lipoprotein-Cholesterol (VLDL-C) (Per Protocol Population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
CI	(−9.529, −4.769)	(−5.671, 1.896)		
P-value[b]	<.0001	.3207		
VLDL-C at Day 0 (mg/dl)	34.10 (11.488)	39.04 (14.997)	.0752	<.0001
VLDL-C at day 120 (mg/dl)	27.20 (8.583)	38.95 (14.306)	<.0001	
Mean Difference	−6.90	−0.08		
CI	(−9.658, −4.138)	(−3.761, 3.594)		
P-value[b]	<.0001	.9638		

Note:
P Value[a]: Two sample t-test.
P value[b]: Paired t-test
P Value[c]: ANCOVA P Value.

TABLE 6B

Sub-Group Analysis:

CATEGORY	Variable	KaraHeart ™ Group (N = 47)	Placebo Group (N = 48)	P-Value[a]	ANCOVA P-Value[c]
VLDL Above 40 mg/dl	N	12	20		
	BASELINE	48.97 (6.655)	53.75 (8.929)	.1193	.0020
	V6	32.67 (7.008)	48.61 (12.840)	.0001	
	Mean Difference	−16.30	−5.14		
	CI	(−20.61, −11.99)	(−11.08, 0.796)		
	P-value[b]	<.0001	.0858		
VLDL 32 to 40 mg/dl	N	18	14		
	BASELINE	34.56 (2.206)	34.13 (1.954)	.5727	.0962
	V6	27.64 (8.792)	33.74 (10.987)	.0911	
	Mean Difference	−6.91	−0.39		
	CI	(−11.14, −2.685)	(−7.108, 6.336)		
	P-value[b]	.0031	.9032		
VLDL Below 32 mg/dl	N	17	14		
	BASELINE	23.12 (7.047)	22.93 (7.373)	.9425	.0132
	V6	22.87 (7.304)	30.37 (11.236)	.0329	
	Mean Difference	−0.25	7.44		
	CI	(−3.176, 2.682)	(1.422, 13.464)		
	P-value[b]	.8603	.0192		

Note:
P Value[a]: Two sample t-test.
P Value[b]: Paired t-test
P Value[c]: ANCOVA P Value.

TABLE 7

Statistical Analysis for Total Cholesterol/HDL-C Ratio (Per Protocol Population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
TC/HDL-C at day 0	4.92 (1.097)	5.03 (1.308)	.6650	.0004
TC/HDL-C at day 30	4.67 (0.864)	5.22 (1.318)	.0202	
Mean Difference	−0.24	0.19		
CI	(−0.386, −0.103)	(−0.044, 0.420)		
P-value[b]	.0011	.1095		
TC/HDL-C at day 0	4.92 (1.097)	5.03 (1.308)	.6650	<.0001
TC/HDL-C at day 60	4.51 (0.838)	5.33 (1.320)	.0006	
Mean Difference	−0.40	0.30		
CI	(−0.567, −0.242)	(0.039, 0.561)		
P-value[b]	<.0001	.0251		
TC/HDL-C at day 0	4.92 (1.097)	5.03 (1.308)	.6650	<.0001
TC/HDL-C at day 90	4.38 (0.899)	5.22 (1.371)	.0007	
Mean Difference	−0.54	0.19		
CI	(−0.732, −0.348)	(−0.108, 0.495)		
P-value[b]	<.0001	.2028		

TABLE 7-continued

Statistical Analysis for Total Cholesterol/HDL-C Ratio (Per Protocol Population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
TC/HDL-C at day 0	4.92 (1.097)	5.03 (1.308)	.6650	<.0001
TC/HDL-C at day 120	4.19 (0.917)	5.08 (1.350)	.0003	
Mean Difference	−0.73	0.06		
CI	(−0.981, −0.487)	(−0.212, 0.327)		
P-value[b]	<.0001	.6689		

Note:
P Value[a]: Two sample t-test.
P value[b]: Paired t-test
P Value[c]: ANCOVA P-Value.

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TABLE 8A

Statistical Analysis for Triglyceride (Per Protocol Population)

Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[a]	ANCOVA P-Value[c]
Triglycerides at day 0 (mg/dl)	171.0 (57.249)	195.2 (74.984)	.0812	.0114
Triglycerides at day 30 (mg/dl)	155.7 (46.590)	186.5 (57.706)	.0054	
Mean Difference (mg/dl)	−15.3	−8.73		
CI	(−22.65, −7.900)	(−20.58, 3.120)		
P-value[b]	.0001	.1450		
Triglycerides at day 0 (mg/dl)	171.0 (57.249)	195.2 (74.984)	.0812	.0001
Triglycerides at day 60 (mg/dl)	140.9 (37.756)	185.5 (57.935)	<.0001	
Mean Difference (mg/dl)	−30.1	−9.67		
CI	(−41.41, −18.76)	(−26.49, 7.160)		
P-value[b]	<.0001	.2536		
Triglycerides at day 0 (mg/dl)	171.0 (57.249)	195.2 (74.984)	.0812	<.0001
Triglycerides at day 90 (mg/dl)	134.7 (37.209)	185.8 (64.177)	<.0001	
Mean Difference (mg/dl)	−36.3	−9.44		
CI	(−48.08, −24.47)	(−28.35, 9.479)		
P--value[b]	<.0001	.3207		
Triglycerides at day 0 (mg/dl)	171.0 (57.249)	195.2 (74.984)	.0812	<.0001
Triglycerides at day 120 (mg/dl)	134.3 (40.114)	194.8 (71.532)	<.0001	
Mean Difference (mg/dl)	−36.7	−0.42		
CI	(−49.76, −23.68)	(−18.80, 17.970)		
P-value[b]	<.0001	.9638		

Note:
P-Value[a]: Two sample t-test.
P-value[b]: Paired t-test
P-Value[c]: ANCOVA P-Value.

TABLE 8B

Sub-group analysis:

CATEGORY	Variable	KaraHeart ™ Group (N = 47)	Placebo Group (N = 48)	P-Value[a]	ANCOVA P-Value[c]
TRIGLYCERIDES	N	12	20		
Above 200 mg/dl	BASELINE	244.8 (33.275)	268.8 (44.646)	.1193	.0020
	V6	163.3 (35.041)	243.1 (64.202)	.0001	
	Mean Difference	−81.50	−25.70		
	CI	(−103.0, −59.97)	(−55.38, 3.979)		
	P-value[(b)]	<.0001	.0858		
TRIGLYCERIDES	N	19	14		
160 TO 200 mg/dl	BASELINE	172.3 (10.954)	170.6 (9.771)	.6636	.0361
	V6	133.7 (35.195)	168.7 (54.937)	.0330	
	Mean Difference	−38.58	−1.93		
	CI	(−54.86, −22.29)	(−35.54, 31.682)		
	P-value[(b)]	<.0001	.9032		

TABLE 8B-continued

Sub-group analysis:					
CATEGORY	Variable	KaraHeart ™ Group (N = 47)	Placebo Group (N = 48)	P-Value[a]	ANCOVA P-Value[c]
TRIGLYCERIDES	N	16	14		
Below 160 mg/dl	BASELINE	114.2 (35.900)	114.6 (36.863)	.9729	.0159
	V6	113.3 (37.423)	151.9 (56.182)	.0331	
	Mean Difference	−0.94	37.21		
	CI	(−16.60, 14.724)	(7.109, 67.319)		
	P-value[(b)]	.9002	.0192		

Note:
P-Value[a]: Two sample t-test.
P-Value[b]: Paired t-test
P-Value[c]: ANCOVA P-Value.

TABLE 9A

Statistical Summary for Secondary parameters (Per Protocol Population)				
Variable	KaraHeart ™ (N = 47)	Placebo (N = 48)	P-Value[(a)]	ANCOVA P-Value[(c)]
HbA1C at Day 0 (%)	5.37 (0.349)	5.42 (0.410)	.5368	.2633
HbA1C at Day 120 (%)	5.54 (0.380)	5.66 (0.621)	.2423	
Mean Difference	0.17	0.24		
CI	(0.095, 0.237)	(0.137, 0.347)		
P-Value[b]	<.0001	<.0001		
CRP at Day 0 (mg/dl)	6.54 (1.518)	6.22 (1.278)	.2571	.4160
CRP at Day 120 (mg/dl)	5.96 (1.210)	6.15 (1.265)	.4604	
Mean Difference	−0.59	−0.07		
CI	(−1.160, −0.010)	(−0.543, 0.405)		
P-value[(b)]	.0463	.7717		
ApoA1 at Day 0 (mg/dl)	136.81 (23.237)	138.81 (26.285)	.6943	.0893
ApoA1 at Day 120 (mg/dl)	142.18 (20.746)	137.44 (32.879)	.4029	
Mean Difference	5.37	−1.37		
CI	(1.226, 9.512)	(−7.768, 5.022)		
P-value(b)	.0122	.6678		

Note:
P Value[a]: Two sample t-test.
P value[b]: Paired t-test
P Value[c]: ANCOVA P Value.

TABLE 9B

Sub-group Analysis of ApoA1:					
CATEGORY	Variable	KaraHeart ™ Group (N = 47)	Placebo Group (N = 48)	P-Value [(a)]	ANCOVA P-Value[(c)]
Apolipoprotein	N	16	15		
A1 above 148	Day 0	161.9 (9.010)	168.9 (18.765)	.2047	.9075
mg/dl	Day 120	159.0 (17.557)	165.8 (29.566)	.4330	
	Mean Difference	−2.99	−3.10		
	CI	(−11.76, 5.790)	(−16.71, 10.506)		
	P-value[(b)]	.4795	.6325		
Apolipoprotein	N	15	18		
A1 125 to 148	Day 0	137.8 (5.814)	135.5 (6.766)	.3088	.3694
mg/dl	Day 120	145.5 (10.117)	136.5 (24.423)	.1651	
	Mean Difference	7.70	0.94		
	CI	(2.585, 12.819)	(−9.643, 11.529)		
	P-value[(b)]	.0061	.8532		

TABLE 9B-continued

Sub-group Analysis of ApoA1:

CATEGORY	Variable	KaraHeart ™ Group (N = 47)	Placebo Group (N = 48)	P-Value [a]	ANCOVA P-Value[c]
Apolipoprotein A1 below 125 mg/dl	N	16	15		
	Day 0	110.7 (11.903)	112.6 (13.771)	.6824	.0320
	Day 120	122.2 (13.445)	110.2 (19.226)	.0512	
	Mean Difference	11.54	−2.42		
	CI	(5.249, 17.825)	(−14.34, 9.494)		
	P-value[b]	.0014	.6695		

Note:
P Value[a]: Two sample t-test.
P Value[b]: Paired t-test.
P Value[c]: ANCOVA P Value .

TABLE 10

Adverse events and dropout subjects.

Sl. No.	Subject ID	Visit No.	AE Description	Concomitant Medication	Severity	Relationship	Action for IP	Outcome	Group
1	SORA005	4	Constipation	—	Moderate	Not Related	No Action	Completely recovered	Placebo
2	RMRA020	5	Headache	Diphenhydramine 25 mg + Phenylephrine 5 mg + Caffeine 30 mg	Mild	Not Related	No Action	Completely recovered	KaraHeart ™
3	ASSA034	4	Constipation	—	Moderate	Not Related	No Action	Completely recovered	KaraHeart ™
4	JBTA043	5	Fever Grade 1	Acetaminophen 650 mg + Cetirizine 10 mg	Mild	Not Related	No Action	Completely recovered	Placebo
5	MACA046	6	Diarrhea	Loperamide 2 mg	Mild	Not Related	No Action	Completely recovered	Placebo
6	BALA086	6	Constipation		Moderate	Not Related	No Action	Completely recovered	Placebo
7	BVVA101	5	Itching	Levocetrizine	Mild	Not Related	No Action	Completely recovered	KaraHeart ™

While this disclosure includes specific examples, it will be apparent after an understanding of the disclosure of this application has been attained that various changes in form and details may be made in these examples without departing from the spirit and scope of the claims and their equivalents.

The invention claimed is:

1. A composition comprising: *Commiphora mukul* extract, *Camellia sinensis* extract, *Trigonella foenum*-graecum extract, *Allium sativum* extract, *Zingiber officinale* extract, and *Cinnamomum verum* extract, wherein the *Commiphora mukul* extract is about 24% to about 36% by weight of the composition, the *Allium sativum* extract is about 20% to about 30% by weight of the composition, the *Camellia sinensis* extract is about 12% to about 18% by weight of the composition, the *Trigonella foenum*-graecum extract is about 12% to about 18% by weight of the composition, the *Zingiber officinale* extract is about 8% to about 12% by weight of the composition, and the *Cinnamomum verum* extract is about 4% to about 6% by weight of the composition.

2. The composition of claim **1**, wherein the *Commiphora mukul* extract is about 30% by weight of the composition, the *Allium sativum* extract is about 25% by weight of the composition, the *Camellia sinensis* extract is about 15% by weight of the composition, the *Trigonella foenum*-graecum extract is about 15% by weight of the composition, the *Zingiber officinale* extract is about 10% by weight of the composition, and the *Cinnamomum verum* extract is about 5% by weight of the composition.

3. The composition of claim **1**, wherein the composition further comprises Turmeric extract, Coriander extract, *Capsicum* annum extract, Horse chestnut extract, Rosehip extract, Radish extract, or *Citrus sinensis* extract.

4. The composition of claim **1**, wherein an active substance of the *Commiphora mukul* extract comprises Commiphytes, and the composition comprises about 0.6% to about 0.9% Commiphytes by weight.

5. The composition of claim **1**, wherein an active substance of the *Camellia sinensis* extract comprises Camitechin, and the composition comprises about 4.8% to about 7.2% Camitechin by weight.

6. The composition of claim **1**, wherein an active substance of the *Zingiber officinale* extract comprises Zinzirols, and the composition comprises about 0.4% to 0.6% Zinzirols by weight.

7. The composition of claim **1**, wherein

an active substance of the *Commiphora mukul* extract comprises Commiphytes and the composition comprises about 0.75% Commiphytes by weight,

an active substance of the *Camellia sinensis* extract comprises Camitechin, and the composition comprises about 6% Camitechin by weight, and

an active substance of the *Zingiber officinale* extract comprises Zinzirols, and the composition comprises about 0.5% Zinzirols by weight.

8. The composition of claim **1**, wherein the composition further comprises excipients.

9. A method of treating hyperlipidemia in a mammal comprising: administering a composition of claim **1** to a mammal.

10. The method of treating hyperlipidemia in a mammal of claim **9**, wherein the hyperlipidemia includes a level of total cholesterol of about 200 mg/dL or more in the mammal's blood.

11. The method of treating hyperlipidemia in a mammal of claim **9**, wherein the *Commiphora mukul* extract is about 24% to about 36% by weight of the composition, the *Allium sativum* extract is about 20% to about 30% by weight of the composition, the *Camellia sinensis* extract is about 12% to about 18% by weight of the composition, the *Trigonella foenum*-graecum extract is about 12% to about 18% by weight of the composition, the *Zingiber officinale* extract is about 8%-12% by weight of the composition, and the *Cinnamomum verum* extract is about 4%-6% by weight of the composition.

12. The method of treating hyperlipidemia in a mammal of claim **11**, wherein the *Commiphora mukul* extract is about 30% by weight of the composition, the *Allium sativum* extract is about 25% by weight of the composition, the *Camellia sinensis* extract is about 15% by weight of the composition, the *Trigonella foenum*-graecum extract is about 15% by weight of the composition, the *Zingiber officinale* extract is about 10% by weight of the composition, and the *Cinnamomum verum* extract is about 5% by weight of the composition.

13. The method of treating hyperlipidemia in a mammal of claim **9**, wherein the composition further comprises Turmeric extract, Coriander extract, *Capsicum* annum extract, Horse chestnut extract, Rosehip extract, Radish extract, or *Citrus sinensis* extract.

14. The method of treating hyperlipidemia in a mammal of claim **9**, wherein

an active substance of the *Commiphora mukul* extract comprises Commiphytes and the composition comprises about 0.6% to about 0.9% Commiphytes by weight,

an active substance of the *Camellia sinensis* extract comprises Camitechin, and the composition comprises about 4.8% to about 7.2% Camitechin by weight, and

an active substance of the *Zingiber officinale* extract comprises Zinzirols, and the composition comprises about 0.4% to about 0.6% Zinzirols by weight.

15. The method of treating hyperlipidemia in a mammal of claim **9**, wherein the amount of total Cholesterol (TC), low density lipoprotein (LDL), very low density lipoprotein (VLDL), or triglycerides (TGL) in the mammal is reduced.

16. The method of treating hyperlipidemia in a mammal of claim **9**, wherein the amount of high-density lipoprotein (HDL) in the mammal is increased.

17. The method of treating hyperlipidemia in a mammal of claim **9**, wherein the mammal is a human.

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