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(54) **Title**: A NOVEL BOSWELLIA LOW POLAR GUM RESIN EXTRACT AND ITS SYNERGISTIC COMPOSITIONS

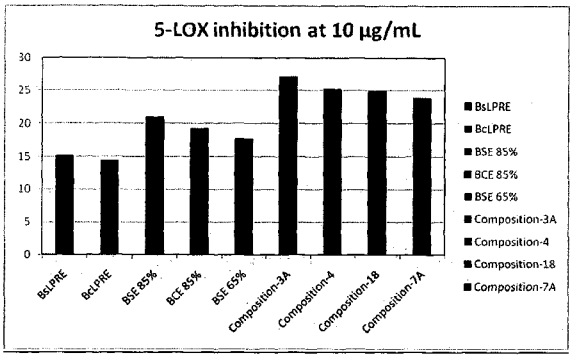

Figure III

(57) **Abstract**: The present invention provides Boswellia low polar gum resin extract (BLPRE) comprising novel phytochemical composition of sesquiterpenes, diterpenes, triterpenes and other phytochemical(s) obtained from gum resin of Boswellia species. The invention also provides compositions comprising BLPRE in combination with one or more component(s) selected from biologically active ingredient(s), functional ingredient(s), excipient(s), diluents(s), carrier(s) and additive(s) or mixtures thereof. Further the invention also provides synergistic composition(s) comprising Boswellia low polar gum resin extract (BLPRE) and at least one component selected from but not limited to extract(s), fraction(s), phytochemical(s) or their salts or mixtures thereof derived from Boswellia species or Curcuma species.

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"A NOVEL BOSWELLIA LOW POLAR GUM RESIN EXTRACT AND ITS SYNERGISTIC COMPOSITIONS"

FIELD OF INVENTION:

The present invention provides Boswellia low polar gum resin extract (BLPRE) comprising novel phytochemical composition(s) of sesquiterpenes, diterpenes, triterpenes and other phytochemical(s) obtained from gum resin of Boswellia species.

The invention also provides compositions comprising Boswellia low polar gum resin extract (BLPRE) and at least one component selected from biologically active ingredient(s), functional ingredient(s), excipient(s), diluents(s), carrier(s) and additive(s) or mixtures thereof.

Further the invention also provides synergistic composition(s) comprising Boswellia low polar gum resin extract (BLPRE) and at least one component selected from extract(s), fraction(s), phytochemical(s) and their salts or mixtures thereof derived from Boswellia species or Curcuma species.

BACK GROUND OF THE INVENTION:

There are numerous pharmaceutical, herbal ingredient(s) and biologically active molecules that are effective in vitro for a disease or disorder. However, several of them are not effective or not bioavailable in vivo (warm blooded animals). It is thus important to explore, identify and invent safe and effective compound(s) or composition(s) that helps increase the in vivo activity of such pharmaceutical or herbal ingredient(s) through synergism. In this process the inventors have screened a number of extracts, fractions, phytochemical(s) and compound(s) originating from plants, animals and microorganisms; individually and in combinations.

The gum resin of Boswellia has been very widely used since ancient times. For example, the gum resin of *Boswellia serrata* (Burseraceae) plant has long been in use for the treatment of rheumatoid arthritis and gout by the practitioners of Ayurvedic medicines in the Indian system of medicine. Various extracts of the gum

resin have shown potent anti-inflammatory and anti-atherogenic activity in laboratory animals [Cuaz-Pérolin et al., *Arterioscler Thromb Vasc Biol* Feb 2008]. The extract of Boswellia was found to be a potent anti-arthritic agent [Kimmatkar et al; *Phytomedicine*. 2003, 10(1): 3-7]. *Boswellia* gum resin and its extracts also demonstrated significant therapeutic improvements in human clinical trials confirming the *in vivo* anti-inflammatory effects. [E Ernest, BMJ 2008; 337: a2813].

The origin of the anti-inflammatory action of *Boswellia* gum resin and its extracts has been attributed to a group of triterpene acids called Boswellic acids that were isolated from the gum resin of *Boswellia serrata*. Boswellic acids exert anti-inflammatory actions by inhibiting 5-lipoxygenase (5-LOX). 5-LOX is a key enzyme for the biosynthesis of leukotrienes from arachidonic acid. Leukotrienes are considered to be involved in the initiation and propagation of a variety of inflammatory diseases. In addition to their 5-lipoxygenase inhibition, Boswellic acids inhibit human leukocyte elastase (HLE), an enzyme of different pro-inflammatory pathway [Safayahi, H., et. al., J. Pharmacol. Exp. Ther., 1997: 281; p 460-463]. 3-O-Acetyl-11-keto-□-Boswellic acid (AKBA) is biologically the most active component among its congeners, with an IC_{50} of 1.5 μM for the inhibition of 5-LOX [Sailer, E. R., et. al., British J. Pharmacol., 1996: 117; p 615-618].

The U.S. patent US5629351 relates to a novel fraction comprising a mixture of Boswellic acids, wherein the fraction exhibits anti-inflammatory and antiulcerogenic activities. Also disclosed is a novel Boswellic acid compound exhibiting anti-inflammatory, antiarthritic and antiulcerogenic activities. Also disclosed is a process for isolating a Boswellic acid fraction and individual Boswellic acids therefrom.

The U.S. patent US20080275117A1 describes compositions comprising Boswellic acids obtained by combining different fractions obtained by supercritical chromatographic extraction of Boswellia serrata gum resin.

The U.S. patent publication US20060280811A1 relates to formulations comprising combinations of analgesic/anti-inflammatory, immunomodulating and cartilage-reconstructing agents in particular comprising saligenin, Boswellic acid, procyanidins, N-acety-glucosamine and either glucoronic acid or glucoronolactone,

for the treatment of rheumatoid arthritis and, more generally, of arthritis conditions. In this pure Boswellic acid or a semi-synthetic derivative thereof or 20% of Boswellic acid-enriched *Boswellia* serrata extract are used in the formulation.

PCT publication WO 02/15916, constituting its priority from German patent DE-A 100 41 217, disclose dihydro Boswellia acids, physiologically acceptable salts thereof and hydrogenated extracts from *Boswellia.* Said publications suggest the use of these compounds for the prophylactic and/or therapeutic treatment of undesired physical and psychic conditions, in particular of somatic, psychosomatic and psychic diseases, such as inflammatory processes caused by increased leukotriene formation, leukocyte elastase or plasmin activity.

There is however no prior art, to the best of inventors knowledge, relating to Boswellia low polar gum resin extract (BLPRE) comprising a novel phytochemical composition and its compositions for the prevention, control and treatment of disorders or diseases in warm blooded animals.

SUMMARY OF THE INVENTION:

In an important aspect, the present invention provides a Boswellia low polar gum resin extract (BLPRE) comprising novel phytochemical composition of sesquiterpenes, diterpenes, triterpenes and other phytochemical(s) obtained from the gum resin of Boswellia species.

Another aspect of the invention is to provide composition(s) comprising Boswellia low polar gum resin extract (BLPRE) in combination with at least one component selected from biologically active ingredient(s), functional ingredient(s), excipient(s), diluents(s), carrier(s) and additive(s) or mixtures thereof.

Another major aspect of the present invention is to provide synergistic composition(s) comprising Boswellia low polar gum resin extract (BLPRE) in combination with at least one component selected from the extract(s), fraction(s), phytochemical(s) and their salts or mixtures thereof derived from Boswellia species.

Another aspect of the present invention is to provide synergistic composition(s) comprising Boswellia low polar gum resin extract (BLPRE) and at least one component selected from the extract(s), fraction(s), phytochemical(s) and their salts or mixtures thereof derived from Curcuma species.

Another aspect of the invention is to provide synergistic composition(s) of Boswellia low polar gum resin extract (BLPRE) with at least one component selected from but not limited to biologically active ingredient(s), functional ingredient(s) or mixtures thereof.

Another aspect of the invention is to provide Boswellia low polar gum resin extract (BLPRE) comprising a novel phytochemical composition and its compositions for use in warm blooded animal(s) in need thereof.

Another aspect of the present invention is to provide Boswellia low polar gum resin extract (BLPRE) comprising a novel phytochemical composition alone and its compositions for the prevention, control and treatment of one or more disorder(s) or disease(s) in warm blooded animals, including but not limited to metabolic disorders, diabetes, obesity, metabolic syndrome, excess body weight, inflammation, asthma, Alzheimer's, cognitive disorders, neurological disorders, cartilage degradation, aging, skin disorders, hyper triglyceridemia, hyperlipidemia, hypercholesterolemia, cholesterol disorders, hypertension, high blood pressure, immune disorders, cancer, coronary heart disease, infectious diseases, osteoporosis, osteoarthritis, rheumatoid arthritis, joint pain, joint discomfort and several other conditions associated thereof.

BRIEF DESCRIPTION OF FIGURES:

Figure I: Figure shows structural formulae **1 - 9** representing prominent compounds of Boswellia low polar gum resin extract (BLPRE).

Figure II: Figure shows the HPLC chromatogram depicting the phytochemical profile of Boswellia low polar gum resin extract (BLPRE).

Figure III: Figure shows comparative 5-Lipoxygenase inhibitory activity of *Boswellia serrata* low polar gum resin extract (BsLPRE), *Boswellia carterii* low

polar gum resin extract (BcLPRE), *Boswellia serrata* extract standardized to 85% total Boswellic acids [BSE 85%], *Boswellia carterii* extract standardized to 85% total Boswellic acids [BCE 85%], *Boswellia serrata* extract standardized to 65% total Boswellic acids [BSE 65%], composition-3A, composition-4, composition-18 and composition-7A. The bars represent percentage inhibition of 5-Lipoxygenase enzyme exhibited by BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, composition-3A, composition-4, composition-18 and composition-7A at 10 µg/mL concentration.

Figure IV: Figure shows bar diagrammatic representations of percentage inhibition of paw edema volume in Freund's Complete Adjuvant induced Sprague Dawley rats by *Boswellia serrata* low polar gum resin extract [BsLPRE, 200 mg/kg body weight (BW)], *Boswellia carterii* low polar gum resin extract (BcLPRE, 200 mg/kg BW), *Boswellia serrata* extract standardized to 85% total Boswellic acids (BSE 85%, 200 mg/kg BW), *Boswellia carterii* extract standardized to 85% total Boswellic acids (BCE 85%, 200 mg/kg BW), *Boswellia serrata* extract standardized to 65% total Boswellic acids (BSE 65%, 200 mg/kg BW), *Curcuma longa* extract standardized to 20% total curcuminoids (CLE 20%, 200 mg/kg BW), *Curcuma longa* extract standardized to 95% total curcuminoids (CLE 95%, 200 mg/kg BW), *Curcuma aromatica* extract standardized to 20% total curcuminoids (CAE 20%, 200 mg/kg BW), *Curcuma aromatica* extract standardized to 95% total curcuminoids (CAE 95%, 200 mg/kg BW), composition-3A (200 mg/kg BW), composition-4 (200 mg/kg BW), composition-18 (200 mg/kg BW), composition-7A (200 mg/kg BW), composition-42 (200 mg/kg BW), composition-26 (200 mg/kg BW), composition-51 (200 mg/kg BW), composition-35 (200 mg/kg BW) and Prednisolone (10 mg/kg BW).

DETAILED DESCRIPTION OF THE INVENTION:

Abbreviations and words used in the description:

1. BLPRE (Boswellia low polar gum resin extract obtained from Boswellia species)
2. BsLPRE (Boswellia serrata low polar gum resin extract obtained from Boswellia serrata)

3. BcLPRE (Boswellia carterii low polar gum resin extract obtained from Boswellia carterii)
4. BSE 85% (Boswellia serrata extract standardized to 85% Boswellic acids)
5. BCE 85% (Boswellia carterii extract standardized to 85% Boswellic acids)
6. BSE 65% (Boswellia serrata extract standardized to 65% Boswellic acids)
7. BCE 65% (Boswellia carterii extract standardized to 65% Boswellic acids)
8. CLE 20% (Curcuma longa extract standardized to 20% Curcuminoids)
9. CLE 95% (Curcuma longa extract standardized to 95% Curcuminoids)
10. CAE 20% (Curcuma aromatica extract standardized to 20% Curcuminoids)
11. CAE 95% (Curcuma aromatica extract standardized to 95% Curcuminoids)
12. The word(s) 'Gum' or 'Gum resin' or 'resin' used in this patent application are meant to be used interchangeably and they all refer to an exudate of Boswellia plant species.
13. The word 'composition(s)' wherever used in the patent application either refers to the novel Boswellia low polar resin extract (BLPRE) as a standalone ingredient or a mixture comprising BLPRE in combination with one or more ingredients such as biologically active ingredient(s), functional ingredient(s), excipient(s), diluents(s), carrier(s) and additive(s) for preparing either general composition(s) or synergistic composition(s).
14. 'Boswellia low polar resin extract' or 'low polar resin extract' wherever used in the patent application refers to the low polar gum resin extract obtained from any of the Boswellia species by any of the processes described.
15. 'Boswellia oil' or 'oily residue' or 'Boswellia oil fraction' wherever used in the present application refers to the total oil fraction/extract (comprising essential oils, volatile oils and Boswellia low polar resin extract) obtained from the gum resin of any of the Boswellia species by any of the processes described.
16. 'volatile oil' or 'volatile fraction' wherever used in the patent application refers to volatile oils obtained by steam distillation or vacuum distillation of any Boswellia gum resin or Boswellia oil.
17. 'Phytochemical' wherever used in the patent application refers to a pure or semi-pure compound or compounds isolated from plants.

18. 'Biologically active ingredient(s)' wherever used in the patent application refers to any pharmaceutically or dietetically acceptable ingredient(s); compound(s), extract(s), fraction(s), phytochemical(s) and their salts or mixtures thereof derived from plants/animals/microorganisms.
19. 'functional ingredient(s)' wherever used in the patent application refers to any herbal extract(s), dietary supplement(s), antioxidants, vitamins, minerals, amino acids, fatty acids, essential oils, fish oils, enzymes, Glucosamine, Chondroitin and probiotics or mixtures thereof derived from plants/animals/ microorganisms.
20. 'excipients' or 'diluents' or 'carriers' or 'additives' wherever used in the patent application refer to one or more pharmaceutically or dietetically acceptable active or inactive ingredients including but not limited to water, saline, aqueous glucose solution, alcohol (e.g. ethanol), propylene glycol, polyethylene glycol, various animal and vegetable oils, white soft paraffin, paraffin, wax, glucose, fructose, sucrose, maltose, yellow dextrin, white dextrin, aerosol, microcrystalline cellulose, calcium stearate, magnesium stearate, sorbitol, stevioside, corn syrup, lactose, citric acid, tartaric acid, malic acid, succinic acid, lactic acid, L-ascorbic acid, dl-alpha-tocopherol, glycerin, propylene glycol, glycerin fatty ester, poly glycerin fatty ester, sucrose fatty ester, sorbitan fatty ester, propylene glycol fatty ester, acacia, carrageenan, casein, gelatin, pectin, agar, vitamin B group, nicotinamide, calcium pantothenate, amino acids, calcium salts, pigments, flavours and preservatives.

***Boswellia serrata* and *Boswellia carterii* low polar gum resin extract:**

The gum resin obtained from *Boswellia serrata/Boswellia carterii/Boswellia papyrifera* or any Boswellia species is a complex mixture comprising essential oil, volatile oils, Boswellic acids, low polar compounds, sugars and polysaccharide fraction. The *Boswellia serrata/Boswellia carterii/Boswellia papyrifera* extracts widely available in the international markets are acidic fractions separated from the gum resin which are standardized to contain 65% or 85% total Boswellic acids by titrimetric method of analysis. During the execution of commercial process for regular Boswellia extracts derived from *Boswellia serrata/Boswellia carterii/Boswellia papyrifera*

(85% total Boswellic acids), the acidic fraction, which contains predominantly triterpene acids including Boswellic acids is separated from the rest of gum resin components. The sugars and other polymeric materials get separated out into the aqueous phase during the enrichment process for total Boswellic acids. The remaining water immiscible low polar compounds, are separated as Boswellia oil fraction/extract. These low polar compounds are either absent or present at very low concentration in both, commercial Boswellia extracts standardized to boswellic acids and Boswellia extracts selectively enriched in 3-O-acetyl-11-keto-□-Boswellic acid (AKBA).

The said Boswellia oil fraction/extract constitutes a significant component in Boswellia gum resin. However, it has very limited commercial utility and it is mostly discarded as a waste material. Potential utilization of this fraction/extract has been long overdue. The inventors found very unexpectedly that Boswellia low polar gum resin extract (BLPRE), a fraction obtained after removing the volatile compounds from the Boswellia oil fraction/extract has several beneficial biological properties. In addition, BLPRE unexpectedly exhibited synergistic activity when combined with other biologically active ingredients.

In our earlier Indian patent application 2229/CHE/2008 filed on 15th September, 2008 and PCT application # PCT/IN2009/000505 filed on 14th September, 2009 we disclosed synergistic compositions comprising *Boswellia serrata* low polar gum resin extract and AKBA enriched fraction, BLPRE composition and its method of identification are also disclosed.

A representative procedure for obtaining *Boswellia serrata* low polar gum resin extract (BsLPRE) comprises:

a) Procuring the gum resin of *Boswellia serrata.*
b) extraction with an water immiscible organic solvent and the insoluble gum materials were separated by filtration and discarded,
c) washing the organic solvent extract repeatedly with dilute aqueous alkali solution to remove the acidic compounds,
d) washing the organic layer successively with water and brine,

e) evaporating the organic layer under vacuum at 60 - 70°C to obtain an oily residue,

f) the volatile components are then removed from the said oily residue under high vacuum and high temperature to obtain a viscous oil, which is referred herein after as Boswellia serrata low polar gum resin extract (BsLPRE).

Alternatively, the BsLPRE can also be prepared by a process comprising:

a) preparing the alcohol or hydroalcohol extract of *Boswellia serrata* gum resin,

b) partitioning the alcohol extract between an aqueous alkali solution and a water immiscible organic solvent,

c) separation of the organic solvent layer , followed by evaporating the organic layer under vacuum at 60 - 70°C to obtain an oily residue,

d) the volatile components are then removed from the said oily residue under high vacuum and high temperature to obtain a viscous oil , which is referred herein after as Boswellia serrata low polar gum resin extract (BsLPRE) .

A representative procedure for obtaining *Boswellia carterii* low polar gum resin extract (BcLPRE) comprises:

a) procuring the gum resin of *Boswellia carterii,*

b) extracting the gum resin with an water immiscible organic solvent and the insoluble gum materials were separated by filtration and discarded,

c) washing the organic solvent extract repeatedly with dilute aqueous alkali solution to remove the acidic compounds,

d) washing the organic layer successively with water and brine,

e) evaporating the organic layer under vacuum at 60 - 70°C to obtain an oily residue.

f) the volatile components are then removed from the said oily residue under high vacuum and high temperature to obtain a viscous oil, which is referred herein after as Boswellia carterii low polar gum resin extract (BcLPRE).

Alternatively, the BcLPRE can also be prepared by process comprising:

a) preparing the alcohol or hydroalcohol extract of *Boswellia carterii* gum resin,

b) partitioning the alcohol extract between an aqueous alkali solution and a water immiscible organic solvent,

c) separation of the organic solvent layer, followed by evaporating the organic layer under vacuum at 60 - 70°C to obtain an oily residue,

d) the volatile components are then removed from the said oily residue under high vacuum and high temperature to obtain a viscous oil, which is referred herein after as Boswellia carterii low polar gum resin extract (BcLPRE).

The representative processes for obtaining Boswellia low polar gum resin extract (BLPRE) from *Boswellia serrata*, *Boswellia carterii* are described above. However, a similar process or processes can be applied to any of the gum resin obtained from Boswellia species for producing the low polar gum resin extract.

In order to understand the chemical composition of BsLPRE, the inventors have carried out extensive separation of BsLPRE using repeated column chromatography and high performance liquid chromatography (HPLC), and isolated several diterpenoid and triterpenoid compounds. The structures of the compounds were rigorously characterized using ^{1}H NMR, ^{13}C NMR, DEPT, HSQC and HMBC, Mass spectral data. The compounds so obtained and identified are guiol (**1**), nephthenol (**2**), serratol (**3**), diterpene X (**4**), lupeol (**5**), olean-12-ene-3β-ol (**6**), olean-12-ene-3α-ol (**7**), lanosta-8, 24-diene-3α-ol (**8**) and urs-12-ene-3α-ol (**9**) as depicted in **Figure I**. The fraction, Boswellia serrata low polar gum resin extract (BsLPRE) was then standardized to three or more of the phytochemical marker compounds selected from **1** to **9**. The typical results obtained are summarized in the **Table 1** and a typical chromatogram depicting the profile of BsLPRE is presented in **Figure II**. However, the inventors have also found that this composition of BsLPRE or any other Boswellia low polar gum resin extract composition (BLPRE) obtained from any other species may vary based on several factors such as Boswellia species used, age of the plant, season of collection of gum resin, geographic location and manufacturing process employed.

The foregoing results manifest that BsLPRE is a novel composition comprising unique combination of sesquiterpenoids, diterpenoids and triterpenoids and other

phytochemical(s). A compound tentatively identified as diterpene X (**4**) and compounds guiol (**1**), nepthenol (**2**) and Lanosta-8, 24-diene-3α-ol (**8**) are not known to be metabolites of Boswellia serrata gum resin. These results suggest that BsLPRE is a novel composition. Surprisingly BsLPRE also exhibited potent biological properties. BsLPRE potently inhibited 5-lipoxygenase enzyme (**Table 2**). It showed 15.13% inhibition of 5-lipoxygenase at 10 μg/mL concentration.

The identification of the composition of low polar gum resin extract obtained from various Boswellia species such as *Boswellia carterii*, *Boswellia papyrifera* is under process. It is contemplated that the low polar gum resin extract of these as well as other Boswellia species comprise a composition having some similarity to that of *Boswellia serrata*. However, the low polar gum resin extract of *Boswellia carterii* (BcLPRE) has shown biological activity and synergistic effect very similar to that exhibited by BsLPRE as summarized in the following in vitro and in vivo studies. The experimental studies are discussed in the examples.

Synergistic composition(s) comprising Boswellia low polar gum resin extract (BLPRE):

The inventors have conducted several cell based and enzyme based in vitro studies on a broad array of Boswellia extracts like *Boswellia serrata* low polar gum resin extract (BsLPRE), *Boswellia carterii* low polar gum resin extract (BcLPRE), Boswellia extracts standardized to Boswellic acids such as *Boswellia serrata* extract standardized to 85% Boswellic acids (BSE 85%), *Boswellia serrata* extract standardized to 65% Boswellic acids (BSE 65%), *Boswellia carterii* extract standardized to 85% Boswellic acids (BCE 85%), and a few other herbal extracts. The individual extracts and different combination(s) of these extracts were tested for their efficacy to inhibit 5-lipoxygenase enzyme (5-LOX).

It was found very surprisingly that the composition(s) comprising either BsLPRE or BcLPRE in combination with any one of the following standardized extracts such as BSE 85%, BCE 85%, and BSE 65% at certain ratios showed synergistic inhibition of 5- lipoxygenase enzyme.

The composition-3A (BsLPRE and BSE 85% in 1:2 ratio), showed 27.12% inhibition at 10 µg/mL compared to 15.13% and 21.04% inhibitions shown respectively by BsLPRE and BSE 85% at the same concentrations.

The comparative 5-lipoxygenase inhibition shown by composition-3A (BsLPRE and BSE 85% in 1:2 ratio), composition-4 (BcLPRE and BCE 85% in 1:2 ratio), composition-18 (BcLPRE and BSE 85% in 1:2 ratio), composition–7A (BsLPRE and BSE 65% in 1:2 ratio), along with those shown by individual ingredients/extracts are presented in **Figure III**.

The synergistic effects shown by composition-3A, composition-4, composition-18, composition-7A in vitro along with few other compositions were then put to test in an in vivo study in Freund's Complete Adjuvant induced arthritis model of Sprague Dawley rats. The anti-inflammatory efficacy of composition-3A, composition-4, composition-18, composition-7A, composition–42 (BsLPRE and CLE 20% in 1:2 ratio), composition–26 (BsLPRE and CLE 95% in 1:2 ratio), composition–51 (BcLPRE and CAE 20% in 1:2 ratio) and composition–35 (BcLPRE and CAE 95% in 1:2 ratio) were evaluated in an in vivo study in Freund's Complete Adjuvant induced arthritis model of Sprague Dawley rats and compared their efficacy with the efficacy shown by the individual ingredients/extracts such as BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, CLE 20%, CLE 95%, CAE 20% and CAE 95%. The rats of either sex were randomly selected and divided into nineteen groups containing six animals per group and the treatment groups were supplemented daily with 200 mg/kg body weight (BW) of one of BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, CLE 20%, CLE 95%, CAE 20%, CAE 95%, composition-3A, composition-4, composition-18, composition-7A, composition–42, composition–26, composition–51 and composition–35 for 14 days. The positive control group was supplemented daily with Prednisolone at 10 mg/kg body weight. At the 14th day, Freund's Complete Adjuvant (FCA) was injected subcutaneously in the sub-plantar region of the left hind paw of each animal. The experiment was terminated on 28th day. Blood samples were collected from each animal at regular intervals and paw volumes were measured by Plethysmography equipment on the day of FCA injection and after 13 days of FCA inoculation. The difference in volume of paw edema is

considered as the inflammatory response. The in vivo anti-inflammatory response of BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, CLE 20%, CLE 95%, CAE 20%, CAE 95%, composition-3A, composition-4, composition-18, composition-7A, composition-42, composition-26, composition-51, composition-35 and Prednisolone were estimated by calculating the percentage inhibition of paw edema when compared to the CMC supplemented control.

The treatment groups supplemented with 200 mg/kg body weight of *Boswellia serrata* low polar gum resin extract (BsLPRE) and 200mg/kg body weight of *Boswellia serrata* extract standardized to 85% total Boswellic acids (BSE 85%) showed 23% and 30% reduction in paw edema respectively. However, the treatment group supplemented with composition-3A (BsLPRE and BSE 85% in 1:2 ratio) at the same dose level showed better reduction and achieved 42% reduction in paw edema volume. The positive control group supplemented with Prednisolone exhibited 46% inhibition at 10 mg/kg dose level. Similarly, the other inventive compositions composition-4, composition-18, composition-7A, composition-42, composition-26, composition-51 and composition-35 also exhibited synergistic effects as summarized in **Figure IV** and **Table 3** confirming the observed in vitro results.

Therefore, the foregoing data shows that the compositions comprising either BsLPRE or BcLPRE in combination with a standardized extract of Boswellia species such as, BSE 85%, BCE 85% and BSE 65% or a standardized extract of Curcuma species such as CLE 20%, CLE 95%, CAE 20% and CAE 95% in the ratio of 1:2 are more potent as anti-inflammatory agents compared to the efficacy shown by the individual components at the same dose levels, manifesting an unexpected synergistic association between these extracts.

Boswellia serrata and *Boswellia carterii* low polar gum resin extracts (BsLPRE and BcLPRE respectively) obtained after removing the volatile compounds have been used to demonstrate the present invention. However, Boswellia oil fraction obtained from any of the Boswellia species or volatile fraction obtained from any of the Boswellia species or fractions obtained after partially removing the volatiles from

Boswellia oil or mixtures thereof can also be used for making the compositions and synergistic composition(s) of the invention, and for obtaining the intended therapeutic/health benefits in warm blooded animal(s).

The Boswellia low polar gum resin extracts, used for demonstrating the present invention, have been obtained from *Boswellia serrata* and *Boswellia carterii* and the names BsLPRE and BcLPRE respectively have been chosen arbitrarily for them. However, the inventors have found that low polar gum resin extract (BLPRE) with similar chemical and biological properties can also be derived from other Boswellia species using similar processes as shown in Example-1 and Example-2.

Commercially available *Boswellia serrata* extract and *Boswellia carterii* extract standardized to 85% Boswellic acids have been used for making the composition(s) to demonstrate the present invention. However, any Boswellia extract(s) or fraction(s) or Boswellia extracts standardized to at least one or more Boswellic acids or their salts; extract(s)/fraction(s) standardized to 50-100% total Boswellic acids by titrimetric method of analysis or extract(s)/fraction(s) standardized to 30%-100% total Boswellic acids by HPLC method of analysis or extract(s)/fraction(s) having 3-O-acetyl-11-keto-β-Boswellic acid (AKBA) concentration in the range of 0.1-99% can also be used to make the compositions described in the present invention.

The BLPRE produced from *Boswellia serrata* or *Boswellia carterii* when combined with an array of Boswellia or Curcuma extracts showed synergistic activity. However it can be contemplated that BLPRE produced from other Boswellia species can also be useful in preparing the synergistic composition(s).

Different embodiments of the present invention are as outlined below:

In an important aspect, the invention provides a Boswellia low polar gum resin extract (BLPRE) comprising novel phytochemical composition of sesquiterpenes, diterpenes, triterpenes, and other phytochemical(s) obtained from Boswellia gum resin.

In another aspect, the invention provides Boswellia low polar gum resin extract (BLPRE) where in the gum resin can be obtained/originated from any of the Boswellia species including but not limited to *Boswellia serrata*, *Boswellia carterii* and *Boswellia papyrifera* or mixtures thereof.

In another aspect, the invention provides a Boswellia low polar gum resin extract from *Boswellia serrata* gum resin, wherein the said extract comprises phytochemical marker compounds selected from but not limited to guiol (**1**), nephthenol (**2**), serratol (**3**), diterpene X (**4**), lupeol (**5**), olean-12-ene-3β-ol (**6**), olean-12-ene-3α-ol (**7**), lanosta-8,24-diene-3α-ol (**8**) and urs-12-ene-3α-ol (**9**).

In another aspect, the invention provides a process for producing Boswellia low polar resin extract (BLPRE) comprising the following steps:

a) extraction of the gum resin of Boswellia species with a water immiscible organic solvent and filtering the extract carefully to remove the insoluble resin material.

b) washing the organic solvent extract repeatedly with an aqueous alkali solution such as aqueous potassium hydroxide

c) washing the organic layer obtained after the alkali wash, with water and brine,

d) evaporating the said organic layer under vacuum and high temperature to obtain the oily residue (Boswellia oil),

e) removing the volatile compounds from the said oily residue under high vacuum and high temperature to obtain Boswellia low polar resin extract (BLPRE).

The water immiscible organic solvent used for extraction can be selected from the group comprising but not limited to 1,2-dichloroethane, hexane, dichloromethane, chloroform, ethyl acetate, n-butanol, methyl iso-butyl ketone (MIBK) or their suitable combination thereof.

The alkali solution used for washing the organic solvent extract can be selected from Group-I or Group-II metal hydroxides, which include but not limited to Sodium hydroxide, Potassium hydroxide, Calcium hydroxide and Magnesium hydroxide or mixtures thereof

In another aspect, an alternative process for producing BLPRE comprise:

a) preparing the alcohol or hydroalcohol extract of Boswellia gum resin,

b) partitioning the alcohol extract between an aqueous alkali solution and a water immiscible organic solvent,

c) separation of the organic solvent layer, followed by evaporation of the solvent to obtain oily residue(Boswellia oil),

d) removal of volatile compounds from the said oily residue under high temperature and high vacuum to obtain Boswellia low polar gum resin extract (BLPRE).

In another aspect, a further alternative process for producing Boswellia low polar gum resin extract (BLPRE) comprise,

a) extracting the gum resin of Boswellia species with alcohol or hydro alcohol,
b) evaporating the organic solvent to an optimum level of total solids and then
c) adjusting the pH to the alkaline side, preferably pH 9 – 12,
d) repeatedly extracting the solution with an organic solvent,
e) evaporating the organic solvent under vacuum and high temperature to obtain the oily residue(Boswellia oil),
f) evaporating the volatiles from the said oily residue under high vacuum and high temperature to obtain BLPRE.

The alcohol used for extraction can be selected from the group comprising but not limited to methanol, ethanol and propanol or their suitable combination thereof.

In a major aspect, the invention provides the synergistic composition(s) comprising Boswellia low polar gum resin extract (BLPRE) and at least one component selected from the extract(s) or fraction(s) or phytochemical(s) or their salt(s) or mixtures thereof derived from Boswellia species.

In another major aspect, the invention provides synergistic composition(s) comprising BLPRE and at least one component selected from the extract(s) or fraction(s) or phytochemical(s) or their salt(s) or mixtures thereof derived from Curcuma species.

In another aspect, the invention provides a Boswellia low polar gum resin extract, which is low polar, obtained after selectively removing the acidic and volatile compounds.

In another aspect, the invention provides the use of one or more components selected from Boswellia oil fraction obtained from any of the Boswellia species or volatile fraction obtained from any of the Boswellia species or fractions obtained after partially removing the volatiles from Boswellia oil in place of BLPRE for preparing composition(s) described in the patent application.

In another aspect, the invention provides the Boswellia extract(s) or fraction(s) or pure phytochemicals or their salts or their mixtures thereof preferably obtained from *Boswellia serrata* or *Boswellia carterii* or *Boswellia papyrifera* for preparing the compositions with BLPRE.

In another aspect, the invention provides the synergistic composition(s) comprising BLPRE with one or more selected from the Boswellia extract(s), fraction(s) and extracts /fractions enriched in total Boswellic acids in the range of 50-100%, by the titrimetric method of analysis or 30-100%, by HPLC method of analysis.

In another aspect, the invention provides synergistic composition(s) comprising BLPRE and one or more component(s) selected from the extract(s), fraction(s) and phytochemical(s) comprising Boswellic acids either individually or in combination selected from α-Boswellic acid, β-Boswellic acid, 3-O-acetyl-α-Boswellic acid, 3-O-acetyl-β-Boswellic acid, 3-O-acetyl-11-keto-α-Boswellic acid, 11-keto-β-Boswellic acid and 3-O-acetyl-11-keto-β-Boswellic acid and their salts.

In another aspect, the invention provides synergistic composition(s) comprising BLPRE and one or more component(s) selected from the extract(s), fraction(s) and phytochemical(s) comprising Boswellic acids either individually or in combination selected from α-Boswellic acid in the range of 0.1–20%, β-Boswellic acid in the range of 0.1–50%, 3-O-acetyl-α-Boswellic acid in the range of 0.1–20%, 3-O-

acetyl-β-Boswellic acid in the range of 0.1–99%, 3-O-acetyl-11-keto-α-Boswellic acid 0.1–20%, 11-keto-β-Boswellic acid in the range of 0.1–99% and 3-O-acetyl-11-keto-β-Boswellic acid in the range of 0.1–99% and their salts.

In another aspect the invention provides, compositions comprising BLPRE and one or more selected from extract(s), fraction(s), phytochemical(s) and their salts derived from the Curcuma species.

In another aspect the invention provides, composition(s) comprising BLPRE and at least one or more component(s) selected from the extract(s), fraction(s), phytochemical(s), and their salts derived from Curcuma species, extracts/fractions enriched/standardized to Curcuminoids either individually or in combination in the range of 20-99% by HPLC method of analysis.

In another aspect the invention provides, compositions comprising BLPRE and one or more Curcuma derived components selected from curcumin, demethoxycurcumin, bisdemethoxycurcumin, monodemethylcurcumin, bisdemethylcurcumin, tetrahydrocurcumin, tetrahydro demethoxycurcumin, tetrahydro bisdemethoxycurcumin, ar-turmerone and their salts obtained naturally or by synthesis or by semi-synthesis.

In another aspect, the invention provides process for producing synergistic composition(s) comprising the steps:

(a) extraction of the gum resin of *Boswellia serrata* or *Boswellia carterii* or *Boswellia papyrifera* with a water immiscible organic solvent,

(b) filtering the extract carefully to remove the insoluble resin material,

(c) washing the organic solvent extract repeatedly with an aqueous alkali solution such as aqueous potassium hydroxide,

(d) washing the said alkali washed organic solvent extract with successively water and brine,

(e) evaporating the organic layer under vacuum and high temperature to obtain an oily residue,

(f) removing the volatile compounds from the said oily residue under high vacuum and high temperature to obtain the Boswellia low polar resin extract (BLPRE).

(g) separately, obtaining a Boswellia derived component selected from the extract(s) or fraction(s) or pure compound(s), extracts/fractions selectively enriched in one or more boswellic acid(s) or mixtures thereof,

(h) combining the said BLPRE and at least one Boswellia derived component(s) in a desired ratio to obtain synergistic composition(s),

(i) optionally mixing the said composition(s) with one or more biologically active ingredients, functional ingredients, excipients, diluents, carriers and additives.

In another aspect, the invention provides process for producing synergistic composition(s) comprising the steps:

(a) extraction of the gum resin of *Boswellia serrata* or *Boswellia carterii* or *Boswellia papyrifera* with a water immiscible organic solvent,

(b) filtering the extract carefully to remove the insoluble resin material,

(c) washing the organic solvent extract repeatedly with an aqueous alkali solution such as aqueous potassium hydroxide,

(d) washing the said alkali washed organic solvent extract successively with water and brine,

(e) evaporating the organic layer under vacuum and high temperature to obtain an oily residue,

(f) removing the volatile compounds from the said oily residue under high vacuum and high temperature to obtain the Boswellia low polar resin extract (BLPRE).

(g) separately, obtaining a Curcuma derived component(s) selected from the extract(s) or fraction(s), extracts/fractions enriched with one or more Curcuminoids, pure Curcuminoid compounds or mixtures thereof,

(h) combining the said BLPRE and at least one Curcuma derived component(s) in a desired ratio to obtain synergistic composition(s),

(i) optionally mixing the said composition(s) with one or more biologically active ingredients, functional ingredients, excipients, diluents, carriers and additives.

In another aspect, the invention provides synergistic composition(s) comprising preferably 5%-95% by weight of Boswellia low polar resin extract (BLPRE) and preferably 95%-5% by weight of at least one Boswellia derived component selected from extract(s), fraction(s), extracts and fractions standardized to one or more boswellic acids, pure boswellic acid(s), phytochemical(s) and their salts or mixtures thereof.

In another aspect, the invention provides synergistic composition(s) comprising more preferably 20%-80% by weight of Boswellia low polar resin extract (BLPRE) and more preferably 80%-20% by weight of at least one Boswellia derived component selected from extract(s), fraction(s), extracts and fractions standardized to one or more boswellic acids, pure boswellic acid(s), phytochemical(s) and their salts or mixtures thereof.

In another aspect, the invention provides Boswellia low polar gum resin extract (BLPRE), Boswellia oil, Boswellic acid(s), extract(s), fraction(s), extracts and fractions enriched in one or more boswellic acids, phytochemical(s) and their salts derived from Boswellia species, wherein the Boswellia species include but not limited to *Boswellia serrata, Boswellia carterii, Boswellia papyrifera, Boswellia sacra, Boswellia ameero, Boswellia bullata, Boswellia dalzielii, Boswellia dioscorides, Boswellia elongata, Boswellia frereana, Boswellia nana, Boswellia neglecta, Boswellia ogadensis, Boswellia pirottae, Boswellia popoviana, Boswellia rivae* and *Boswellia socotrana.*

In another aspect of the invention, the composition of BsLPRE or BLPRE varies based on several factors such as Boswellia species used, age of the plant, season of collection of gum resin, geographic location and manufacturing process employed.

In another aspect, the invention provides the synergistic compositions comprising preferably 5%-95% by weight of Boswellia low polar resin extract (BLPRE) and preferably 95%-5% by the weight of at least one Curcuma derived component selected from extract(s), fraction(s), extracts/fractions standardized to one or more curcuminoids, pure curcuminoid(s), phytochemical(s) and their salts or mixtures thereof.

In another aspect, the invention provides synergistic composition(s) comprising more preferably 20%-80% by weight of BLPRE and more preferably 80%-20% by weight of at least one Curcuma derived component selected from extract(s), fraction(s), extracts and fractions standardized to one or more curcuminoids, pure curcuminoid(s), phytochemical(s) and their salts or mixtures thereof.

In another aspect, the invention provides extract(s), fraction(s), extract(s)/fraction(s) selectively enriched in curcuminoids, Curcuminoids, phytochemical(s) and their salts derived from Curcuma species, wherein the Curcuma species include but not limited to *Curcuma longa, Curcuma aromatica, Curcuma zedoaria, Curcuma domestica, Curcuma aeruginosa, Curcuma albicoma, Curcuma albiflora, Curcuma alismatifolia, Curcuma angustifolia, Curcuma elata, Curcuma ferruginea, Curcuma flaviflora, Curcuma yunnanensis,* and *Curcuma zedoaroides.*

In another major aspect, the invention provides composition(s) comprising Boswellia low polar resin extract (BLPRE) and one or more component(s) selected from biologically active ingredient(s), functional ingredient(s), excipient(s), diluent(s), carrier(s) and additive(s).

In another aspect, the Biologically active ingredients used for preparing the composition(s) include but not limited to pharmaceutically or dietetically acceptable active ingredient(s), anti-inflammatory agents, anti-obese agents, anti-diabetic agents, anti-arthritic agents, anti-asthmatic agents, anti-cancer agents, compound(s), extract(s), fraction(s), phytochemical(s) and their salts or mixtures thereof derived from plants, animals or microorganisms.

In another aspect, the functional ingredient(s) used for preparing composition(s) include but not limited to herbal ingredient(s), dietary supplements, antioxidants, vitamins, minerals, amino acids, fatty acids, essential oils, fish oils, enzymes, Glucosamine, chondroitin and probiotics.

In another aspect, the herbal ingredient(s) used for preparing composition(s) include extracts/fractions/phytochemicals derived from plants selected from but not limited to *Withania somnifera, Garcinia mangostana, Garcinia cambogia, Piper nigrum, Piper betle, Piper longum, Bacopa monniera, Centella asiatica, Amorphophallus campanulatus, Amorphophallus konjac, Emblica officinalis, Holoptelea integrifolia, Ocimum tenuiflorum, Annona squamosa* and *Sphaeranthus indicus*.

In another aspect, the invention provides composition(s) for the prevention, control or treatment of one or more diseases or disorders in warm blooded animal(s).

In another embodiment of the invention excipients/diluents/additives/sweetening agents/flavoring agents/wetting agents/absorbents/solution retarding agents include but not limited to distilled water, saline, aqueous glucose solution, alcohol (e.g. ethanol), propylene glycol, polyethylene glycol, various animal and vegetable oils, white soft paraffin, paraffin, wax, glucose, fructose, sucrose, maltose, saccharin, yellow dextrin, white dextrin, aerosol, microcrystalline cellulose, calcium stearate, magnesium stearate, sorbitol, stevioside, corn syrup, lactose, citric acid, tartaric acid, malic acid, succinic acid, lactic acid, L-ascorbic acid, dl-alpha-tocopherol, glycerin, propylene glycol, glycerin fatty ester, poly glycerin fatty ester, sucrose fatty ester, sorbitan fatty ester, propylene glycol fatty ester, acacia, carrageenan, casein, gelatin, pectin, agar, vitamin B group, nicotinamide, calcium pantothenate, amino acids, calcium salts, cetyl alcohol, glyceryl monostearate, kaolin, betonite clay pigments, peppermint, methyl salicylate, orange flavor, vanilla flavor and preservatives alone or in a suitable combination thereof.

In another aspect, the invention provides for administration of Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) in comminuted form or in unmodified form in a suitable dosage form selected from but not limited to an

infusion solution, injection solution, tablet, capsule, cream, gel, granules, precipitate, extract, liquid, syrup, shots, exudates, ointment, enema, medicinal pack, topical patches, controlled release tablets, controlled release capsules or food supplement.

In another aspect, the invention provides for formulation of Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) into suitable forms including but not limited to oral agents such as tablets, capsules, soft capsules, hard capsules, pills, granules, powders, emulsions, suspensions, syrups and pellets; as parenteral agents such as injection solution, drops and suppositories; and as transdermal agents such as patches, topical creams and gel and food ingredients or beverages.

In another aspect the invention provides use of the composition(s) for the prevention, control and treatment of disorders or diseases in warm-blooded animals in need thereof.

In another aspect, the invention provides a method of using a therapeutically effective amount of Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) for the prevention, control and treatment of diseases or disorders selected from but not limited to inflammation, metabolic disorders, inflammatory disorders, asthma, atherosclerosis, endothelial dysfunction, osteoarthritis, rheumatoid arthritis, allergic rhinitis, dermatitis, psoriasis, cystic fibrosis, inflammatory bowel diseases, multiple sclerosis, diabetes, memory loss, neurological disorders, cartilage degradation, aging, skin disorders, disorders in cholesterol levels (LDL, VLDL and HDL), hyper triglyceridemia, hyperlipidemia, hypercholesterolemia, hypertension, high blood pressure, immune disorders, coronary heart disease, vasculitis, ulcerative colitis, gastrointestinal allergies, nephritis, conjunctivitis, chronic obstructive pulmonary disease, occupational asthma, eczema, bronchitis, hay fever, hives, adult respiratory distress syndrome, allergic disorders and for conditions like wheezing, dyspnea, non productive cough, chest tightness, neck muscle tightness, rapid heart rate, chest pain, infectious diseases, osteoporosis, joint pain, joint discomfort, cognitive disorders and several other conditions associated thereof in warm blooded animals in need thereof.

In another aspect, administration of a therapeutically effective amount of Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) for the prevention, control and treatment of disease conditions related to or associated with inflammation, which include but not limited to asthma, occupational asthma, eczema, bronchitis, hay fever, hives, rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, osteoarthritis, refractory rheumatoid arthritis, chronic non-rheumatoid arthritis, osteoporosis, coronary heart disease, atherosclerosis, endothelial dysfunction, multiple sclerosis, vasculitis, nephritis, uveitis, glomerulonephritis, systemic lupus erythematosis, post-angioplasty restenosis, ulcerative colitis, conjunctivitis, dermatitis, psoriasis, cystic fibrosis, adult respiratory distress syndrome, IBS (inflammatory bowel syndrome), IBD (inflammatory bowel disease), chronic obstructive pulmonary disease, adult respiratory distress syndrome, allergic rhinitis, gastrointestinal allergies, allergic disorders and for conditions like wheezing, dyspnea, non productive cough, chest tightness, neck muscle tightness, rapid heart rate, joint pain, and delayed-type hypersensitivity in warm blooded animals in need thereof.

In another aspect, the invention provides Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) for the amelioration of one or more biological markers, which include but not limited to 5-lipoxygenase (5-LOX), 5-Lipoxygenase activating protein(FLAP), Macrophage/Adipocyte Fatty acid binding protein (aP2), IFN-γ, IL-4, ICAM, VCAM , MMPs, TNFα, NFκB and IL-1β by composition(s) in warm blooded animals in need thereof.

In another aspect, the invention provides a method of use of Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) for the amelioration of one or more biological markers, which include but not limited to 5-lipoxygenase (5-LOX), 5-Lipoxygenase activating protein (FLAP), Macrophage/Adipocyte Fatty acid binding protein (aP2), IFN-γ, IL-4, ICAM, VCAM , MMPs, TNFα, NFκB and IL-1β by composition(s) in warm blooded animals in need thereof.

Examples

Example 1

Preparation of *Boswellia serrata* low polar gum resin extract (BsLPRE):

The *Boswellia serrata* gum resin (100 g) was dispersed in 600 mL of methyl isobutyl ketone (MIBK) solvent and stirred at room temperature for 60 min. The insoluble gum materials were separated by filtration. The MIBK solution was extracted repeatedly with 2% KOH solution (3 x 200 mL) to remove the acidic compounds. The MIBK layer was then washed successively with water (400 mL) and brine (200 mL). The MIBK layer was evaporated under vacuum at 60 – 70°C and the volatile components are then removed from the oily residue under high vacuum at 75 – 85°C to obtain BsLPRE as viscous oil (12 g).

Alternatively, the gum resin (250 g) collected from *Boswellia serrata* was extracted with methanol (300 mLx3) and the combined methanol extract was concentrated. The residue (50 g) was dissolved in ethyl acetate (400 mL) and extracted thrice with 1N KOH (3 x 100 mL). The organic layer was washed with water (2 x 200 mL) and brine (200 mL) and evaporated to obtain oily residue (Boswellia oil). The volatile compounds were evaporated from the oil under high vacuum at 75-85°C to obtain 22 g of BsLPRE.

The BsLPRE was subjected to column chromatography over normal silica gel using solvents of increasing polarity starting from hexane to hexane/ethyl acetate mixtures to ethyl acetate. The identical fractions were combined based on TLC and the combined fractions were subjected individually to repeated column over silica gel using mixtures of hexane/ethyl acetate or hexane/acetone as eluants to obtain pure compounds. Some of the impure fractions were further subjected to preparative HPLC using a reversed phase C18 silica column to obtain pure compounds. The structures of individual compounds were established by analyzing the ^{1}H NMR, ^{13}C NMR, DEPT, HSQC and HMBC and mass spectral data and then comparing the data with that of known compounds. Nine of the prominent compounds are identified as guiol (**1**), nephthenol (**2**), serratol (**3**), diterpene X (**4**), lupeol (**5**), olean-12-ene-3β-ol (**6**), olean-12-ene-3α-ol (**7**), lanosta-8,24-diene-3α-ol (**8**) and urs-12-ene-3α-ol (**9**)

as depicted in **Figure I**. The pure compounds were then utilized to standardize the Boswellia serrata low polar extract (BLPRE) using HPLC method. The novel composition of BLPRE, evaluated based on analytical HPLC method, along with the retention times (R_t) is summarized in **Table 1**. The HPLC chromatogram for BLPRE is depicted in **Figure II**.

Guaiol (1):

^{1}H NMR ($CDCl_3$, 400MHz): δ 2.57-2.53(1H, m), 2.46-2.39 (1H, m), 2.33-2.30 (1H, m), 2.28-2.22 (1H, m), 2.09-1.89 (2H, m), 1.84-1.75(2H, m), 1.67-1.52 (2H, m), 1.48-1.28 (3H, m), 1.18 (6H, s), 1.03 (3H, d, J = 7.2 Hz), 0.99 (3H, d, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): δ 140.98, 140.02, 73.80, 49.84, 45.10, 35.27, 33.83, 33.32, 31.28, 29.20, 27.35, 27.11, 26.27, 19.61, 19.26.

Nephthenol (2):

^{1}H NMR ($CDCl_3$, 400MHz): δ 5.12 (1H, t, J = 7.0 Hz), 5.00 (1H, t, J = 6.4 Hz), 4.94 (1H, t, J = 6.4 Hz), 2.20 (2H, m), 2.14 (2H, m), 2.12 (1H, m), 2.07 (2H, m), 2.03 (2H, m), 2.00 (2H, m), 1.90 (1H, dd, J = 14.0, 7.0Hz), 1.65 (1H, m), 1.57 (6H, s), 1.56 (3H, s), 1.34 (1H, m), 1.28 (1H, m), 1.20 (6H, s); ^{13}C NMR ($CDCl_3$, 100MHz): δ 134.09, 133.39, 133.08, 125.98, 125.80, 125.02, 73.94, 48.59, 39.42, 38.88, 37.81, 31.93, 29.69, 28.54, 28.34, 27.70, 27.57, 27.35, 24.73, 24.07, 15.61, 15.58, 15.33.
Mass 290 $C_{20}H_{34}O$

Diterpene X (4)

^{1}H NMR ($CDCl_3$), 400MHz: δ 6.17 (1H, dd, J = 10.8, 15.2 Hz), 5.78 (1H, d, J = 7.2 Hz), 5.28 (1H, d, J = 15.2 Hz), 4.87 (1H, m), 4.41 (1H, d, J = 11.2 Hz), 2.44 (1H, m), 2.26 (1H, dt, *J* = 3.2, 11.6 Hz), 2.11 (1H, m), 2.20 (2H, m), 1.75 (3H, s), 1.75 (6H, s),1.72 (1H,d) 1.66 (3H, s), 1.60 (2H, m), 1.49 (3H, d, J = 0.8Hz), 1.34 (1H, m), 1.19 (3H, s), 0.94 (1H, m); ^{13}C NMR($CDCl_3$), 100MHz: δ 12.05, 16.55, 18.22, 20.80, 25.84, 26.00, 26.45, 28.77, 29.66, 30.58, 37.08, 41.15, 121.48, 125.08, 125.12, 129.10, 132.05, 140.50, 141.89.

Lanosta-8, 24- diene-3α-ol (8):

^{1}H NMR ($CDCl_3$, 400MHz): δ 5.10 (1H, t, J = 6.8 Hz), 3.43 (1H, t, J = 2.4Hz), 2.12-1.85 (8H, m), 1.71 (2H, m), 1.65 (3H, s), 1.59 (3H,s), 1.65 -1.29 (10H, m), 1.26 (3H, s), 1.213-1.16 (1H, m), 0.97 (3H,s), 0.96 (3H, s), 0.92 (3H, d, J = 6.4Hz), 0.87 (6H, s), 0.77 (3H, s); ^{13}C NMR ($CDCl_3$, 100MHz): δ 134.44, 133.42, 130.87, 125.35,

76.02, 50.24, 50.09, 44.92, 44.20, 37.73, 37.27, 36.48, 36.36, 30.92, 29.88, 29.72, 28.09, 27.31, 25.94, 25.70, 25.01, 24.43, 22.30, 21.46, 20.00, 18.90, 18.75, 17.63, 15.60.

Table 1

Composition of Boswellia serrata low polar gum resin extract (BsLPRE)

S. No	Test substance	R_t in min	Percentage
1	Guiol (**1**)	4.5	0.96
2	Nephthenol (**2**)	7.087	2.01
3	Serratol (**3**)	8.027	13.32
4	Diterpene X (**4**)	15.777	0.12
5	Lupeol (**5**)	26.901	0.06
6	Olean-12-ene-3β-ol (**6**)	31.460	1.29
7	Olean-12-ene-3α-ol (**7**)	33.718	5.36
8	Lanosta-8,24-diene-3α-ol (**8**)	35.371	1.34
9	Urs-12-ene-3α-ol (**9**)	37.207	4.55

Example 2

Preparation of *Boswellia carterii* low polar gum resin extract (BcLPRE):

The *Boswellia carterii* gum resin (100 g) was dispersed in 600 mL of methyl isobutyl ketone (MIBK) solvent and stirred at room temperature for 60 min. The insoluble gum materials were separated by filtration. The MIBK solution was extracted repeatedly with 2% KOH solution (3 x 200 mL) to remove the acidic compounds. The MIBK layer was then washed successively with water (400 mL) and brine (200 mL). The MIBK layer was evaporated under reduced pressure at 60 – 70°C and the volatile components are then removed from the oily residue under high vacuum at 75 – 85°C to obtain BcLPRE as a viscous oil (9.5 g).

Alternatively, the gum resin (250 g) collected from *Boswellia carterii* was extracted with methanol (300 mLx3) and the combined methanol extract was concentrated. The residue (50 g) was dissolved in ethyl acetate (400 mL) and extracted thrice with 1N KOH (3 x 100 mL). The organic layer was washed with water (2 x 200 mL) and brine (200 mL) and evaporated to obtain oily residue. The volatile compounds were

evaporated from the oil under high vacuum at 75-85°C to obtain 17.75 g of BcLPRE.

Example 3

Boswellia serrata extract standardized to 50 - 100% total boswellic acids by titrimetric method or to 30 – 100% total boswellic acids by HPLC method of analysis: Boswellia serrata extracts standardized to 85% or 65% total Boswellic acids by titrimetric method of analysis are commercially available. Alternately, these extracts can be prepared using a known procedure. For example, by extracting the gum resin of *Boswellia serrata* using a water immiscible organic solvent and then selectively extracting the acidic compounds from the organic solvent extract using aqueous alkali solution through phase separation. Finally acidification of the alkali solution to precipitate the Boswellic acids followed by filtration and vacuum drying of the resultant solid to yield *Boswellia serrata* extract standardized to 85% Boswellic acids (BSE85%). *Boswellia serrata* extracts standardized to a selected concentration of total Boswellic acids in the range of 50 – 100% by titrimetric method of analysis or 30 – 100% by HPLC method of analysis can be obtained by purification of the *Boswellia serrata* gum resin or *Boswellia serrata* extracts or by dilution of higher grade material.

Example 4

Boswellia carterii extract standardized to 50 - 100% total Boswellic acids (titrimetric method): *Boswellia carterii* extracts standardized to 85% or 65% total Boswellic acids by titrimetric method of analysis can be prepared using a procedure described in Example 3 for Boswellia serrata. For example, by extracting the gum resin of *Boswellia carterii* using a water immiscible solvent and then selectively extracting the acidic compounds from the organic solvent extract using aqueous alkali solution through phase separation. Finally acidification of the alkali solution to precipitate the Boswellic acids followed by filtration and vacuum drying of the solid to yield *Boswellia carterii* extract standardized to 85% total boswellic acids (BCE85%). *Boswellia carterii* extracts standardized to a selected concentration of total Boswellic acids in the range of 50 – 100% by titrimetric method of analysis or 30 – 100% by HPLC method of analysis can be obtained by purification of the *Boswellia carterii* gum resin or *Boswellia carterii* extracts or by dilution of higher grade material.

Example 5

Preparation of composition-1: Composition-1 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and one part of *Boswellia serrata* extract standardized to 85% total Boswellic acids (BSE 85%) (1 g).

Example 6

Preparation of composition-2: Composition-2 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and one part of *Boswellia carterii* extract standardized to 85% total Boswellic acids (BCE 85%) (1 g).

Example 7

Preparation of composition-3A: Composition-3A was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Boswellia serrata* extract standardized to 85% total Boswellic acids (BSE 85%) (2 g).

Preparation of composition-3B: Composition-3B was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Boswellia carterii* extract standardized to 85% total Boswellic acids (BCE 85%) (2 g).

Example 8

Preparation of composition-4: Composition-4 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and two parts of *Boswellia carterii* extract standardized to 85% total Boswellic acids (BCE 85%) (2 g).

Example 9

Preparation of composition-5: Composition-5 was prepared by mixing unit doses of the following components; two parts of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g) and one part of *Boswellia serrata* extract standardized to 85% Boswellic acids (BSE 85%) (1g).

Example 10

Preparation of composition-6: Composition-6 was prepared by mixing unit doses of the following components; two parts of *Boswellia carterii* low polar gum resin

extract (BcLPRE) (2 g) and one part of *Boswellia carterii* extract standardized to 85% Boswellic acids (BCE 85%) (1 g).

Example 11

Preparation of composition-7A: Composition-7A was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1g) and two parts of *Boswellia serrata* extract standardized to 65% Boswellic acids (BSE 65%) (2 g).

Preparation of composition-7B: Composition-7B was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1g) and two parts of *Boswellia carterii* extract standardized to 65% Boswellic acids (BCE 65%) (2 g).

Example 12

Preparation of composition-8: Composition-8 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and two parts of *Boswellia carterii* extract standardized to 65% Boswellic acids (BCE 65%) (2 g).

Example 13

Preparation of composition-9: Composition-9 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and one part of *Boswellia serrata* extract standardized to 65% Boswellic acids (BSE 65%) (1 g).

Example 14

Preparation of composition-10: Composition-10 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and one part of *Boswellia carterii* extract standardized to 65% Boswellic acids (BCE 65%) (1 g).

Example 15

Composition-11: Composition-11 was prepared by mixing unit doses of the following components; two parts of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g), two parts of *Boswellia serrata* extract standardized to 85% Boswellic acids (BSE 85%) (2 g) and one part of white dextrin (1 g).

Example 16

Composition-12: Composition-12 was prepared by mixing unit doses of the following components; two parts of *Boswellia carterii* low polar gum resin extract (BcLPRE) (2 g), two parts of *Boswellia carterii* extract standardized to 85% Boswellic acids (BCE 85%) (2 g) and one part of white dextrin (1 g).

Example 17

Composition-13: Composition-13 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g), two parts of *Boswellia serrata* extract enriched with 95% of 3-O-acetyl-11-keto-β-Boswellic acid (4 g).

Example 18

Composition-14: Composition-14 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (2 g), two parts of *Boswellia carterii* extract enriched with 95% of 3-O-acetyl-11-keto-β-Boswellic acid (4 g).

Example 19

Composition-15: Composition-15 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g), two parts of *Boswellia serrata* extract enriched with 40% of 3-O-acetyl-β-Boswellic acid (4 g).

Example 20

Composition-16: Composition-16 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (2 g), two parts of *Boswellia carterii* extract enriched with 40% of 3-O-acetyl-β-Boswellic acid (4 g).

Example 21

Preparation of composition-17: Composition-17 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and one part of *Boswellia serrata* extract standardized to 85% total Boswellic acids (BSE 85%) (1 g).

Example 22

Preparation of composition-18: Composition-18 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin

extract (BcLPRE) (1 g) and two parts of *Boswellia serrata* extract standardized to 85% total Boswellic acids (BSE 85%) (2 g).

Example 23

Preparation of composition-19: Composition-19 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g), two parts of *Boswellia serrata* extract standardized to 85% total Boswellic acids (BSE 85%) (2 g) and one part of white dextrin (1 g).

Example 24

Preparation of composition-20: Composition-20 was prepared by mixing unit doses of the following components; two parts of *Boswellia carterii* low polar gum resin extract (BcLPRE) (2 g) and one part of *Boswellia serrata* extract standardized to 85% Boswellic acids (BSE 85%) (1 g).

Example 25

Preparation of composition-21: Composition-21 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and one part of *Boswellia carterii* extract standardized to 85% total Boswellic acids (BCE 85%) (1 g).

Example 26

Preparation of composition-22A: Composition-22A was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Boswellia carterii* extract standardized to 85% total Boswellic acids (BCE 85%) (2 g).

Preparation of composition-22B: Composition-22B was prepared by mixing unit doses of the following components; two parts of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g) and one part of *Boswellia carterii* extract standardized to 85% Boswellic acids (BCE 85%) (1 g).

Example 27

Preparation of composition-23: Composition-23 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g), two parts of *Boswellia carterii* extract standardized to 85% total Boswellic acids (BCE 85%) (2 g) and one part of white dextrin (1 g).

Example 28

Preparation of Curcuma longa extract 20-99% Curcuminoids (CLE 20-99%) or Curcuma aromatica extract 20-99% Curcuminoids (CAE 20-99%):

The Curcuma extract standardized to 95% curcuminoids is an enriched product obtained from Curcuma species and it comprises curcumin, demethoxycurcumin and bisdemethoxycurcumin. These and low assay curcuma extracts can be procured from the commercially available extracts or can be produced using one or more of the following procedures. Extraction of *Curcuma longa* rhizome with methanol followed by evaporation of the solvent and washing the residue with hexane gives 20 – 25% total Curcuminoids by HPLC. Precipitation of this 20 – 25% total Curcuminoids product in n-butanol / hexane mixture gives a residue, which on vacuum drying gives 90 – 95% total Curcuminoids by HPLC. Optionally, extraction of *Curcuma longa* rhizome with acetone or ethyl acetate followed by evaporation of the solvent gives Curcuma longa extract comprising 50 - 60% total Curcuminoids. Alternately the low grade extracts can be purified to required concentration of total Curcuminoids using, precipitations, washings, chromatography techniques, resin purifications or combinations thereof. Similar processes or techniques can also be applied to other Curcuma species including but not limited to *Curcuma aromatica, Curcuma zedoaria* and *Curcuma amada* to obtain required concentration of total Curcuminoids.

Example 29

Preparation of composition-24: Composition-24 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and one part of *Curcuma longa* extract standardized to 95% total Curcuminoids (CLE 95%) (1 g).

Example 30

Preparation of composition-25: Composition-25 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and one part of *Curcuma longa* extract standardized to 95% total Curcuminoids (CLE 95%) (1 g).

Example 31

Preparation of composition-26: Composition-26 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin

extract (BsLPRE) (1 g) and two parts of *Curcuma longa* extract standardized to 95% total Curcuminoids (CLE 95%) (2 g).

Example 32

Preparation of composition-27: Composition-27 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and two parts of *Curcuma longa* extract standardized to 95% total Curcuminoids (CLE 95%) (2 g).

Example 33

Preparation of composition-28: Composition-28 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g), two parts of *Curcuma longa* extract standardized to 95% total Curcuminoids (CLE 95%) (2 g) and one part of white dextrin (1 g).

Example 34

Preparation of composition-29: Composition-29 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g), two parts of *Curcuma longa* extract standardized to 95% total Curcuminoids (CLE 95%) (2 g) and one part of white dextrin (1 g).

Example 35

Preparation of composition-30: Composition-30 was prepared by mixing unit doses of the following components; two parts of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g) and one part of *Curcuma longa* extract standardized to 95% total Curcuminoids (CLE 95%) (1 g).

Example 36

Preparation of composition-31: Composition-31 was prepared by mixing unit doses of the following components; two parts of *Boswellia carterii* low polar gum resin extract (BcLPRE) (2 g) and one part of *Curcuma longa* extract standardized to 95% total Curcuminoids (CLE 95%) (1 g).

Example 37

Preparation of composition-32: Composition-32 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and one part of *Curcuma aromatica* extract standardized to 95% total Curcuminoids (CAE 95%) (1 g).

Example 38

Preparation of composition-33: Composition-33 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and one part of *Curcuma aromatica* extract standardized to 95% total Curcuminoids (CAE 95%) (1 g).

Example 39

Preparation of composition-34: Composition-34 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Curcuma aromatica* extract standardized to 95% total Curcuminoids (CAE 95%) (2 g).

Example 40

Preparation of composition-35: Composition-35 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and two parts of *Curcuma aromatica* extract standardized to 95% total Curcuminoids (CAE 95%) (2 g).

Example 41

Preparation of composition-36: Composition-36 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g), two parts of *Curcuma aromatica* extract standardized to 95% total Curcuminoids (CAE 95%) (2 g) and one part of white dextrin (1 g).

Example 42

Preparation of composition-37: Composition-37 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g), two parts of *Curcuma aromatica* extract standardized to 95% total Curcuminoids (CAE 95%) (2 g) and one part of white dextrin (1 g).

Example 43

Preparation of composition-38: Composition-38 was prepared by mixing unit doses of the following components; two parts of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g) and one part of *Curcuma aromatica* extract standardized to 95% total Curcuminoids (CAE 95%) (1 g).

Example 44

Preparation of composition-39: Composition-39 was prepared by mixing unit doses of the following components; two parts of *Boswellia carterii* low polar gum resin

extract (BcLPRE) (2 g) and one part of *Curcuma aromatica* extract standardized to 95% total Curcuminoids (CAE 95%) (1 g).

Example 45

Preparation of composition-40: Composition-40 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and one part of *Curcuma longa* extract standardized to 20% total Curcuminoids (CLE 20%) (1 g).

Example 46

Preparation of composition-41: Composition-41 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and one part of *Curcuma longa* extract standardized to 20% total Curcuminoids (CLE 20%) (1 g).

Example 47

Preparation of composition-42: Composition-42 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Curcuma longa* extract standardized to 20% total Curcuminoids (CLE 20%) (2 g).

Example 48

Preparation of composition-43: Composition-43 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and two parts of *Curcuma longa* extract standardized to 20% total Curcuminoids (CLE 20%) (2 g).

Example 49

Preparation of composition-44: Composition-44 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g); two parts of *Curcuma longa* extract standardized to 20% total Curcuminoids (CLE 20%) (2 g) and one part of white dextrin (1 g).

Example 50

Preparation of composition-45: Composition-45 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g), two parts of *Curcuma longa* extract standardized to 20% total Curcuminoids (CLE 20%) (2 g) and one part of white dextrin (1 g).

Example 51

Preparation of composition-46: Composition-46 was prepared by mixing unit doses of the following components; two parts of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g) and one part of *Curcuma longa* extract standardized to 20% total Curcuminoids (CLE 20%) (1 g).

Example 52

Preparation of composition-47: Composition-47 was prepared by mixing unit doses of the following components; two parts of *Boswellia carterii* low polar gum resin extract (BcLPRE) (2 g) and one part of *Curcuma longa* extract standardized to 20% total Curcuminoids (CLE 20%) (1 g).

Example 53

Preparation of composition-48: Composition-48 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and one part of *Curcuma aromatica* extract standardized to 20% total Curcuminoids (CAE 20%) (1 g).

Example 54

Preparation of composition-49: Composition-49 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and one part of *Curcuma aromatica* extract standardized to 20% total Curcuminoids (CAE 20%) (1 g).

Example 55

Preparation of composition-50: Composition-50 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Curcuma aromatica* extract standardized to 20% total Curcuminoids (CAE 20%) (2 g).

Example 56

Preparation of composition-51: Composition-51 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g) and two parts of *Curcuma aromatica* extract standardized to 20% total Curcuminoids (CAE 20%) (2 g).

Example 57

Preparation of composition-52: Composition-52 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin

extract (BsLPRE) (1 g), two parts of *Curcuma aromatica* extract standardized to 20% total Curcuminoids (CAE 20%) (2 g) and one part of white dextrin (1 g).

Example 58

Preparation of composition-53: Composition-53 was prepared by mixing unit doses of the following components; one part of *Boswellia carterii* low polar gum resin extract (BcLPRE) (1 g), two parts of *Curcuma aromatica* extract standardized to 20% total Curcuminoids (CAE 20%) (2 g) and one part of white dextrin (1 g).

Example 59

Preparation of composition-54: Composition-54 was prepared by mixing unit doses of the following components; two parts of *Boswellia serrata* low polar gum resin extract (BsLPRE) (2 g) and one part of *Curcuma aromatica* extract standardized to 20% total Curcuminoids (CAE 20%) (1 g).

Example 60

Preparation of composition-55: Composition-55 was prepared by mixing unit doses of the following components; two parts of *Boswellia carterii* low polar gum resin extract (BcLPRE) (2 g) and one part of *Curcuma aromatica* extract standardized to 20% total Curcuminoids (CAE 20%) (1 g).

Example 61

Preparation of composition-56: Composition-56 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Withania somnifera* methanol extract (2 g).

Example 62

Preparation of composition-57: Composition-57 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Garcinia mangostana* methanol extract (2 g).

Example 63

Preparation of composition-58: Composition-58 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Annona squamosa* ethanol extract (2 g).

Example 64

Preparation of composition-59: Composition-59 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin

extract (BsLPRE) (1 g) and two parts of *Sphaeranthus indicus* ethyl acetate extract (2 g).

Example 65

Preparation of composition-60: Composition-60 was prepared by mixing unit doses of the following components; one part of *Boswellia serrata* low polar gum resin extract (BsLPRE) (1 g) and two parts of *Bacopa monniera* 90% methanol/water extract (2 g).

Example 66

Evaluation of 5-Lipoxygenase inhibitory activity of BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, composition-3A, composition-4, composition-18 and composition-7A:

5-Lipoxygenase enzyme inhibitory activity was measured using the method of Schewe et al. (Adv Enzymol, Vol 58, 191-272, 1986), modified by Reddanna et. al., (Methods of Enzymology, Vol 187, 268-277, 1990). The assay mixture contained 80 μM linoleic acid and sufficient amount of potato 5-lipoxygenase in 50 mM phosphate buffer (pH 6.3). The reaction was initiated by the addition of enzyme buffer mix to linoleic acid and the enzyme activity was monitored as the increase in absorbance at 234 nm. The reaction was monitored for 120 sec and the inhibitory potential of the test substances, BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, composition-3A, composition-4, composition-18 and composition-7A was measured by incubating various concentrations of test substances two minutes before the addition of linoleic acid. All assays were performed three times. Percentage inhibition was calculated by comparing slope of the curve obtained for test substances with that of the control. The percentage inhibitions of BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, composition-3A, composition-4, composition-18 and composition-7A are summarized in **Table 2** and depicted in the **Figure III**.

Table 2

5-Lipoxygenase inhibitory activity

S. No	Test substance	5-LOX inhibition at 10 μg/ml
1	BsLPRE	15.13

2	BcLPRE	14.36
3	BSE 85%	21.04
4	BCE 85%	19.26
5	BSE 65%	17.68
6	Composition-3A	27.12
7	Composition-4	25.23
8	Composition-18	24.95
9	Composition-7A	23.83

Example 67

The in vivo anti-inflammatory activity of Boswellia low polar gum resin extract (BsLPRE and BcLPRE), a few Boswellia extracts, Curcuma extracts and their compositions:

The anti-inflammatory efficacy of BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, CLE 20%, CLE 95%, CAE 20%, CAE 95%, composition-3A, composition-4, composition-18, composition-7A, composition-42, composition-26, composition-51 and composition-35 were evaluated in an *in vivo* study in Freund's Complete Adjuvant induced arthritis model of Sprague Dawley rats. Prednisolone was used as a positive control. The rats of either sex were randomly selected and divided into nineteen groups containing six animals per group. The treatment group rats were supplemented daily with 200 mg/kg body weight of one of BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, CLE 20%, CLE 95%, CAE 20%, CAE 95%, composition-3A, composition-4, composition-18, composition-7A, composition-42, composition-26, composition-51 and composition-35 for 14 days. The positive control group was supplemented daily with Prednisolone at 10 mg/kg body weight. All supplements were diluted in 10 mL of 1% CMC for administration. The animals of control group received same volume of 1% CMC. At the 14th day, Freund's Complete Adjuvant (FCA) was injected subcutaneously in the sub-plantar region of the left hind paw of each animal. The experiment was terminated on 28th day. Blood samples were collected from each animal at regular intervals and paw volumes were measured by Plethysmography equipment on the day of FCA injection and after 13 days of FCA inoculation. The difference in volume of paw edema is considered as

the inflammatory response. The in vivo anti-inflammatory response of BsLPRE, BcLPRE, BSE 85%, BCE 85%, BSE 65%, CLE 20%, CLE 95%, CAE 20%, CAE 95%, composition-3A, composition-4, composition-18, composition-7A, composition-42, composition-26, composition-51, composition-35 and Prednisolone were estimated by calculating the percentage inhibition of paw edema when compared to the CMC supplemented control.

The treatment groups supplemented with 200 mg/kg body weight of Boswellia serrata low polar gum resin extract (BsLPRE) and 200mg/kg body weight of Boswellia serrata extract standardized to 85% total Boswellic acids (BSE 85%) showed 23% and 30% reduction in paw edema respectively. However, the treatment group supplemented with composition-3A at the same dose level showed better reduction and achieved 42% reduction in paw edema volume. The positive control group supplemented with Prednisolone exhibited 46% inhibition at 10 mg/kg dose level. Similarly, the other inventive compositions composition-4, composition-18, composition-7A, composition-42, composition-26, composition-51 and composition-35 also exhibited synergistic effects as summarized in **Figure IV** and **Table 3** confirming the observed in vitro results.

Table 3

Reduction in Paw volume activity

S. No	Test substance	Reduction in Paw edema	Concentration mg/kg body weight
1	BsLPRE	23	200
2	BcLPRE	19	200
3	BSE 85%	30	200
4	BCE 85%	28	200
5	BSE 65%	24	200
6	CLE 20%	10	200
7	CLE 95%	25	200
8	CAE 20%	8	200

9	CAE 95%	23	200
10	Composition-3A	42	200
11	Composition-4	38	200
12	Composition-18	35	200
13	Composition-7A	31	200
14	Composition-42	26	200
15	Composition-26	35	200
16	Composition-51	21	200
17	Composition-35	33	200
18	Prednisolone	46	10

It will be appreciated by those of ordinary skilled in the art that changes could be made to the embodiments described above without departing from the broad inventive concept thereof. It is understood, therefore, that this invention is not limited to the particular embodiments or examples disclosed, but is intended to cover modifications within the embodiments and scope of the present invention.

We Claim,

1. A Boswellia low polar gum resin extract (BLPRE) comprising novel phytochemical composition of sesquiterpenes, diterpenes, triterpenes, and other phytochemical(s) derived from gum resin of Boswellia species.
2. The Boswellia low polar gum resin extract (BLPRE) as claimed in claim 1, wherein the Boswellia species used for obtaining BLPRE is selected from one or more plant(s) comprising *Boswellia serrata*, *Boswellia carterii* and *Boswellia papyrifera*.
3. A process for preparation of the Boswellia low polar gum resin extract (BLPRE) as claimed in claim 1, wherein the process comprises:

a) procuring the gum resin of one or more plant(s) selected from *Boswellia serrata*, *Boswellia carterii* and *Boswellia papyrifera*,

b) extraction of the gum resin with a water immiscible organic solvent,

c) filtering the extract carefully to remove the insoluble resin material,

d) washing the organic solvent extract repeatedly with an aqueous alkali solution followed by,

e) washing the organic layer with water and brine,

f) evaporating the organic layer under vacuum and high temperature to obtain an oily residue,

g) removing the volatile compounds from the said oily residue under high vacuum and high temperature to obtain BLPRE.

4. A Boswellia low polar gum resin extract derived from *Boswellia serrata* gum resin, wherein the said extract can be identified by the presence of at least three compounds selected from guiol (**1**), nephthenol (**2**), serratol (**3**), diterpene X (**4**), lupeol (**5**), olean-12-ene-3β-ol (**6**), olean-12-ene-3α-ol (**7**), lanosta-8,24-diene-3α-ol (**8**) and urs-12-ene-3α-ol (**9**).
5. The process as claimed in claim 3, wherein the water immiscible organic solvent is selected from one or more solvents comprising 1,2-dichloroethane, hexane, dichloromethane, chloroform, ethyl acetate, n-butanol and methyl iso-butyl ketone (MIBK).
6. The process as claimed in claim 3, wherein the alkali solution is derived from one or more Group-I/Group-II metal hydroxides, which comprise Sodium

hydroxide, Potassium hydroxide, Calcium hydroxide and Magnesium hydroxide.

7. A process as claimed in claim 3, wherein an alternative process comprises:
   a) extracting the gum resin with alcohol or hydro alcohol,
   b) evaporating the organic solvent to optimum total solids,
   c) adjusting the pH to alkaline side, preferably the pH between 9 – 12,
   d) repeatedly extracting the solution with an organic solvent
   e) evaporating the organic solvent under vacuum at high temperature to obtain an oily residue,
   f) evaporation of volatile compounds from the said oily residue under high vacuum and high temperature to obtain BLPRE.
8. The process as claimed in claim 7, wherein the alcohol is selected from the group comprising methanol, ethanol and propanol or their suitable combination thereof.
9. The Boswellia low polar gum resin extract (BLPRE) as claimed in claims 1 and 4, wherein the said BLPRE is obtained after selectively removing the acidic and volatile compounds.
10. A synergistic composition comprising Boswellia low polar gum resin extract (BLPRE) and one or more component(s) selected from biologically active ingredient(s), functional ingredient(s), excipient(s), diluents(s), carrier(s) and additive(s).
11. A synergistic composition as claimed in claim 10, wherein the composition comprises Boswellia low polar gum resin extract and one or more component(s) selected from the extract(s), fraction(s), extracts and fractions standardized to one or more boswellic acids, boswellic acid(s), phytochemical(s) and their salt(s) derived from Boswellia species.
12. A synergistic composition as claimed in claim 10, wherein the composition comprises Boswellia low polar gum resin extract and one or more component(s) selected from the extract(s), fraction(s), extracts and fractions standardized to one or more Curcuminoid(s), Curcuminoid(s), phytochemical(s) and their salt(s) derived from Curcuma species.

13. The Boswellia derived component(s) as claimed in claim 11, comprise total Boswellic acids preferably in the range of 30-100% by titrimetric or HPLC method of analysis.
14. The Boswellia derived component(s) as claimed in claim 11, comprise total Boswellic acids more preferably in the range of 50-95% by titrimetric or HPLC method of analysis.
15. The Boswellia derived component(s) as claimed in claim 11, comprise one or more Boswellic acid(s) selected from α-Boswellic acid, β-Boswellic acid, 3-O-acetyl-α-Boswellic acid, 3-O-acetyl-β-Boswellic acid, 3-O-acetyl-11-keto-α-Boswellic acid, 11-keto-β-Boswellic acid and 3-O-acetyl-11-keto-β-Boswellic acid.
16. The Curcuma derived component(s) as claimed in claim 12, comprise Curcuminoid(s) in the range of 20-99% by HPLC method of analysis.
17. The Curcuma derived component(s) as claimed in claim 12, comprise one or more component(s) selected from curcumin, demethoxycurcumin, bisdemethoxycurcumin, monodemethylcurcumin, bisdemethylcurcumin, tetrahydrocurcumin, tetrahydro demethoxycurcumin, tetrahydro bisdemethoxycurcumin and ar-turmerone.
18. A process for making synergistic composition(s) as claimed in claim 11, wherein the said process comprise:
    (a) obtaining Boswellia low polar gum resin extract using a process as claimed in claim 3 or claim 7,
    (b) separately obtaining one or more Boswellia derived component(s) selected from extract(s), fraction(s), extracts/fractions selectively enriched in one or more boswellic acid(s) in the range of 30-100% by titrimetric or HPLC method of analysis, phytochemicals and their salts,
    (c) combining the said Boswellia low polar gum resin extract and said Boswellia derived component(s) in a desired ratio to obtain synergistic composition(s),
    (d) optionally combining the said synergistic composition(s) with one or more component(s) selected from biologically active ingredients, functional ingredients, excipients, diluents, carriers and additives.

19. The Boswellia derived component(s) as claimed in any of the preceding claims, is/are derived from one or more species selected from the group comprising *Boswellia serrata*, *Boswellia carterii* and *Boswellia papyrifera.*

20. A process for making synergistic composition(s) as claimed in claim 12, wherein the said process comprise:

(a) obtaining Boswellia low polar gum resin extract using a process as claimed in claim 3 or claim 7,

(b) separately obtaining one or more Curcuma derived component(s) selected from the extract(s), fraction(s), extracts/fractions enriched in one or more Curcuminoids and pure Curcuminoid compounds,

(c) combining the said Boswellia low polar gum resin extract and said Curcuma derived component(s) in a desired ratio to obtain synergistic composition(s),

(d) optionally combining the said synergistic composition(s) with one or more component(s) selected from biologically active ingredients, functional ingredients, excipients, diluents, carriers and additives.

21. The Curcuma derived component(s) as claimed in claims 12, 16, 17 and 20 is derived from one or more species selected from the group comprising *Curcuma longa and Curcuma aromatica.*

22. The synergistic composition as claimed in claim 11, preferably comprises 5%-95% by weight of the Boswellia low polar gum resin extract and 95%-5% by weight of Boswellia derived component(s).

23. The synergistic composition as claimed in claim 22, wherein the composition preferably comprises 5%-95% by weight of *Boswellia serrata* derived Boswellia low polar gum resin extract and 95%-5% by the weight of *Boswellia serrata* derived component(s).

24. The synergistic composition as claimed in claim 22, wherein the composition preferably comprises 5%-95% by weight of *Boswellia carterii* derived Boswellia low polar gum resin extract and 95%-5% by the weight of *Boswellia carterii* derived component(s).

25. The synergistic composition as claimed in claim 22, wherein the composition preferably comprises 5%-95% by weight of *Boswellia serrata* derived

Boswellia low polar gum resin extract and 95%-5% by the weight of *Boswellia carterii* derived component(s).

26. The synergistic composition as claimed in claim 22, wherein the composition more preferably comprises 20%-80% by weight of *Boswellia serrata* derived Boswellia low polar gum resin extract and 80%-20%by the weight of *Boswellia serrata* derived component(s).
27. The synergistic composition as claimed in claim 22, wherein the composition more preferably comprises 20%-80% by weight of *Boswellia carterii* derived Boswellia low polar gum resin extract and 80%-20% by the weight of *Boswellia carterii* derived component(s).
28. The synergistic composition as claimed in claim 22, wherein the composition more preferably comprises 20%-80% by weight of *Boswellia serrata* derived Boswellia low polar gum resin extract and 80%-20% by the weight of *Boswellia carterii* derived component(s).
29. The synergistic composition as claimed in claim 22, wherein the composition more preferably comprises 20%-80% by weight of *Boswellia carterii* derived Boswellia low polar gum resin extract and 80%-20% by the weight of *Boswellia serrata* derived component(s).
30. The synergistic composition as claimed in claim 12, wherein the composition comprises 95%-5% by weight of Boswellia derived Boswellia low polar gum resin extract and 5%-95% by the weight of Curcuma derived component(s).
31. The synergistic composition as claimed in claim 30, wherein the composition preferably comprises 5%-95% by weight of *Boswellia serrata* derived Boswellia low polar gum resin extract and 95%-5% by the weight of *Curcuma longa* derived component(s).
32. The synergistic composition as claimed in claim 30, wherein the composition preferably comprises 5%-95% by weight of *Boswellia serrata* derived Boswellia low polar gum resin extract and 95%-5% by the weight of *Curcuma aromatica* derived component(s).
33. The synergistic composition as claimed in claim 30, wherein the composition preferably comprises 5%-95% by weight of *Boswellia carterii* derived Boswellia low polar gum resin extract and 95%-5% by the weight of *Curcuma longa* derived component(s).

34. The synergistic composition as claimed in claim 30, wherein the composition preferably comprises 5%-95% by weight of *Boswellia carterii* derived Boswellia low polar gum resin extract and 95%-5% by the weight of *Curcuma aromatica* derived component(s).
35. The synergistic composition as claimed in claim 30, wherein the composition more preferably comprises 20%-80% by weight of *Boswellia serrata* derived Boswellia low polar gum resin extract and 80%-20% by the weight of *Curcuma longa* derived component(s).
36. The synergistic composition as claimed in claim 30, wherein the composition more preferably comprises 20%-80% by weight of *Boswellia serrata* derived Boswellia low polar gum resin extract and 80%-20% by the weight of *Curcuma aromatica* derived component(s).
37. The synergistic composition as claimed in claim 30, wherein the composition more preferably comprises 20%-80% by weight of *Boswellia carterii* derived Boswellia low polar gum resin extract and 80%-20% by the weight of *Curcuma longa* derived component(s).
38. The synergistic composition as claimed in claim 30, wherein the composition more preferably comprises 20%-80% by weight of *Boswellia carterii* derived Boswellia low polar gum resin extract and 80%-20% by the weight of *Curcuma aromatica* derived component(s).
39. The composition(s) comprising Boswellia low polar gum resin extract (BLPRE) and one or more component(s) selected from biologically active ingredient(s), functional ingredient(s), excipient(s), diluent(s) and additive(s).
40. The synergistic composition(s) as claimed in claims 11 and 12, optionally comprise one or more component(s) selected from biologically active ingredient(s), functional ingredient(s), excipient(s), diluent(s), carrier(s) and additive(s) or mixtures thereof.
41. The Biologically active ingredients as claimed in claims 10, 39 and 40, comprise one or more pharmaceutically or dietetically acceptable ingredient(s); compound(s), extract(s), fraction(s), phytochemical(s) and their salts or mixtures thereof derived from plants/animals/microorganisms.

42. The functional ingredients as claimed in claims 10, 39 and 40, comprise one or more herbal ingredients, antioxidants, vitamins, minerals, amino acids, fatty acids, essential oils, fish oils, enzymes and probiotics.
43. The excipients/diluents/additives/carriers as claimed in claims 10, 39 and 40, include one or more but not limited to distilled water, saline, aqueous glucose solution, alcohol (e.g. ethanol), propylene glycol, polyethylene glycol, various animal and vegetable oils, white soft paraffin, paraffin, wax, glucose, fructose, sucrose, maltose, yellow dextrin, white dextrin, aerosol, microcrystalline cellulose, calcium stearate, magnesium stearate, sorbitol, stevioside, corn syrup, lactose, citric acid, tartaric acid, malic acid, succinic acid, lactic acid, L-ascorbic acid, dl-alpha-tocopherol, glycerin, propylene glycol, glycerin fatty ester, poly glycerin fatty ester, sucrose fatty ester, sorbitan fatty ester, propylene glycol fatty ester, acacia, carrageenan, casein, gelatin, pectin, agar, vitamin B group, nicotinamide, calcium pantothenate, amino acids, calcium salts, pigments, flavours and preservatives.
44. Method of use of Boswellia low polar gum resin extract (BLPRE) according to claims 1 and 4, in warm blooded animal(s).
45. Method of use of synergistic compositions according to claims 10, 11 and 12, in warm blooded animal(s).
46. Method of use of compositions according to claims, 39 and 40 in warm blooded animal(s).
47. The method of use as claimed in claims 44, 45 and 46, wherein the said composition(s) is/are administered in the form of oral, dermal, intravenous, subcutaneous, intra-peritoneal rectal or intra-muscular route.
48. The method of use as claimed in claims 44, 45 and 46, wherein the said composition(s) is/are administered in the form of an infusion solution, injection solution, tablet, capsule, cream, gel, granules, ointment, enema, medicinal pack, topical patches, controlled release tablets, controlled release capsules or food supplement.
49. The method of use as claimed in claims 44, 45 and 46, wherein the said composition(s) are formulated as oral agents such as tablets, capsules, soft capsules, hard capsules, pills, granules, powders, emulsions, suspensions, syrups and pellets; and parenteral agents such as injection solution, drops and

suppositories; and transdermal agents such as patches, topical creams, and gel and food ingredients or beverages.

50. A method of use of the composition(s) as claimed in claims 42, 44, 45 and 46, in comminuted form or in unmodified form at a daily dosage administered in any of the forms comprising powder, capsules, tablets, granules, precipitate, extract, dried extract, liquid, syrup, shots and exudates.

51. The species of Boswellia as claimed in claims 1, 2, 3 and 11, can further be selected from *Boswellia ameero, Boswellia bullata, Boswellia dalzielii, Boswellia dioscorides, Boswellia elongata, Boswellia frereana, Boswellia nana, Boswellia neglecta, Boswellia ogadensis, Boswellia pirottae, Boswellia popoviana, Boswellia rivae, Boswellia sacra and Boswellia socotrana.*

52. The species of Curcuma as claimed in claim 21, can further be selected from *Curcuma domestica, Curcuma aeruginosa, Curcuma albicoma, Curcuma albiflora, Curcuma alismatifolia, Curcuma angustifolia, Curcuma elata, Curcuma ferruginea, Curcuma flaviflora, Curcuma yunnanensis* and *Curcuma zedoaria.*

53. The Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) as claimed in any of the preceding claims for the prevention, control and treatment of disease(s) or disorder(s) in warm blooded animal(s) in need thereof.

54. A method of use according to claim 53, wherein the disease/disorder include but not limited to metabolic disorders, diabetes, obesity, metabolic syndrome, excess body weight, inflammation, neurological disorders, cartilage degradation, aging, skin disorders, hyper tryglyceridemia, hyperlipidemia, hypercholesterolemia, hypertension, immune disorders, cancer, coronary heart disease, infectious diseases, osteoporosis, osteoarthritis, joint pain, joint discomfort, Alzheimer's, memory loss, cognitive disorders and several other conditions associated thereof comprising administering to warm blooded animal(s) in need thereof.

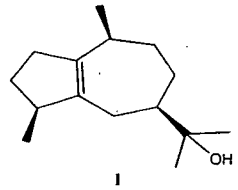
55. A method of use according to claim 54, wherein the conditions associated with inflammation include but not limited to asthma, occupational asthma, eczema, bronchitis, hay fever, hives, rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, osteoarthritis, refractory rheumatoid

arthritis, chronic non-rheumatoid arthritis, osteoporosis, coronary heart disease, atherosclerosis, endothelial dysfunction, multiple sclerosis, vasculitis, nephritis, uveitis, glomerulonephritis, systemic lupus erythematosis, post-angioplasty restenosis, ulcerative colitis, conjunctivitis, dermatitis, psoriasis, cystic fibrosis, adult respiratory distress syndrome, IBS (inflammatory bowel syndrome), IBD (inflammatory bowel disease), chronic obstructive pulmonary disease, adult respiratory distress syndrome, allergic rhinitis, gastrointestinal allergies, allergic disorders and for conditions like wheezing, dyspnea, non productive cough, chest tightness, neck muscle tightness, rapid heart rate and delayed-type hypersensitivity comprising administering to a warm blooded animals in need thereof a therapeutically effective amount of composition(s).

56. The method of treatment by amelioration of one or more biological markers in warm blooded animal(s) in need thereof, by Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) as claimed in any of the preceding claims, wherein the markers include but not limited to 5-lipoxygenase (5-LOX), 5-Lipoxygenase activating protein (FLAP), Macrophage/Adipocyte Fatty acid binding protein (aP2), IFN-γ, IL-4, ICAM, VCAM, MMPs, TNFα, NFκB and IL-1β.

57. A method of use of Boswellia low polar gum resin extract (BLPRE) alone or its composition(s) as claimed in any of the preceded claims in warm blooded animal(s) in need thereof for the amelioration of one or more biological markers, which include but not limited to 5-lipoxygenase (5-LOX), 5-Lipoxygenase activating protein (FLAP), Macrophage/Adipocyte Fatty acid binding protein (aP2), IFN-γ, IL-4, ICAM, VCAM, MMPs, TNFα, NFκB and IL-1β.

Figure I



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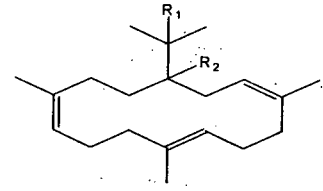
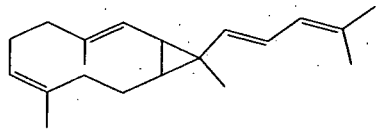


2 R_1 = OH and R_2 = H
3 R_1 = H and R_2 = OH



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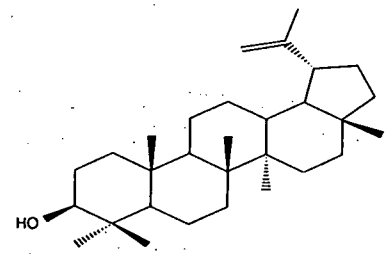

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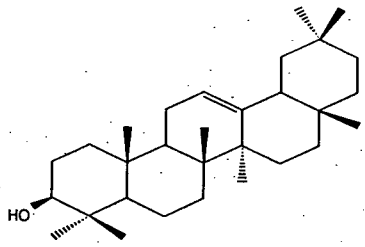

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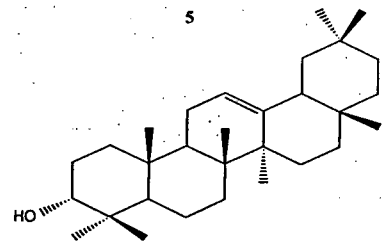

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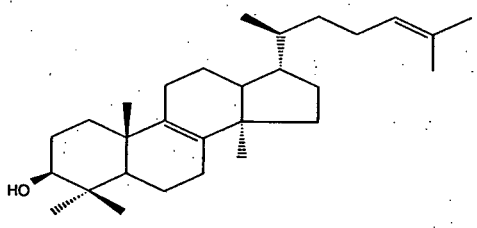

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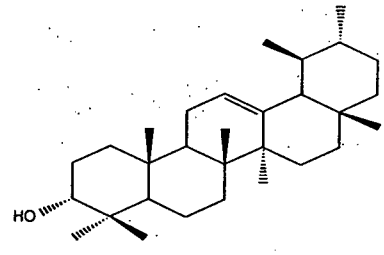
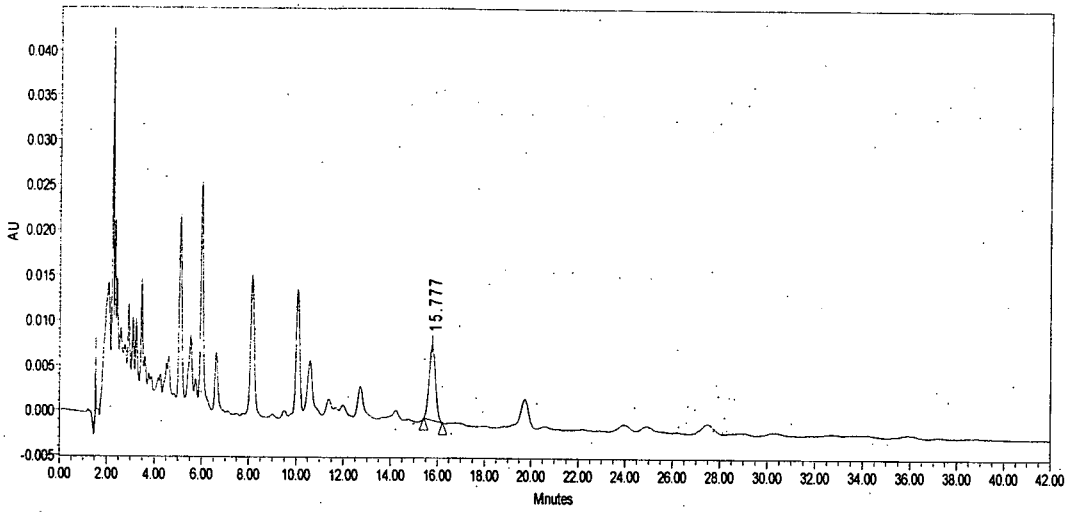
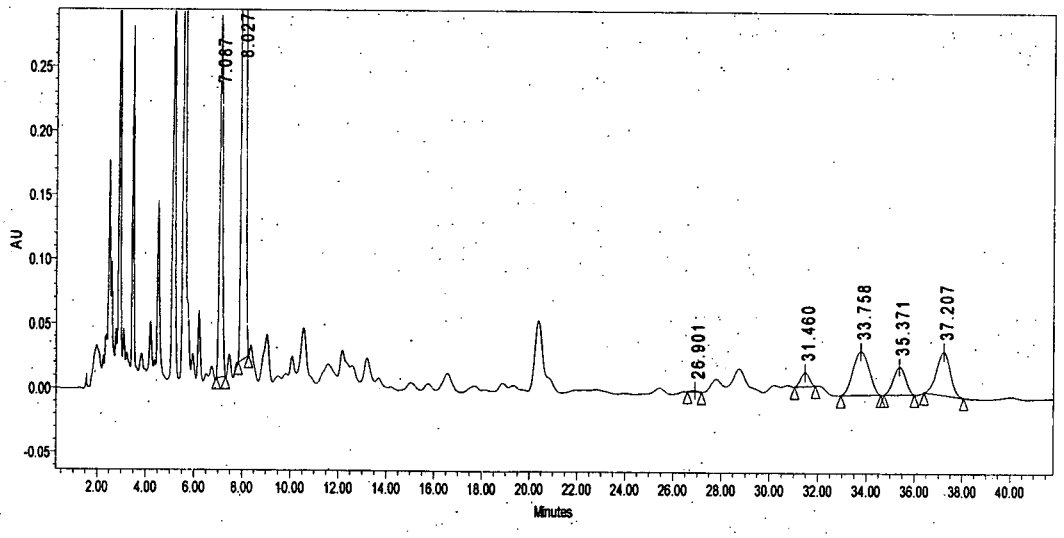


9

Figure II



A: chromatogram at 252 nm



B: chromatogram at 210 nm

Figure III

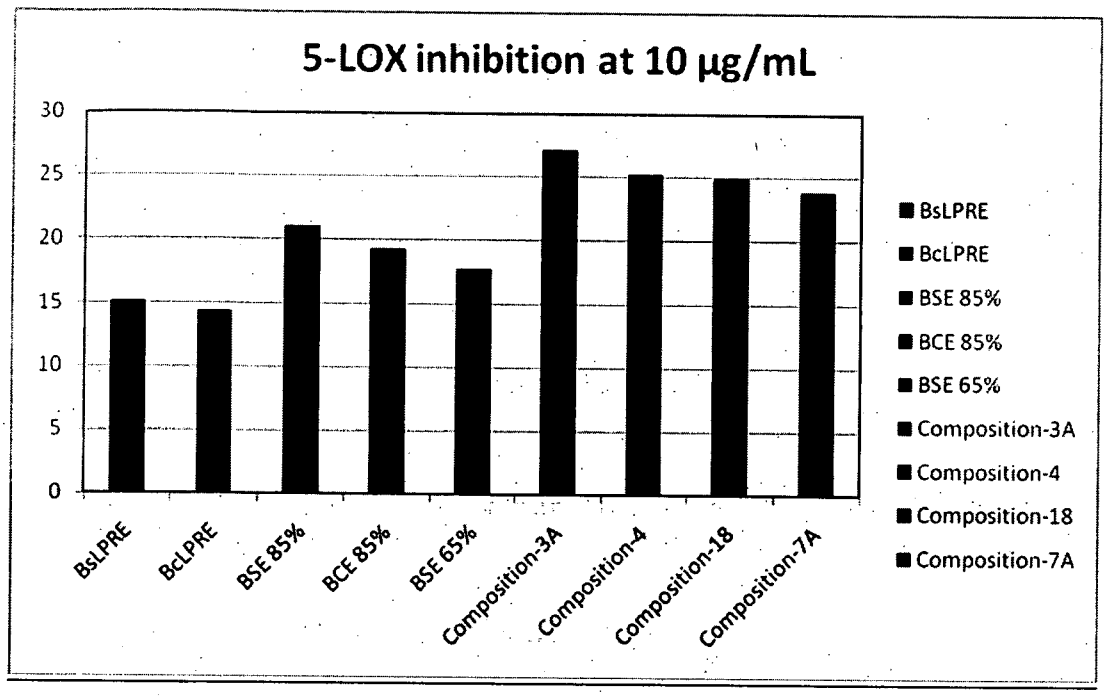
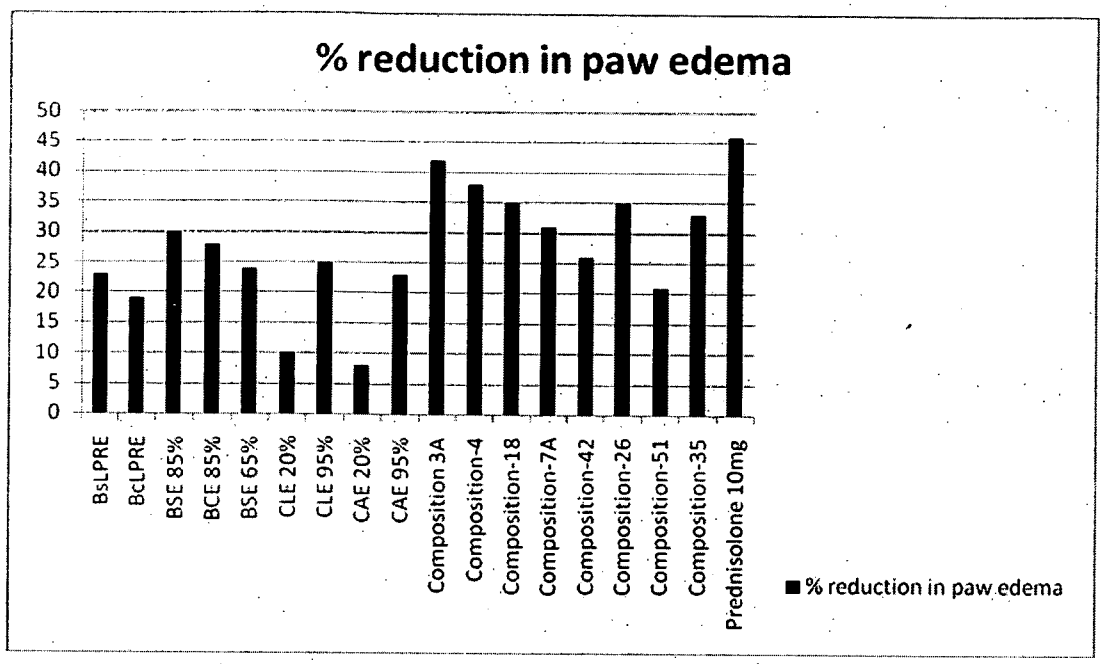

5-LOX inhibition at 10 µg/mL
30
25
20
15
10
5
0
BsLPRE
BcLPRE
BSE 85%
BCE 85%
BSE 65%
Composition-3A
Composition-4
Composition-18
Composition-7A
BsLPRE
BcLPRE
BSE 85%
BCE 85%
BSE 65%
Composition-3A
Composition-4
Composition-18
Composition-7A

Figure IV


% reduction in paw edema
50
45
40
35
30
25
20
15
10
5
0
BsLPRE
BcLPRE
BSE 85%
BCE 85%
BSE 65%
CLE 20%
CLE 95%
CAE 20%
CAE 95%
Composition 3A
Composition-4
Composition-18
Composition-7A
Composition-42
Composition-26
Composition-51
Composition-35
Prednisolone 10mg
% reduction in paw edema

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN 10/00233

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A01N 61/00; A01N 65/00; A61K 31/00; A61K 35/00
USPC - 424/195.18
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC- A01N 61/00; A01N 65/00; A61K 31/00; A61K 35/00;
USPC- 424/195.18

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC- 424/769;
Patents and NPL

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPTO PubWest (USPT, PGPUB, EPO, JPO: classification, keyword), GoogleScholar;
search terms: boswellia, gum, resin, phytochemical, low, polar, alkali, basic, brine, vacuum, curcuma

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BASAR, S. Chemical Investigations on Boswellia Species. University of Hamburg [online], 18 March 2005 (18.05.2005) [retrieved on: 2010-09-02], pp 1-256, Retrieved from the Internet: <http://www.sub.uni-hamburg.de/opus/volltexte/2005/2503/pdf/Dissertation-Simla_Basar.pdf>, pp 3-12, 36, 38, 41, 108, 114-117, 125, 132, 139, 151, 195, 203, 209, 212.	1-18, 20-40, 44, 45, 51
Y	US 2004/0202709 A1 (KIRBY, et al.) 14 October 2004 (14.10.2004), para [0019], [0074], [0091], [0092], [0099], [0109], [0111], [0191]	1-18, 20-40, 44, 45, 51
Y	US 2008/0317885 A1 (BAKER) 25 December 2008 (25.12.2008), para [0009], [0010], [0038], [0039], [0054]	16, 17, 20, 21, 30-38
A	AL-HARRASI, A., et al. Phytochemical Analysis of the Essential Oil from Botanically Certified Oleogum Resin of Boswellia Sacra (Omani Luban). Molecules. 16 September 2008 (16.09.2008), Vol. 13, No. 9, pp 2181-2189.	1-18, 20-40, 44, 45, 51
A	US 2007/0281045 A1 (TRIPP, et al.) 06 December 2007 (06.12.2007), entire document	1-18, 20-40, 44, 45, 51
A	EHRMAN, T. M., et al. Phytochemical Databases of Chinese Herbal Constituents and Bioactive Plant Compounds with Known Target Specificities. Journal of Chemical Information and Modelling, 09 January 2007 (09.01.2007), Vol. 47, No. 2, pp 254-263.	1-18, 20-40, 44, 45, 51
A	US 2006/0062859 A1 (BLUM, et al.) 23 March 2006 (23.03.2006), entire document	1-18, 20-40, 44, 45, 51
A	US 2006/0040000 A1 (GOKARAJU, et al.) 23 February 2006 (23.02.2006), entire document	1-18, 20-40, 44, 45, 51

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 September 2010 (23.09.2010)	05 OCT 2010

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN 10/00233

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 19, 41-43, 46-50, 52-57
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.