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(54) Title: ANTIULCER HERBAL COMPOSITION(S)

(57) Abstract: The invention provides a novel herbal synergistic formulation for treatment of acute and chronic ulcers in stomach. Formulation(s) comprises of plant extracts together with the conventional additives to form the oral dosage forms which include tablets, capsules and powders ready for suspension. Uleria solicifolia along with this plants used traditionally like Asparagus racemosus, Foeniculum vulgare, and Ficus glomerata are added which are used in intestinal discomforts and as an galactagogue.



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ANTIULCER HERBAL COMPOSITION(S)

TECHNICAL FIELD

The present invention relates to development of an antiulcer herbal composition(s), process of preparing the extracts useful for preparing herbal formulation to treat ulcers.

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BACKGROUND ART

Peptic ulcer represents a major health problem, both in terms of morbidity and mortality. Research advances during the last decade have offered new insights in the therapy and prevention of gastroduodenal ulceration by measures directed at strengthening the mucosal defense system rather than by attenuating the aggressive acid-pepsin factors held responsible for the induction of ulcers. The rise in gastric acidity and peptic activity are usually a manifestation of a physiological disturbance affecting one or more mechanisms which normally regulate gastric secretion. Neurotransmitters or hormones that directly stimulate secretion of hydrochloric acid and pepsin by the gastric glands are acetylcholine, gastrin and histamine. In addition there are other factors which play an important role in the manifestation of peptic ulcers. Activity of the gastric secretory cells has been found to be stimulated by caffeine, alcohol, hydrochloric acid, sodium chloride, non steroidal anti-inflammatory drugs (NSAIDS) and stress^{3,4,5}.

The recent daily life is called a stress age and the chances of receiving stress have been increased by the kaleidoscopic change of the living environment and the increase of the complexity of personal relations. Also, the chance of taking many virtual, which do not exist in nature has been increased².

Thus, the number of persons suffering from a stomach ulcer, a duodenal ulcer, etc., by these factors has been increased and various antiulcer agents have been developed and utilized at present. The antiulcer agents which have been used at present are largely classified into a digestive power depressant, a gastric juice secretion depressant, a mucous membrane protective tissue reparative agent, etc., and are orally or subcutaneously administered. However, these preparations are isolated medicaments or synthesized medicaments, each medicament has each side effects, whereby the restrictions about the applicable objects and the using amount become severe, and an effective and safe antiulcer agent has not yet been developed and utilized¹.

Thus, since these conventional antiulcer agents can not be regularly used from the point of the safety, they can not be utilized for the prophylaxis and the recurrence prevention.

On the other hand, as preventives for ulcer, medicines for intestinal disorders and medicaments having the secretion preventing effect of gastric juice only are used and hence, they are not said to be preventives for a ulcer in true meaning. At present, side effects of medicaments to a human being become a problem and hence the
5 development of a medicament having an antiulcer effect, which is a natural product, gives no side effects, and is sufficiently safe even when the medicament is regularly used as a preventive or a recurring preventing agent has been required^{1,2}.

Hitherto only on oral tradition of Malasar and Kadar tribes of Kerala use *Utleria solifolia* for treatment of intestinal ailments like colic and bleeding in stomach. The synthetic
10 conventional drugs either inhibit acid secretion or cure the ulcer. The long term treatment of the present synthetic drugs completely inhibits the acid and pepsin secretion which is normally responsible for digestion and function of stomach and causes cancer. The offensive acid, pepsin and defensive mucin of the stomach plays a critical role in stomach function. The *Helicobacter pylori* bacteria, offensive acid, pepsin, consumption of hot food
15 disrupts the continuity of the cells and leads to ulcer and gastric cancer, yet there is no complete cure. Therefore for the treatment of acute gastric/duodenal ulcer, and *H. pylori*, a novel herbal formulation is required. Accordingly studies were undertaken to develop a oral formulation containing herbal drugs along with additives for oral ingestion^{6,7} to treat acute gastric/duodenal ulcer and also to treat internal bleeding.

20 OBJECTS OF THE INVENTION

The main object of the present invention to provide a novel anti-ulcer herbal formulation useful for the treatment of acute and chronic ulcers of stomach and duodenum

Another objective of the present invention is to prepare herbal formulation(s) that gives immediate relieves the acidity of the stomach by neutralizing the excess acid.

25 Yet another object of the present invention is to prepare herbal formulation(s) with a combination of the plants which are used in diarrhea, intestinal discomforts and antimicrobial.

SUMMARY OF THE INVENTION

Accordingly, the present invention provides a herbal formulation useful in the treatment of
30 acute and chronic ulcers in stomach. The herbal formulation comprising of *Utleria solifolia* that has been used by Malasar and Kadar tribes, Kerala as mentioned in prior art for the above mentioned purpose as the active ingredient. Along with this plants used traditionally like *Asparagus racemosus*, *Foeniculum vulgare*, and *Ficus glomerata* are added which are used in intestinal discomforts and as an galactagogue together with conventional additives.

DETAILED DESCRIPTION OF THE INVENTION

Accordingly, the present invention provides a novel anti-ulcer herbal synergistic formulation useful for the treatment of acute and chronic ulcers of stomach and duodenum, said formulation comprising:

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a) 50 % aqueous alcoholic extracts of the plants comprising *Utlaria solicifolia* 2-5wt. %, *Asparagus racemosus* 1-3wt. %, *Foeniculum vulgare* 2-4wt. %, and *Ficus glomerata* 3-5wt. % in an oral dosage form selected from a group consisting of a tablet, a capsule, a powder and a liquid.

10 The novelty of the present investigation is (1) herbal formulation for the treatment of gastric and duodenal ulcers (2) the herbal formulation neutralizes the excess acid in the stomach (3) the herbal formulation is useful in healing and curing of ulcers (4) unlike the commercial antiulcer agents, the herbal formulation also checks the internal bleeding.

In an embodiment, the plant extracts used may be *Utlaria solicifolia*, *Asparagus*
15 *racemosus*, *Foeniculum vulgare*, and *Ficus glomerata*.

In still another embodiment, the formulation may be made into tablet, capsule or powder ready for suspension.

In yet another embodiment, the binder used may be either starch or gum acacia or carboxymethyl cellulose

20 In still another embodiment, the diluent used to make up the dosage form may be lactose.

In another embodiment, the extracts of plants used are 50 % aqueous alcoholic extracts.

In another embodiment, alcohol used is ethanol.

In still another embodiment, formulation(s) treats stomach discomforts, gastric cancer, stomachache, intestinal discomforts, gastric and duodenal ulcers.

25 In yet another embodiment, the extracts of the plants are mixed in the ratio *Utlaria solicifolia* 2-5wt. %, *Asparagus racemosus* 1-3wt. %, *Foeniculum vulgare* 2-4wt. %, and *Ficus glomerata* 3-5wt. % along with conventional additives to form oral solid dosage forms.

In another embodiment, formulation(s) comprises about 8-17% wt of the total formulation.

30 In still another embodiment, extract of *Utlaria solicifolia* is a rhizome extract.

In yet another embodiment, the plant extracts are obtained: from plant parts selected from leaf, rhizome and aerial parts.

In still another embodiment, the lubricants used are from starch and lactose.

In an embodiment, the formulation is used in treating diarrhea, intestinal discomforts and is an antimicrobial agent.

In another embodiment, the formulation immediately relieves the acidity of the stomach by neutralizing the excess acid.

5 In another embodiment, the formulation at a dose of 100 to 200 mg/kg in cold restraint stress induced ulcers gives an ulcer index of 11.2 ± 3.1 to 4.2 ± 1.0

In yet another embodiment, the formulation at a dose of 100 to 200 mg/kg in cold restraint stress induced ulcers gives an % curative ratio of 83.59 to 56.25.

10 In still another embodiment, the formulation at a dose of 100 to 200 mg/kg in pylorus ligation induced ulcers gives an ulcer index of 6.1 ± 0.8 to 4.8 ± 1.2 .

In another embodiment, the formulation at a dose of 100 to 200 mg/kg in pylorus ligation induced ulcers gives an % curative ratio of 57.93 to 66.90.

In yet another embodiment, the formulation at a dose of 100 to 200 mg/kg showed lipid peroxidation capacity in rat gastric mucosa of 0.1 ± 0.01 to 0.21 ± 0.01 .

15 In still another embodiment, the formulation at a dose of 100 to 200 mg/kg in ethanol induced changes in gastric ulcers of 64.94 to 86.75 % protection and significant increase in gastric wall mucus in rats.

In yet another embodiment, the formulation at a dose of 100 to 200 mg/kg in aspirin induced changes in gastric ulcers in rats showed an ulcer index of 7.1 ± 2.2 to 6.2 ± 1.3 and
20 % curative ratio of 61.41 to 66.30.

In still another embodiment, the formulation at a dose of 100 to 200 mg/kg in acetic acid induced (ulcer healing) chronic ulcers in rats showed 2.1 to 0.0 % incidence of perforations and 31.2 in control.

25 As a result of intensive study conducted by the inventors with the aim of achieving aforementioned objectives, new formulations for oral ingestion were developed employing herbal drugs which are from natural origin, incorporating them into binders and diluents to form oral dosage forms.

Accordingly, the present investigation deals with the oral dosage form formulation(s). Each formulation has been described in detail giving the formula of the ingredients along
30 with the method of preparation. These examples are for illustration only and should not be construed to limit the scope of the invention.

The first step in the preparation of these formulations involves a process for making, the plant material suitable for formulating into a tablet/ capsule. The specified portion of the

plant is collected and dried under shade at room temperature (25 -35⁰C) for 72 hours or until the material gets dried. The material is then powdered into a fine powdered. A specified amount of the powdered material is then extracted exhaustively with 50 % aqueous alcohol at room temperature (25-35 ⁰C). Extraction was carried out in a closed
5 container immersing specified amount of the plant material in specified solvent (1:8-1:15 ratio) for 4-7 days. At the end of this stage, solvent is decanted and filtered if necessary to make it free from plant debris. The solvent is then concentrated by evaporating under vacuum at less than 40-60⁰C. The concentrate is then freeze dried to obtain final product in powder form. The final product is then made into oral dosage form by using it as an
10 ingredient for making tablets and capsules. Suitable binders like starch and diluents like lactose are added to make up the formulation.

EXAMPLE – 1

	<i>Utlaria solicifolia</i>	3wt. %
	<i>Asparagus racemosus</i>	2wt. %
15	<i>Foeniculum vulgare</i>	3wt. %
	<i>Ficus glomerata</i>	3wt. %
	Starch paste	15wt. %
	Talc	1wt. %
	Lactose	q.s. to make 100 %

20 *Utlaria solicifolia*, *Asparagus racemosus*, *Foeniculum vulgare*, *Ficus glomerata* were collected and dried in shade. The dried material (1Kg) is then powdered and extracted with 50 % aqueous alcohol (3 L) for 5 days. At the end of this, the solvent is decanted and filtered if necessary to remove the plant debris. The extract is then concentrated under vacuum at less than 50 ⁰C. Then the extract is lyophilized to obtain the extract in powder
25 form.

15 g of starch is mixed with water and heated to form a paste. The weighed quantities of the plant extracts are then blended with starch paste and then lactose is added quantity sufficient to make 100 g. The ingredients are then mixed properly with the starch paste to form a mass. The mass is then granulated in a granulator and then the dry at 104 ⁰F and
30 screen through 16 mesh screen. Talc is added to the dried granules and then they are punched in the tablet-punching machine to form uniform tablets.

The formulation is useful for the treatment of acute and chronic gastric and duodenal ulcers and internal bleeding

EXAMPLE -2

	<i>Utlaria solicifolia</i>	2wt. %
	<i>Asparagus racemosus</i>	1wt. %
5	<i>Foeniculum vulgare</i>	4wt. %
	<i>Ficus glomerata</i>	4wt. %
	Lactose	q.s to make 100 %

Utlaria solicifolia, *Asparagus racemosus*, *Foeniculum vulgare*, *Ficus glomerata* were collected and dried in shade. The dried material (1Kg) is then powdered and extracted with 10 50 % aqueous alcohol (3 L) for 5 days. At the end of this, the solvent is decanted and filtered if necessary to remove the plant debris. The extract is then concentrated under vacuum at less than 50 °C. Then the extract is lyophilized to obtain the extract in powder form. The weighed quantities of the plant extracts as mentioned are mixed with the diluent lactose and then are filled in hard gelatin capsules and are dispensed.

15 The formulation is useful for the treatment of acute and chronic gastric and duodenal ulcers and internal bleeding

Procedures for antiulcer activity screening:

1. *Ethanol induced ulcers*: The gastric ulcers were induced in rats by administering ethanol (1 ml/200g, 1 h) and the animals were sacrificed by cervical dislocation and 20 stomach was incised along the greater curvature and examined for ulcers.
2. *Aspirin induced ulcers*: Aspirin in dose of 200 mg/kg was administered to the animals and ulcers were scored after 4 hours. The stomach was taken out and cut open along with greater curvature and the ulcers were scored by a person unaware of experimental protocol in the glandular portion of the stomach.
- 25 3. *Cold restraint stress – induced ulcers*: Rats were strapped on a wooden plank and kept them at 4-6 °C for 2 hours. The animals were then sacrificed by cervical dislocation and ulcers were scored on the dissected stomach.
4. *Pylorus ligated induced ulcers*: Animals were anaesthetized using pentobarbitone (35mg/kg, i.p.), the abdomen was opened and pylorus ligation was done without 30 causing any damage to its blood supply. The stomach was replaced carefully and the abdomen wall was closed in 2 layers with interrupted sutures. The animals were deprived of water during postoperative period. After 4 hours stomach were dissected out and contents were collected and ulcer index was calculated.

5. *Acetic acid induced ulcers*: The rats were anaesthetized with pentobarbitone (35 mg/kg, i.p.). The abdomen was opened and the stomach was visualized. Cylindrical glass tube of 6 mm diameter was tightly placed upon the anterior serosal surface of the glandular portion on the stomach 1 cm away from the pyloric end. 50 % acetic acid (0.06 ml/ animal) was instilled into the tube and allowed to remain 60 s on the gastric wall. After removal of the acid solution, the abdomen was closed in 2 layers and animals were caged and fed normally. The animals were sacrificed after the last dose of treatment either on 6th or 11th of day of experiment to assess the ulcer size healing. Ulcer index was calculated based upon the product of length and width (mm²/ rat) of ulcers.
6. *Cysteamine induced duodenal ulcers*: Cysteamine in 2 doses of 400 mg/ Kg of 4 intervals time were administered to induce duodenal ulcers. The animals were sacrificed after drug treatment and observed for the presence or absence of ulcers.

Table 1. Effect of antiulcer Herbal composition (HC₁) and formulation without *Utlaria solicifolia* (HC₂) on cold restraint stress (CRS) and pylorus ligation (PL) - induced changes in gastric ulcers in rats.

Treatment	Dose	CRS - induced ulcers		PL - induced ulcers	
		Ulcer Index	%Curative Ratio	Ulcer Index	%Curative Ratio
Control	--	25.6 ± 4.2	--	14.5 ± 2.5	--
HC ₁	100	11.2 ± 3.1 ^a	56.25	6.1 ± 0.8 ^b	57.93
HC ₁	200	4.2 ± 1.0 ^c	83.59	4.8 ± 1.2 ^b	66.90
HC ₂	100	17.2 ± 3.1	32.81	10.5 ± 2.8	27.59
HC ₂	200	13.3 ± 4.5	48.05	7.8 ± 1.6 ^a	46.21
Ranitidine	50	5.2 ± 1.1 ^c	79.68	5.1 ± 1.3 ^b	64.82

Values are mean ± SEM for six rats.

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 HC₁ herbal preparation.

HC₁ showed dose dependent and significant (P: ^a<0.05 to P: ^a<0.001) ulcer protective effect ranged 56.25 – 83.59 %. The H₂ receptor blocker ranitidine showed significant protection and % protection (64.82 and 79.68 %) in CRS and pylorus ligation induced ulcers.

5 EXAMPLE –3

	<i>Utlaria solicifolia</i>	4wt. %
	<i>Asparagus racemosus</i>	2wt. %
	<i>Foeniculum vulgare</i>	3wt. %
	<i>Ficus glomerata</i>	3wt. %
10	Sodium bicarbonate	0.5wt. %
	Citric acid	0.5wt. %
	Lactose	q.s to make 100%

Utlaria solicifolia, *Asparagus racemosus*, *Foeniculum vulgare*, *Ficus glomerata* were collected and dried in shade. The dried material (1Kg) is then powdered and extracted with
 15 50 % aqueous alcohol (3 L) for 5 days. At the end of this, the solvent is decanted and filtered if necessary to remove the plant debris. The extract is then concentrated under vacuum at less than 50 °C. Then the extract is lyophilized to obtain the extract in powder form. The extracts of the plants are mixed with sodium bicarbonate, and citric acid. It is then dry granulated, sieved and punched to form effervescent tablets.

20 The formulation is useful for the treatment of acute and chronic gastric and duodenal ulcers and internal bleeding

EXAMPLE –4

	<i>Asparagus racemosus</i>	2wt. %
	<i>Foeniculum vulgare</i>	4wt. %
25	<i>Ficus glomerata</i>	4wt. %
	Starch paste	15wt. %
	Talc	1.5wt. %
	Lactose	q.s. to make 100 %

Asparagus racemosus, *Foeniculum vulgare*, *Ficus glomerata* were collected and dried in
 30 shade. The dried material (1Kg) is then powdered and extracted with 50 % aqueous alcohol (3 L) for 5 days. At the end of this, the solvent is decanted and filtered if necessary to remove the plant debris. The extract is then concentrated under vacuum at less than 50 °C. Then the extract is lyophilized to obtain the extract in powder form.

15 g of starch is mixed with water and heated to form a paste. The weighed quantities of the plant extracts are then blended with starch paste and then lactose is added quantity sufficient to make 100 g. The ingredients are then mixed properly with the starch paste to form a mass. The mass is then granulated in a granulator and then the dry at 104 °F and
5 1screen through 16-mesh screen. Talc is added to the dried granules and then they are punched in the tablet-punching machine to form uniform tablets.

The formulation is useful for the treatment of acute ulcers.

In case of HC2 formulation (without *Ulteria solicifolia*) the significant (P<0.05) ulcer
10 protection observed at 200 mg/ Kg in Pylorus induced ulcers only.

ADVANTAGES

1. Neutralizes the excess acid in the stomach.
2. Used in acute and chronic gastric/ duodenal ulcers.
- 15 3. Used in healing and curing of ulcers.
4. Useful in curing internal bleeding.

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Claims

1. An antiulcer synergistic herbal formulation, the said formulation comprising of:

INGREDIENTS	wt./wt. %
a) an extract of <i>Utlaria solicifolia</i>	2 to 5
b) an extract of <i>Asparagus racemosus</i>	1 to 3
c) an extract of <i>Foeniculum vulgare</i>	2 to 4
d) an extract of <i>Ficus glomerata</i>	3 to 5 and
e) pharmaceutically acceptable excipient	83 to 92

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2. A formulation(s) as claimed in claim 1 can be administered orally in the form of a tablet, capsule, powder or liquid.

3. A formulation of claim 1, wherein the extract of plants used is obtained by extracting with 50% aqueous alcoholic solution.

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4. A formulation of claim 3, wherein the alcohol used is ethanol.

5. A formulation of claim 1, wherein the total wt % of the plant extracts used ranges between 8 and 17 of the total formulation.

6. The formulation of claim 1, wherein the extract of *Utlaria solicifolia* is a rhizome extract.

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7. A formulation of claim 1, wherein the plant extracts used may be obtained from the plant parts selected from leaf, rhizome or aerial parts.

8. A formulation of claim 1, wherein the pharmaceutically acceptable excipient used is selected from binder, diluent, lubricant, glidant, disintegrant or combinations thereof.

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9. A formulation of claim 8, wherein the diluents are lactose, starches, sugars such as mannitol, sorbitol, xylitol, dextrose, sucrose, microcrystalline cellulose, basic calcium phosphate, calcium sulfate and mixtures thereof.

30

10. A formulation of claim 8, wherein the binders used are starch paste, sorbitol, alginates, polyvinyl pyrrolidone, gum acacia, cellulose derivatives such as hydroxypropylmethyl cellulose, hydroxypropyl cellulose, methyl cellulose, carboxymethyl cellulose, methylcellulose, ethylcellulose, pregelatinized starch, or mixtures thereof.

11. A formulation of claim 8, wherein the glidants used are silica derivatives, talc, starch and mixtures thereof.

12. A formulation of claim 8, wherein the lubricants used are metallic stearates, stearic acid, talc, polyethylene glycols, soluble salts such as sodium chloride, sodium benzoate, sodium lauryl sulfate, spray dried magnesium lauryl sulfate, boric acid, starch, lactose or mixtures thereof.
- 5 13. A method of preparing formulation of claim 1, wherein the said method comprises steps of :
- a) obtaining the required part of medicinal plants,.
 - b) drying the plant material of step (a) in shade,
 - c) powdering the dried plant material of step (b) to obtain a coarse plant
10 powder,
 - d) extracting the powdered plant material of step (c) with aqueous ethanol at a temperature range of 25 – 35 °C for a time period of 4 to 7 days to obtain an aqueous alcoholic extract,
 - e) concentrating the obtained extract of step (d) under reduced pressure at a
15 temperature range of 40-60 °C to obtain a concentrated extract,
 - f) lyophilising the concentrated extract of step (e) for complete removal of solvent to obtain the required plant extract, and
 - g) mixing and formulating the plant extract of step (f) with suitable pharmaceutically acceptable excipient to obtain the required formulation
- 20
14. A method of claim 13, wherein in step (a) the medicinal plant are used from *Utlaria solicifolia*, *Asparagus racemosus*, *Foeniculum vulgare*, and *Ficus glomerata*.
15. A method of claim 14, wherein the parts of the medicinal plant used is selected from leaf, rhizome or aerial parts.
- 25 16. A method of claim 13, wherein in step (d) the aqueous ethanol used contains water:ethanol in the ratio of 6:4 to 1:1.
17. A method of claim 13, wherein in step (d) the ratio of plant and aqueous ethanol used is in the range of 1:8 to 1:15.
18. A method of claim 13, wherein the total plant extracts used ranges between 8 to 17
30 wt.% of the total formulation.
19. A method of claim 13, wherein the pharmaceutically acceptable excipients are selected from a group consisting of binder, diluent, lubricant, glidant, disintegrant or mixtures thereof.

20. A method of claim 19, wherein the diluents are lactose, starches, sugars such as mannitol, sorbitol, xylitol, dextrose, sucrose, microcrystalline cellulose, basic calcium phosphate, calcium sulfate and mixtures thereof.
21. A method of claim 19, wherein the binders used are starch paste, sorbitol, alginates, polyvinyl pyrrolidone, gum acacia, cellulose derivatives such as hydroxypropylmethyl cellulose, hydroxypropyl cellulose, methyl cellulose, carboxymethyl cellulose, methylcellulose, ethylcellulose, pregelatinized starch, or mixtures thereof.
22. A method of claim 19, wherein the glidants used is silica derivatives, talc, starch or mixtures thereof.
23. A method of claim 19, wherein the lubricants used are metallic stearates, stearic acid, talc, polyethylene glycols, soluble salts such as sodium chloride, sodium benzoate, sodium lauryl sulfate, spray dried magnesium lauryl sulfate, boric acid, starch, lactose or mixtures thereof.
24. Use of formulation of claim 1 for relieving the acidity of the stomach by neutralizing the excess acid.
25. Use of formulation of claim 1 to treat stomach discomforts, gastric cancer, stomachache, intestinal discomfort, gastric ulcer, duodenal ulcer and diarrhea.
26. Use of formulation of claim 1 as an antimicrobial agent.
27. Use of formulation of claim 1 at a dose of 100 to 200 mg/kg in cold restraint stress induced ulcers having an ulcer index in the range of 11.2 ± 3.1 to 4.2 ± 1.0 .
28. Use of formulation of claim 1 at a dose of 100 to 200 mg/kg in cold restraint stress induced ulcers having a percentage curative ratio of 83.59:56.25.
29. Use of formulation of claim 1 at a dose of 100 to 200 mg/kg in pylorus ligation induced ulcer having an ulcer index in the range of 6.1 ± 0.8 to 4.8 ± 1.2 .
30. Use of formulation(s) of claim 1, at a dose of 100 to 200 mg/kg in pylorus ligation induced ulcer gives a percentage curative ratio of 57.93:66.90.
31. Use of formulation of claim 1 at a dose of 100 to 200 mg/kg showed lipid peroxidation capacity in rat gastric mucosa in the range of 0.1 ± 0.01 to 0.21 ± 0.01 .
32. Use of formulation of claim 1 at a dose of 100 to 200 mg/kg in an ethanol induced gastric ulcers, provides 64.94 to 86.75% protection and significant increase in gastric wall mucus in rats.

33. Use of formulation of claim 1 at a dose of 100 to 200 mg/kg in aspirin induced gastric ulcers in rats, showed an ulcer index of 7.1 ± 2.2 to 6.2 ± 1.3 and %curative ratio of 61.41 to 66.30.
34. Use of formulation of claim 1 at a dose of 100 to 200 mg/kg in acetic acid induced chronic ulcer healing in rats showed 0.0 to 2.1% incidence of perforations in comparison to 31.2% in control.
35. Use of formulation of claim 1 at a dose of 100 to 200 mg/kg in cysteamine induced duodenal ulcers in rats showed 0 to 20 % incidence when compared to 80 % incidence of ulcers in control.

INTERNATIONAL SEARCH REPORT

Interna Application No
PCT/IB 02/05518

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K35/78 A61P1/04

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, PAJ, WPI Data, BIOSIS, EMBASE, 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.
A	K.RADHAKRISHNAN E.A.: "Utleria salicifolia" FITOTERAPIA, vol. 69, no. 5, 1998, pages 403-405, XP009009827 page 403 page 404	1
A	PATENT ABSTRACTS OF JAPAN vol. 1996, no. 04, 30 April 1996 (1996-04-30) & JP 07 316062 A (DAI ICHI SEIAKU), 5 December 1995 (1995-12-05) abstract --- -/--	1

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

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Date of the actual completion of the international search

4 June 2003

Date of mailing of the international search report

13/06/2003

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INTERNATIONAL SEARCH REPORT

Internationa	Application No
PCT/IB 02/05518	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>A.M.FORESTIERI E.A.: "Antiinflammatory, analgesic and antipyretic activity in rodents of plant extracts used in African Medicine"</p> <p>PHYTOTHERAPY RESEARCH, vol. 10, no. 2, 1996, pages 100-106, XP008018024 page 100 -page 101</p> <p style="text-align: center;">---</p>	1
A	<p>G.K.DATTA E.A.: "Antiulcerogenic activity of Satavari mandur-an ayurvedic herbo-mineral preparation "</p> <p>INDIAN JOURNAL OF EXPERIMENTAL BIOLOGY, vol. 40, no. 10, 2002, pages 1173-1177, XP008018011 page 1173</p> <p style="text-align: center;">-----</p>	1

INTERNATIONAL SEARCH REPORT

in on patent family members

Internal	Application No
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PCT/IB 02/05518

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 07316062	A	05-12-1995	NONE