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(54) Title: ANTI-ALLERGIC HERBAL FORMULATION(S)

(57) Abstract: The invention provides a novel herbal preparation useful in treatment of allergy. Formulation(s) comprises of plant preparation or active component of plant extract together with conventional additives to form the oral dosage forms, which includes tablets, capsules and liquid dosage forms viz. syrup and suspension as anti-allergic. Formulation(s) comprises of *Tinospora cardifolia*, *Piper longum*, *Albizia lebbeck* and *Curcuma amada*. Conventionally used as solid or liquid or encapsulated as a soft/hard gelatin capsule for easy consumption as a solid or liquid dosage forms.



WO 2006/067802 A1

ANTI-ALLERGIC HERBAL FORMULATION(S)**FIELD OF THE INVENTION**

The present invention relates to novel herbal formulation(s) useful as anti-allergens.

BACKGROUND AND PRIOR ART OF THE INVENTION

5 Stress is known to alter the physiological homeostasis of the organism and results in the break down of the integrated adaptational processes. In response to extreme environmental demands various endocrinal and visceral responses occur naturally in a variety of experimental situations. For example, changes in plasma corticosterone and gastric mucosal integrity are widely reported during stress and both peripheral and central
10 mechanisms seemingly regulate these changes. Much interest has recently been generated on the immunological changes during stress with reports indicating that the immune status of the organism is actually modified by experimental stressors. The central nervous system, besides being crucial for stress, also regulates immune function and studies show that common neural substrates like the hypothalamus are clearly involved in such central nervous system-immune
15 system interactions.

 Neuro-pharmacological data have shown that complex neurochemical mechanisms regulates stress responses and transmitters like gamma-aminobutyric acid (GABA) and endogenous opiates are crucially involved. For example, benzodiazepenes (BZD), which modulate GABA, and opioid antagonists, modify several stress responses like gastric ulcer
20 formation and plasma corticosterone. Evidence indicates that central nervous system innervation of lymphoid tissue is possible. Lymphocytes bear receptors for several hormones and neurotransmitters and pharmacological alterations in neural activity influence immunocompetence. (Ray 1991)

 Scientists now use the word anaphylaxis to mean any immune reaction of this type,
25 even if it is not serious. But most doctors use it to mean life-threatening rapid allergic reaction. Unfortunately this kind of harmful immunization happens to a few of us not just from injections but also from ordinary foods such as nuts. Our immune system is there to protect us from infection, goes wrong and harms or even kills us. In recent years, there has been an upsurge in the clinical use of indigenous drugs. Such herbal plants, originally used in
30 the traditional system of medicine, are now being effectively tried in a variety of pathophysiological states. Non-specific mechanisms like restoration of normal physiological milieu and generalized increase in resistance against infections are proposed and the role of the immune system in these drug effects is suggested. (Sen P et al., 1992).

OBJECT OF THE INVENTION

The main object of the present invention is to provide a novel Anti-allergic herbal formulation(s) in various dosage forms viz; tablet, capsule and ointment form for easy consumption.

5 Another objective of the present invention is to prepare herbal dosage form that improves in the treatment of allergy.

SUMMARY OF THE INVENTION

Accordingly, the present invention provides a novel of the invention of an herbal formulation(s) obtained from plants having the property of stimulant and resistant to various
10 pathogens and acts as an immunomodulation as a tablet, injection and as a liquid formulation(s).

The herbal synergistic formulation has anti-allergy properties and comprises extracts of *Tinospora cardifolia*, *Piper longum*, *Albizia lebbeck* and *Curcuma amada*.

In an embodiment the extracts/juice of the plants are mixed in the ratio viz *Tinospora*
15 *cardifolia* (2-3 wt %), *Piper longum* (0.5-2 wt %), *Albizzia lebbeck* (3-5 wt %), and *Curcuma amada* (3-5 wt %) and balance being conventional additives.

In another embodiment, the plant used is *Tinospora cardifolia*.

In another embodiment, the plant used is *Piper longum*.

In another embodiment, the plant used is *Albizia lebbeck*.

20 In still another embodiment, the plant used is *Curcuma amada*.

In another embodiment, composition is used a syrup or suspension.

In another embodiment, the formulation is also used as anti- oxidant and nerves relaxant.

In still another embodiment, the formulation is also used to treat allergic related
25 diseases, blood purifier, anti-periodic and externally applied sprain and wound.

In another embodiment, the formulation is also used as a blood purifier and for jaundice treatment.

In yet another embodiment, the said formulation has specific gravity ranging between 0.972 – 1.405 and a refractive index ranging between 1.5263 –1. 6812.

30 In another embodiment, the formulation at a dose of 400 mg/kg did not show any abnormality of general condition.

In another embodiment, the formulation form at a dose ranging from 100-200 mg/kg shown a 22.70 – 80.04 % protection in hypoxia time and works as a stress relaxant.

In another embodiment, the formulation form at a dose ranging from 100-200 mg/kg shown a 24.18 – 82.83 % protection in swimming endurance and works as a stress relaxant.

DETAILED DESCRIPTION OF THE INVENTION

Accordingly the present invention provides a novel Anti-allergic herbal formulation(s) in various dosage forms viz; tablet, capsule and ointment form for easy consumption. The herbal formulation comprising of *Tinospora cardifolia*, *Piper longum*, *Albizia lebbeck* and *Curcuma amada*. *Tinospora cardifolia* extract brown in color. It is used as nourishing food. It was shown that it produce a significant improvement in general ability and behavioural pattern.

10 *Tinospora cordifolia*

Family: Menispermaceae

Botanical Descriptions: A large glabrous climbing shrub. Stems rather succulent with long filiform, aerial roots arising from branches. Bark; warty, papery thin, creamy white or grey brown. Peels off easily. Wood, soft, perforated. Leaves; membranous, cordate with broad sinus. Pointed at the tip. Flowers; unisexual and greenish, in long clusters. Seeds; curved. 15 Drupes; ovoid, succulent, lustrous, red, pea sized. Fruits; fleshy, one seeded. It is found throughout tropical India, ascending to an altitude of 300m.

Medicinal Uses:

Useful in bilious fever, rheumatism, general debility, seminal weakness, splenic diseases and urinary affections. Fresh plant is considered more efficacious. It is mostly used for preparing a kind of starch known as Guduchi satva or Sat giloe. 20

Phytochemistry: Sesquiterpene tinocordifolin, sesquiterpene glucoside tinocordifolioside, tinosponone, tinocordioside, cordioside, furanoid diterpenes, a new clerodane furanoditerpene viz. columbin, tinosporaside, an immunologically active arabinogalactan, two phytoecdyyones viz., ecdysterone and makisterone and several glycosides isolated as polyacetates. Other alkaloids viz., jatrorrhizine, palmatine, berberine, tembeterine, 25 phenylpropene disaccharides cordifolioside A, B and C, choline, tinosporic acid, tinosporal, tinosporon, 20- β -hydroxyecdysone, palmatoside C and F, cordifolisides D and E, diterpenoid furanolactones.

Pharmacology: The water and ethanolic extract inhibited the cyclophosphamide induced immunosuppression. Aqueous extract of the stem showed anti-inflammatory, analgesic and antipyretic properties in rats. In clinical studies, it also showed immunosuppressive effect in obstructive jaundice patients, antioxidant activity and amelioration of cyclophosphamide-induced toxicity. 30

Piper longum L.

Family: Piperaceae

Botanical Description: A slender, aromatic climber with perennial woody roots; stems jointed, creeping, young shoots downy. Leaves simple, alternate, 5-12cm long and 3-6cm wide, glabrous, ovate base cordate with broad rounded lobes, apex sub acute, and margins entire. Flowers minute on unisexual, axillary, cylindrical spikes; green at first, turning yellow, up to 5cm long; male spikes longer than female. Fruits ovoid, yellowish orange turning dark red to blackish, sunk in fleshy spikes 2.5-3.8 cm long.

Pharmacology: The dried roots, as well as the immature and mature fruits, are used extensively, alone and in combination with other plant drug to treat a broad range of ailments in traditional Indian medicine. The dried roots and thicker stems, known commercially as piplamul, are an important drug in the ayurvedic and unani systems. The roots and fruits are used to treat dysentery and leucoderma, as a cholagogue for treating bile duct and gallbladder obstruction, and as a counter-irritant and analgesic for relieving muscular pains and inflammations. A decoction of dried immature fruit and root, or the powdered fruits mixed with honey, is used to treat chronic bronchitis, cough and cold. An infusion of the powdered fruits is given to women after childbirth to check bleeding and fever. It is an important ingredient in medicated oil used externally for sciatica and paraplegia.

Albizia lebbek

Family: Mimosoideae

Botanical description: It is common throughout India, from the plains up to 900m elevations in the Himalayas. It is a large, unarmed, deciduous tree to about 20m tall with a spreading crown; bark pale; young shoots glabrous. Leaves bipinnate; rachis with a gland near the base of the petiole and one below uppermost pairs of pinnae; pinnae usually 2-3 pairs, 7-12 cm long; leaflets 5-9 pairs, 2.5-4.5 cm long and 1.6-2cm wide, with glands between their bases, elliptic-oblong or obovate-oblong, unequal-sided, retuse or obtuse at apex, base obliquely rounded or truncate; petiolules very short. Flowers fragrant, white to greenish-yellow, borne in globose umbellate heads 2-3.8 cm in diameter; peduncles 3.8-7.5 cm long, solitary or 2-4 together from the axils of the upper leaves, pedicels 2.5-3 mm long; calyx 4mm long, pubescent, teeth short, deltoid; corolla 1cm long, tube glabrous, lobes 2.5mm long, triangular, acute, pubescent outside; stamens longer than the corolla. Fruits (pods) 10-30 cm long and 2-4.5 cm wide, linear-oblong, bluntly pointed, thin green turning straw-coloured on maturity, reticulately veined above the seeds, smooth, shining; seeds 4-12, pale brown, ellipsoid-oblong, compressed. Flowers from April to June and fruits mature in December in northern and central India; in southern India flowering occurs earlier, from January to April. In central India trees remain leafless for a month or more between March and June.

Medicinal uses: In Ayurveda the astringent root is used to treat hemicrania; the acrid bark is reportedly used to treat diseases of the blood, leucoderma, itching, skin diseases, piles, inflammation, and bronchitis; the leaves are used to treat opthalmia, and the flowers for asthma. In unani medicine the root is used to treat opthalmia; the bark is regarded as anthelmintic and used to relieve toothache and to strengthen the gums and teeth, and to treat leprosy, deafness, boils, scabies, syphilis and paralysis; the leaves are reportedly useful for treating night blindness; and the seeds are used to treat gonorrhoea and tuberculous glands, their oil applied locally for leucoderma. The flower are used as a cooling medicine and as an external application to relieve boils, skin eruption and swelling. the seed oil is used externally to promote healing of lesions in leprosy among the Irulars of Tamilnadu.

Phytochemistry: A new acyclic ester isolated and characterized as heneicos-7 (2)-enyl-24-hydroxytetracos-10 (2)-enoate; lupeol, oleanolic acid, docosanoic acid and β -sitosterol also was isolated (*Ind J Pharm Sci*, 1991, 53, 24). Echinocystic acid β -sitosterol identified in bark and seeds (*Ind J Appl. Chem*, 1969, 32, 73; *Chem Abstr* 1971, 75, 160352). Mature leaves contained ketoacids including phosphoenol pyruvate, glyoxalate, oxaloacetate and α -oxoglutarate (*Plant Biochem J*, 1977, 4, 34; *Chem Abstr* 1977, 17, 148762s); vicenin-2, reynoutrin, rutin, myricitrin and robinin from leaves (*Shoyakugaku Zasshi*; 1977, 31, 172; *Chem Abstr* 1978, 88, 14897h).

Pharmacology: Bark and flowers decoction protected guinea pig against histamine and acetylcholine –induced bronchospasm. Chronic treatment with bark decoction also protected sensitized guinea pigs against antigen challenge. Drug showed anti-asthmatic and anti-anaphylactic activities due to inhibition of phenomenon of sensitization (*Ind J Pharmacol*, 1977, 9, 189). Saponin showed β -haemolysis against buffalo and sheep blood and α -haemolysis against human blood. Purified saponin showed antifungal activity against *marcophomina phaseolina* (mic 32.8 μ g), *stemplilum* species and *fusarium solani* (*Pak Vet J* 1990, 10, 146; *Chem Abstr* 1992, 116, 102686j). The plant has been showed to poses antidiarrhoeal and antifertility activities. It posses anti anaphylactic and anticonvulsive properties. The leaves are reportedly useful for treating night blindness; and the seeds are used to treat gonorrhoea and tuberculous glands, their oil applied locally for leucoderma.

Curcuma amada

Family: Zingiberaceae

Botanical description: A tall herb, rootstock large, ovoid, with cylindrical tubers that are bright yellow or orange inside. Leaves very large, in tufts up to 1.2 m long including petioles, blade up to 50 cm long and 8 cm wide, oblong lanceolate, tapering to the base; petiole about as long as leaf blade. Flowers are pale yellow.

Pharmacology: The dried, powdered rhizome is the source of turmeric, widely used in Indian cuisine as well as in traditional medicine. Turmeric is considered to have strong antiseptic properties and is used to treat poisonous affections, ulcers and wounds. In Ayurveda, is considered to be alterative, antiperiodic, germicidal, carminative, stimulant, tonic and vermifuge. It is used to treat diabetes, eye diseases, ulcers, oedema, anaemia, anorexia, leprosy, scrofula; its paste, sometimes combined with that of neem leaves, is used to cure ring worm, itching, eczema and other parasitic skin diseases, and in the treatment of chicken pox and small pox. In unani medicine it is considered carminative, mutant and diuretic and useful for treating jaundice and other liver disorders. An essential oil obtained from the rhizome is used as a carminative, stoma chic and tonic. A paste made of the flowers is used externally to treat ringworm and other parasitic skin diseases, as well as gonorrhoea.

Medicinal uses: It is used to treat diabetes, eye diseases, ulcers, oedema, anaemia, anorexia, leprosy, scrofula; its paste, sometimes combined with that of neem leaves, is used to cure ring worm, itching, eczema and other parasitic skin diseases, and in the treatment of chicken pox and small pox.

The present invention provides a novel of the invention of an herbal formulation(s) obtained from plants having the property of stimulant and resistant to various pathogens and acts as an immunomodulation as a tablet, injection and as a liquid formulation(s).

The herbal synergistic formulation has anti-allergy properties and comprises extracts of *Tinospora cardifolia*, *Piper longum*, *Albizia lebbeck* and *Curcuma amada*. The extracts/juice of the plants are mixed in the ratio viz *Tinospora cardifolia* (2-3 wt %), *Piper longum* (0.5-2 wt %), *Albizzia lebbeck* (3-5 wt %), and *Curcuma amada* (3-5 wt %) and balance being conventional additives.

In another embodiment, the plant used is *Tinospora cardifolia*.

In another embodiment, the plant used is *Piper longum*.

In another embodiment, the plant used is *Albizia lebbeck*.

In still another embodiment, the plant used is *Curcuma amada*.

In another embodiment, composition is used a syrup or suspension.

The formulation is also used as anti- oxidant and nerves relaxant. The formulation can also be used to treat allergic related diseases, blood purifier, anti-periodic and externally applied sprain and wound. The formulation is also used as a blood purifier and for jaundice treatment.

The formulation has specific gravity ranging between 0.972 – 1.405 and a refractive index ranging between 1.5263 –1. 6812. At a dose of 400 mg/kg did not show any

abnormality of general condition. The formulation form at a dose ranging from 100-200 mg/kg shown a 22.70 – 80.04 % protection in hypoxia time and works as a stress relaxant.

The formulation form at a dose ranging from 100-200 mg/kg shows 24.18 – 82.83 % protection in swimming endurance and works as a stress relaxant.

5 The invention is further illustrated by the following non-limiting examples.

Formulation 1 (F1)

	<i>Tinospora cardifolia</i>	3wt. %
	Lactose	66.7g
	Starch	10g
10	Water	q.s. to make 100 ml

Dry mature seed of *Tinospora cardifolia* are washed in purified distilled water, and were immersed in hot water (30-60⁰ c) for 2-3 hr. Mix the plant constituents and filter the solution and add specified quantity of starch and heat until the starch dissolves and then cool and make up the volume with required amount of water to make 100 ml. Oral dosage form
15 has been described in detail giving the formula of the ingredients along with the method and mode of usage of the standardized formulation. Kindly refer table I and II.

Formulation 2 (F2)

	<i>Piper longum</i>	1wt. %
	Lactose	66.7g
20	Starch	10.0g
	Water	q.s. to make 100 ml

Dry mature seed of *Piper longum* are washed in purified distilled water, and were immersed in hot water (30-60⁰ c) for 2-3 hr. Mix the plant constituents and filter the solution and add specified quantity of starch and heat until the starch dissolves and then cool and
25 make up the volume with required amount of water to make 100 ml. Oral dosage form has been described in detail giving the formula of the ingredients along with the method and mode of usage of the standardized formulation. Kindly refer table I and II.

Formulation 3 (F3)

	<i>Albizia lebbeck</i>	4 wt. %
30	Lactose	66.7g
	Starch	10.0g
	Water	q.s. to make 100 ml

Dry mature seed of *Albizia lebbeck* are washed in purified distilled water, and were immersed in hot water (30-60⁰ c) for 2-3 hr. Mix the plant constituents and filter the solution

and add specified quantity of starch and heat until the starch dissolves and then cool and make up the volume with required amount of water to make 100 ml. Oral dosage form has been described in detail giving the formula of the ingredients along with the method and mode of usage of the standardized formulation. Kindly refer table I and II.

5 Formulation 4 (F4)

<i>Curcuma amada</i>	5 wt %
Lactose	66.7g
Starch	10g
Water	q.s. to make 100 ml

10 Dry mature seed of *Curcuma amada* are washed in purified distilled water, and were immersed in hot water (30-60° c) for 2-3 hr. Mix the plant constituents and filter the solution and add specified quantity of starch and heat until the starch dissolves and then cool and make up the volume with required amount of water to make 100 ml. Oral dosage form has been described in detail giving the formula of the ingredients along with the method and
15 mode of usage of the standardized formulation (Tables I and II)

Formulation 5 (F5)

<i>Tinospora cardifolia</i>	3wt. %
<i>Piper longum</i>	1 wt %
Lactose	63.7g
20 Starch	10g
Water	q.s. to make 100 ml

Dry mature seed of *Tinospora cardifolia* and *Piper longum* are washed in purified distilled water, and immersed in hot water (30-60° c) for 2-3 hr. Mix the plant constituents and filter the solution and add specified quantity of starch and heat until the starch dissolves
25 and then cool and make up the volume with required amount of water to make 100 ml. Oral dosage form has been described in detail giving the formula of the ingredients along with the method and mode of usage of the standardized formulation (Tables I and II).

Formulation 6 (F6)

<i>Tinospora cardifolia</i>	3wt. %
30 <i>Piper longum</i>	1 wt %
<i>Albizia lebbbeck</i>	3 wt. %
Lactose	60.7g
Starch	10g
Water	q.s. to make 100 ml

Dry mature seed of *Tinospora cardifolia*, *Piper longum* and *Albizia lebbeck* are washed in purified distilled water, and immersed in hot water (30- 60⁰ c) for 2-3 hr. The plant constituents were mixed and the solution filtered and specified quantity of starch added and heated till starch dissolves and then cooled and volume made up with required amount of water to make 100 ml. Oral dosage form has been described in detail giving the formula of the ingredients along with the method and mode of usage of the standardized formulation. Kindly refer table I and II.

Formulation 7(F7)

	<i>Tinospora cardifolia</i>	3 wt. %
10	<i>Piper longum</i>	1 wt %
	<i>Albizia lebbeck</i>	4 wt. %
	<i>Curcuma amada</i>	3 wt. %
	Lactose	56.7g
	Starch	10g
15	Water	q.s. to make 100 ml

Dry mature seed of *Tinospora cardifolia*, *Piper longum*, *Albizia lebbeck* and *Curcuma amada* are washed in purified distilled water, and were immersed in hot water (30-60⁰ c) for 2-3 hr. Mix the plant constituents and filter the solution and add specified quantity of starch and heat until the starch dissolves and then cool and make up the volume with required amount of water to make 100 ml. Oral dosage form has been described in detail giving the formula of the ingredients along with the method and mode of usage of the standardized formulation. Kindly refer table I and II.

Table I: Effect of formulation on hypoxia and swimming performance time in mice.

S.No	Treatment	Dose (mg/kg, p.o)	Hypoxia time	Swimming endurance
1.	Control + Stress	-	23.34 ± 1.15	238.21± 25.11
2.	F1	200	24.34 ± 1.55	241.21 ± 27.41
3.	F2	200	22.54 ± 2.11	239.45 ± 25.05
4.	F3	200	26.01 ± 2.28	245.52 ± 26.74
5.	F4	200	27.89 ± 2.15	246.32 ± 25.53
6.	F5	200	27.01 ± 2.58	248.14 ± 26.85
7.	F6	200	35.23 ± 2.95 ^a	369.52 ± 26.74 ^a
8.	F7	200	45.89 ± 3.05 ^b	435.54 ± 28.85 ^b

Values are mean ± S.E.M.

25 P: ^a<0.01 and ^b<0.001 compared to control + stress group.

NOTE: No mortality was found in any of the treated group.

No gross abnormality in behavior was observed in the animal exposed with herbal preparation. The formulation (F1) contains *Tinospora cardifolia* (3%) with balance being conventional additives. The formulation (F2) contains *Piper longum* (1%) with balance being conventional additives. The formulation (F3) contains *Albizia lebbeck* (4%) with balance being conventional additives. The formulation (F4) contains *Curcuma amada* (3%) with balance being conventional additives. The formulation (F5) contains *Tinospora cardifolia* (3%) and *Piper longum* (1%) with balance being conventional additives. The formulation (F6) contains *Tinospora cardifolia* (3%), *Piper longum* (1%) and *Albizia lebbeck* (3%) with balance being conventional additives. The formulation (F7) contains *Tinospora cardifolia* (3%), *Piper longum* (1%), *Albizia lebbeck* (4%) and *Curcuma amada* (3%) with balance being conventional additives

The results showed in table 1 that formulations F7 showed significant hypoxia time when compared with control + stress and formulation F1 – F6. The value of formulation F7 hypoxia time has significantly increased and swimming endurance value is decreased which leads to stress relaxation.

Immunological assay

Hypoxia time: The animals were placed in an empty glass jar of 300 mL capacity attached with an electronic watch; the jars were made air tight with greased glass stoppers and the time until the onset of convulsion was recorded (Singh B et al 2001).

Swimming performance time: The animals were allowed to swim inside a Perspex glass beaker (30 cm high with 20 cm diameter containing water up to 25 cm high) maintained at $26^{\circ} \pm 1^{\circ}$ C with a continuous air current from the bottom. The end point of swimming endurance was taken as when the mice remained at the bottom for more than 10 s (Singh B et al 2001).

Table II: Effect of formulation on mast cell degranulation in rats.

S.No	Treatment	Dose (mg/kg, p.o)	Histamine released ($\mu\text{g/ml}$)
1.	Control	--	0.899 $\pm$ 0.05
2.	F1	200	0.895 $\pm$ 0.04
3.	F2	200	0.886 $\pm$ 0.06
4.	F3	200	0.892 $\pm$ 0.05
5.	F4	200	0.879 $\pm$ 0.05
6.	F5	200	0.885 $\pm$ 0.02
7.	F6	200	0.671 $\pm$ 0.02 ^a
8.	F7	200	0.254 $\pm$ 0.05 ^c
9.	Avil	25	0.345 $\pm$ 0.04 ^b

Values are mean $\pm$ S.E.M.

P: ^a<0.05, ^b<0.01 and ^c<0.001 compared to control group.

NOTE: No mortality was found in any of the treated group.

No gross abnormality in behavior was observed in the animal exposed with herbal preparation.

5 The formulation (F1) contains *Tinospora cardifolia* (3%) with balance being conventional additives. The formulation (F2) contains *Piper longum* (1%) with balance being conventional additives. The formulation (F3) contains *Albizia lebbeck*. (4%) with balance being conventional additives. The formulation (F4) contains *Curcuma amada* (3%) with balance being conventional additives. The formulation (F5) contains *Tinospora cardifolia*
10 (3%) and *Piper longum* (1%) with balance being conventional additives. The formulation (F6) contains *Tinospora cardifolia* (3%), *Piper longum* (1%) and *Albizia lebbeck* (3%) with balance being conventional additives. The formulation (F7) contains *Tinospora cardifolia* (3%), *Piper longum* (1%), *Albizia lebbeck* (4%) and *Curcuma amada* (3%) with balance being conventional additives.

15 The results showed in table 2 formulations F7 showed significant effect when compared with control. The release of histamine is tremendously decreased which shows the anti allergic activity. The formulation F7 is more significant than that of standard drug Avil. Disadvantages of Avil are dizziness and drowsiness.

Mast cell degranulation: Tyrode solution (10ml) containing 5 units/ml of heparin was
20 injected in the peritoneal cavity of sensitized male rats lightly anaesthetized with ether. After a gentle abdominal massage for about 30 to 45 sec, the mast cell rich peritoneal fluid was collected over ice and centrifuged at 2000 rpm for 5 min. The cells were washed thrice with chilled Tyrode and resuspended in about 1 ml of Tyrode solution. The peritoneal fluid was obtained from 10 rats and the final volume of the fluid was pooled and used for the studies
25 (Nair AM et al, 1997).

Table III: Effect of formulation (F7) on lipid peroxidation, superoxide dismutase and catalase activities in tissues.

S.No	Treatment	Liver	Kidney	Heart
Lipidperoxidation(LPO)				
1.	Control	32.2±1.5	25.1± 1.3	17.7± 0.5
2.	F7	18.5± 1.2 ^c	13.65± 2.7 ^c	21.5±2.1 ^a
Superoxide dismutase(SOD)				
1.	Control	9.2± 0.6	5.8± 0.9	4.3±0.5
2.	F7	2.6±0.8 ^c	3.6±0.2 ^b	4.9±0.4 ^a
Catalase activity				
1.	Control	96.3±1.8	126.5±1.9	92.5±2.5
2.	F7	185.6± 7.1 ^c	256.9±8.3 ^c	132.2±3.4 ^c

Values are mean $\pm$ S.E.M.

P: ^a<0.05, ^b<0.01 and ^c<0.001 compared to respective control group.

NOTE: No mortality was found in any of the treated group.

No gross abnormality in behavior was observed in the animal exposed with herbal preparation.

The formulation (F7) contains *Tinospora cardifolia* (3%), *Piper longum* (1%), *Albizia lebbbeck* (4%) and *Curcuma amada* (3%) with balance being conventional additives.

Table IV: Effect of formulation(s) on relative mean $\pm$ SEM organ weights of rats.

Treatment group	Body weight (g)	Kidney (g)	Liver (g)	Spleen (g)
Control	182.5 $\pm$ 9.3	0.94 $\pm$ 0.04	5.92 $\pm$ 0.65	0.61 $\pm$ 0.07
F (5)	171.3 $\pm$ 8.6	0.87 $\pm$ 0.05	5.68 $\pm$ 0.58	0.68 $\pm$ 0.05
F (6)	178.1 $\pm$ 9.7	0.92 $\pm$ 0.07	5.82 $\pm$ 0.61	0.70 $\pm$ 0.08
F (7)	185.4 $\pm$ 8.4	0.85 $\pm$ 0.09	5.13 $\pm$ 0.69	0.65 $\pm$ 0.06

The formulation (F5) contains *Tinospora cardifolia* (3%) and *Piper longum* (1%) with balance being conventional additives. The formulation (F6) contains *Tinospora cardifolia* (3%), *Piper longum* (1%) and *Albizia lebbbeck* (3%) with balance being conventional additives. The formulation (F7) contains *Tinospora cardifolia* (3%), *Piper longum* (1%), *Albizia lebbbeck* (4%) and *Curcuma amada* (3%) with balance being conventional additives.

The results of the Table IV shows there is no significant changes in body weight of various vital organs in the body in toxicity studies.

The formulation F5, F6 and F7 is highly effective (Table I) and it is safe.

Note: No mortality/ gross abnormality was observed in the animals during the treatment of formulations (F5, F6 and F7).

We Claim:

1. A herbal anti-allergy synergistic formulation(s) comprising extracts of *Tinospora cardifolia*, *Piper longum*, *Albizia lebbeck* and *Curcuma amada* in pharmaceutically acceptable dosages optionally along with an additive.
- 5 2. Herbal anti-allergy formulation(s) as claimed in claim 1, wherein the extracts/juice of the plants are mixed in the ratio viz *Tinospora cardifolia* (2-3 wt %), *Piper longum* (0.5-2 wt %), *Albizzia lebbeck* (3-5 wt %), and *Curcuma amada* (3-5 wt %) and balance being conventional additives.
- 10 3. Herbal formulation(s) as claimed in claim 1, wherein the plant used is *Tinospora cordifolia*
4. Herbal formulation(s) as claimed in claim 1, wherein the plant used is *Piper longum*.
5. Herbal formulation(s) as claimed in claim 1, wherein the plant used is *Albizia lebbeck*.
6. Herbal formulation(s) as claimed in claim 1, wherein the plant used is *Curcuma amada*.
- 15 7. Herbal formulation(s) as claimed in claim 1, wherein said composition is used as a syrup or suspension.
8. Herbal formulation(s) as claimed in claim 1, wherein the formulation is also used as anti-oxidant and nerve relaxant.
9. Herbal formulation(s) as claimed in claim 1, wherein the formulation is also used to
- 20 treat allergic related diseases, anti-periodic and externally applied sprain and wound.
10. Herbal formulation(s) as claimed in claim 1, wherein the formulation is also used as blood purifier.
11. Herbal formulation(s) as claimed in claim 1 and 2, wherein the formulation is used to cure asthma, cough and also act as an analgesic and anti-inflammatory agent.
- 25 12. Herbal formulation(s) as claimed in claim 1, wherein formulation has specific gravity ranging between 0.972 – 1.405.
13. Herbal formulation(s) as claimed in claim 1, wherein the formulation has refractive index ranging between 1.5263 – 1.6812.
14. Herbal formulation(s) as claimed in claim 1, wherein the formulation at a dose of 400
- 30 mg/kg did not show any abnormality of general condition.
15. Herbal formulation(s) as claimed in claim 1, where in the formulation form at a dose ranging from 100-200 mg/kg showed a 22.70 – 80.04 % protection in hypoxia time and worked as a stress relaxant.

16. Herbal formulation(s) as claimed in claim 1, where in the formulation form at a dose ranging from 100-200 mg/kg showed a 24.18 – 82.83 % protection in swimming endurance and worked as a stress relaxant.
17. A method for the treatment of allergy in a subject comprising administering to the
5 subject a herbal anti-allergy synergistic formulation(s) comprising extracts of *Tinospora cardifolia*, *Piper longum*, *Albizia lebbeck* and *Curcuma amada* in pharmaceutically acceptable dosages optionally along with an additive.
18. A method as claimed in claim 17 wherein the extracts/juice of the plants are taken in a
10 ratio *Tinospora cardifolia* (2-3 wt %), *Piper longum* (0.5-2 wt %), *Albizia lebbeck* (3-5 wt %), and *Curcuma amada* (3-5 wt %) balance being conventional additives.
19. A method as claimed in claim 17 wherein the formulation is used at a dose of 400 mg/kg body weight.
20. A method as claimed in claim 17 wherein the dosage is in the range of 100-200 mg/kg
15 body weight and shows a 22.70 – 80.04 % protection in hypoxia time and worked as a stress relaxant.
21. A method as claimed in claim 17 wherein the formulation at a dose ranging from 100-200 mg/kg body weight shows a 24.18 – 82.83 % protection in swimming endurance and worked as a stress relaxant.
22. Use of a herbal anti-allergy synergistic formulation(s) comprising extracts of
20 *Tinospora cardifolia*, *Piper longum*, *Albizia lebbeck* and *Curcuma amada* in pharmaceutically acceptable dosages optionally along with an additive for the treatment of allergy in a subject.
23. Use as claimed in claim 22 wherein the extracts/juice of the plants are taken in a ratio
25 *Tinospora cardifolia* (2-3 wt %), *Piper longum* (0.5-2 wt %), *Albizia lebbeck* (3-5 wt %) and *Curcuma amada* (3-5 wt %) balance being conventional additives.
24. Use as claimed in claim 22 wherein the formulation is used at a dose of 400 mg/kg body weight.
25. Use as claimed in claim 22 wherein the dosage is in the range of 100-200 mg/kg body
30 weight and shows a 22.70 – 80.04 % protection in hypoxia time and worked as a stress relaxant.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IN2004/000409

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K35/78 A61P37/02

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 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 693 327 A (SHAH ET AL) 2 December 1997 (1997-12-02) *cf. abstract, col. 1, lines 48-60, col. 5, lines 28-30*	1-25
Y	WO 01/64163 A (NATURAL REMEDIES PRIVATE LIMITED; AGARWAL, RAVINDRA, KUMAR; AGARWAL, A) 7 September 2001 (2001-09-07) *cf. abstract, page 1, lines 1-7, page 10, lines 3-9, example 4, on page 26, claims 1 and 2*	1-25
Y	US 6 413 553 B1 (BANDYOPADHYAY SANTU ET AL) 2 July 2002 (2002-07-02) *cf. abstract, col. 3, lines 55-67, col. 5, lines 4-7, claims 1-3*	1-25
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IN2004/000409

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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PCT/IN2004/000409

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