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[54] **USE OF TARCHONANTHUS
CAMPHORATUS FOR REPELLING INSECTS
AND ALLEVIATING EDEMA, CONGESTION
AND IRRITATION OF THE SKIN**

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[58] **Field of Search** **424/195.1**

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[73] **Assignee:** **Gisquare Technologies B.V.**, Amsterdam, Netherlands

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[57] **ABSTRACT**

Utilization of the *Tarchanthus camphoratus* and its derivatives in formulations and compositions having insect repellent, anti-irritant, anti-edema, decongestant and soothing properties.

[30] **Foreign Application Priority Data**

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2 Claims, No Drawings

**USE OF TARCHONANTHUS
CAMPHORATUS FOR REPELLING INSECTS
AND ALLEVIATING EDEMA, CONGESTION
AND IRRITATION OF THE SKIN**

This application is a 371 of PCT/EP93/02997 filed Oct. 28, 1993.

This invention relates to new uses of the *Tarchonanthus camphoratus*, utilization of its leaves, roots and branches either fresh, dried, soaked, extracted or in the form of essential oil.

The *Tarchonanthus camphoratus* is a shrub rearing in the wild in different African regions especially in the Rift uplands area. An experimental growing took also place in Italy (Canzonieri and Spica; Gazz. Chim. Ital. 1882, 227).

The shrub, mostly unknown by botanists, has different nares such as: Wild cotton, Sage wood, Wildesalie, Kamferhout, Kamferbos, Sieriehout, Vaalbos, Veld-vaalbos, Vaaibos, Sauto Mofahlana, Rolog e Thaalaping mohathla, well known in the local Swahili dialect with the name of "Leleshua", in the abissianian language "Ebok" and so on, or simply with the botanic name of *Tarchonanthus camphoratus*.

The *Tarchonanthus camphoratus* is a shrub reaching 2-4 m height; belonging to the Composite family, it has regular branches with velutinous white-greenish oval or lanceolate shaped leaves ranging from 4 to 13 cm lenght having a strong camphorated aromatic smell, whence its Linneana denomination.

This plant, with its wool-like, spike shaped flower heads is mentioned only in "The Medicinal and Poisonous Plants of Southern Africa" by John Mitchell Watt and Maria Gerdina Breyer-Brandwijk—Edinburgh, 1932 and in Paolo Rovesti's communication, presented at the XXIX International Congress of Industrial Chemistry in Paris in December 1956, "Ecological influences on the composition of the essential oils".

In the literature, mentioned herewith, various applications of this plant are known.

Engler mentions this species as used only for wood by the Usambara in Tanzania (Die Pflanzenwelt Afrikas—Tell B. Berlin, 1895, 357).

Braun tells the Masai (Tanzania) use it for wood-carving (Neil Gew. Pfl. Bd. XI, 2, 47).

Thonner is generally speaking about the plant precious medicinal properties using its leaves in fumigations and infusions (Die Blütenpflanzen Afrikas—Berlin 1908).

Dragerdorff tells that this species have the same therapeutic applications as *Salvia officinalis* (sage) (Die Heilpflanzen—Stuttgart 1898, 589).

Canzonieri and Spica made some studies about the supposed antipyretic properties/activities of *Tarchonanthus Camphoratus* leaves (Gazz. Chim. Ital. 1882, 227).

Watt and Breyer tell the Ottentotti and other indigenous in the South Africa smoke the plant leaves using it as tobacco thanks to their slight narcosis forms. They are also used in fumigations against heathache, rheumatism and infusions (The medicinal and poisonous Plants of South Africa—Edimburg—1932, 189) against dyspepsia and toothache.—Pappe tells leaves contain some camphor but he gives no practical proof (Floras Capensis Medicae Prodromus—Capetown—1868, 178).

Pijper distilled an essential oil but he gave no details on its characteristics (De Volksgeneskunst in Transvaal—Leyden, 1919).

De Stefanis distilled, using some small branches with leaves sent from Eritrea to the Farmacognosia Labora-

tory of Turin University, an essence having a strong camphorated smell, with a yield of 0.1% and the following peculiarity: D 0,9152; i.a. 2,1; i.s. 11,8; i.s. after acethylene 85; I. Iodine 188,5; solubility 1:0.5 in alcohol at 95° (Boll. Inf. Econ. Minist. Colonie—Roma, 1924, n. 1).

Further details come from Rovesti's documentation which shows two plant distillations made in February (dried season) and in August (damp season) which took place in the Ethiopian tableland (XXIX International Congress of Industrial Chemistry, above cited).

	Yield %	d ₁₅ ^o	n _D ²⁰	n _D ²⁰	I.S.	I.S. after acethyl.	Sol.
February essence	0.108	0.9171	-7°23'	1.4681	31.73	149.33	1:3A 70°
August essence	0.209	0.8968	-2°15'	1.4718	18.67	41.07	1:3A 90°

It has now been found, and this is the subject of this invention, that some parts of the plant, in particular its leaves, fresh or dried and their derivatives, have some special insect repelling, insecticide, anti-edema, decongestant, anti-irritating and soothing properties that might be profitably used for therapeutic applications both for humans and animals.

The derivatives of this invention concern the *Tarchonanthus camphoratus* extracts obtained through an extraction as mentioned for example in the Italian Pharmacopeia.

Examples of extraction methods are: maceration, decoction, percolation and distillation.

There are then different derivatives such as the aqueous, the glycolic, the alcoholic, the hydroalcoholic, the soft and dried ones and, preferably, the essential oils.

One of the main goals of this invention is the use of the essential oil. According to the present invention, the application of this plant and of their derivatives concerns not only its insect repelling and insecticide action but also the treatment of irritations and inflammations caused by insect bites.

The efficacy of the *Tarchonanthus camphoratus* derivatives has been also found during some irritation and inflammatory conditions on cutis as for example eczema, ache, reddening, swelling and on genital and mouth mucosa.

The *Tarchonanthus Camphoratus* essential oil obtained through a distillation in a steam flow, has been characterized using a GC/MS analysis, in this way 44 components were identified. Among these elements we find:

Alpha Pinene	15.40%
Camphene	4.35%
Beta Pinene	3.50%
Delta-2-Carene	4.30%
Alpha Phellandrene	1.60%
Limonene	3.00%
Gamma Terpinene	2.05%
Terpinolene	1.35%
1,8 Cineole	12.10%
Fenchol	14.40%
1-Terpinen-4-ol	2.30%
Alpha Terpineol	4.50%
Fenchone	0.85%
Trans Caryophyllene	1.15%
Bergamotene	4.50%
Delta Cadinene	1.40%
Alpha Curcumene	1.70%

The results of this research were presented at the Digne Congress in September 1992 (Ghizzoni, Rovesti, Colombo, Bottini).

Basing on a test of primary cutis irritation on human, it appears that the *Tarhconanthus camphoratus* oil spread as it is on 20 volunteers' healthy cutis in occlusive conditions, gave a medium irritation index of 0.4 after 15 minutes and of 0.35 after 24 hours the sample removal. Basing on the above mentioned parameter the product is then classified as non irritating.

The essential oil showed some surprising therapeutic anti-edema properties. The information about the applications of the essential oil, concerns in detail the edema status on lower limbs.

Another object of the present invention is the preparation and use of topical pharmaceutical compositions containing from 0.01 to 10% of *Tarhconanthus camphoratus* essential oil used as an active ingredient, alone or combined with other active materials.

The compositions can be made according to conventional methods as reported, for example, in the "Remington's Pharmaceutical Sciences Handbook" Mack Pub. New York U.S.A.

Some examples of pharmaceutical topical compositions are: solutions, suspensions, emulsions, ointments, creams, toothpastes in get form, sprays, prolonged release compositions such as transdermic plasters, and soaps.

One of the preferred embodiments of this invention is the preparation of insect-repelling and insecticide formulations containing from 0.01 to 10% of *Tarhconanthus camphoratus* essential oil as active ingredient, alone or with other similar components having the same activity.

Some examples of these preparations are: mosquito-fumigants, fumigants, vaporizing solutions, plates, sprays, stick, lotions, creams and gels.

The *Tarhconanthus* essential oil, put in different topical compositions having anti-edema, decongestant, anti-irritating, soothing activity, can be used in quantities ranging from 0.01% to 5%, preferably from 0.03% to 0.5%.

On the other side the *Tarhconanthus* essential oil, put in different topical formulations with insect-repelling and insecticide activity, can be used in quantities ranging from 0.03% to 7%, preferably from 0.05% to 3%.

In insect-repelling formulations, where the shrub or its essential oil are used at their natural state, the quantity must be 5% up to 95%. In this case it is advisable to use the plant during its balsamic period and immediately after its picking up; this, unfortunately, sets a limit to the *Tarhconanthus* use at natural state, while no limit is fixed for its essential oil.

The activity of the essential oil, being part of this invention, has been tested in more than one pharmacological and clinical test.

1. Insect-repelling and insecticide activity.

A spray lotion containing 0.05% *Tarhconanthus* essential oil, in respect to the below mentioned formulation in example n. 1, was spreaded on 10 volunteers' skin who, during summer season evenings, laid in places with a high mosquitoes concentration.

It has been showed that among the 10 volunteers only 2 of them had mosquito-bites on two cutis areas.

A spray lotion containing 3% *Tarhconanthus* essential oil, in respect to the below mentioned formulation in example n. 3, was spread on 10 volunteers' skin who laid in places with a high mosquito concentration during summer evenings. It was shown that none of them had bites on the skin.

A *Tarhconanthus camphoratus* essential oil alcoholic lotion, in respect to the below mentioned formulation in example n. 4, was used in a diffusor with absorbant tampon and put in a dimly airy room of about 60 mc infested with bothersome insects. Once the diffuser worked, an insecticide action started.

2. Anti-edema, decongestant, anti-irritating and soothing activity.

An application of 0.1% *Tarhconanthus* essential oil gel, as per formulation in example 5, was spreaded on edematous legs, which gave immediate relief.

A gel containing 0.05% *Tarhconanthus* essential oil, as per formulation in example 6, was put on female genitals with itching problems. That brought an immediate relief.

A gel containing 0.054% *Tarhconanthus* essential oil was used as per formulation in example 5, against bags under one's eyes. A rapid and surprising recovery took place.

A gel on 0.3% *Tarhconanthus* essential oil basis, as mentioned in example n. 9, was used on a right ear as a remedy for a swelling due to a mosquito, or some other unidentified insect-bite. The problem was immediately solved. The same result was obtained after an application on different skin areas on 10 persons with various insect bites.

A gel on 0.05% *Tarhconanthus* essential oil basis, as mentioned in example n. 6, was spread on 10 persons suffering from frequent erythema generally treated with a cortisone cream. It was found that all the subject recovered rapidly and both the painful and itching sensations disappeared.

An alcoholic solution containing 0.1% *Tarhconanthus* essential oil, see example n. 12, was put, by means of a tampon, on a pimply skin full with acne on 10 patients. In all the above mentioned situations the problem was totally solved. The same preparation was put on recent pimples that disappeared 24 hours later.

A gel with 0.1% *Tarhconanthus* essential oil was used, as per example n. 7, on 5 subjects' face and neck skin and on armpits and legs suffering from irritation after shaving and depilation treatments. They both declared a relief and freshness sensation.

A fluid emulsion containing 0.1% *Tarhconanthus* essential oil, as per example n.13, was spreaded on genital and anal areas on 2 aged people and on 3 new borns, suffering from itching conditions due to napkins use. All the cases were solved rapidly.

A fluid emulsion on 0.1% *Tarhconanthus* essential oil, see example 14, was spreaded on bedsores on 3 patients. In all these cases the recovery was rapid, the edema and the irritation improved.

A gel containing 0.5% *Tarhconanthus* essential oil, as per example n. 6, was spreaded on 7 subject with itching problems on the anal area due to hemorrhoids and rhagades. They recovered rapidly declaring a freshness and relief sensation.

A mouthwash with 20% infusion, worked at cold state, obtained from *Tarhconanthus* grinded fresh leaves, as in example n.16, was used on 5 patients having irritated gums. In these cases a constant and periodic application brought a relief with a consequent decongestion of gums together with a freshness sensation and a good smelling breath.

A toothpaste with 0.2% *Tarhconanthus* essential oil, as mentioned in example n. 15, was used in 5 cases suffering from slightly irritated gums. A constant and periodic use of the formulation was of help in the gums decongestion. A freshness sensation and a good smelling breath was also noticed.

An alcoholic gel containing 1% *Tarhconanthus* essential oil, as per example n. 10, was used on legs suffering from phlebitis. A constant and periodic use was of help to solve the problem.

An alcoholic gel containing 0.8% *Tarhconanthus* essential oil as per example n. 11, was spreaded on haematoma on 3 subjects. In both cases, a constant and periodic use, was of help to improve the edema problem.

The following examples further illustrate the invention. For sake of brevity, the essential oil is called E.O.

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EXAMPLE N. 1

Insecticide spay lotion

PEG 40 Hydrogenated Castor Oil	0.2%	
Glycerine	3%	
Tarchonanthus camphoratus E.O.	0.05%	
Preservatives (antibacterial/antimould)	q.s.	
Demineralized water	q.s.	to 100%

EXAMPLE N. 2

Insecticide spray lotion

PEG 40 Hydrogenated Castor oil	4%	
Glycerine	3%	
Tarchonanthus camphoratus E.O.	1%	
Preservatives (antibacterial/antimould)	q.s.	
Demineralized water	q.s.	to 100%

EXAMPLE N. 3

Insecticide spray lotion

Peg 40 Hydrogenated Castor Oil	12%	
Glycerine	3%	
Tarchonanthus camphoratus E.O.	3%	
Preservatives (antibacterial/antimould)	q.s.	
Demineralized water	q.s.	to 100%

EXAMPLE N. 4

Insecticide alcoholic solutions for environmental purposes

Methylated alcohol type A	42%	
Tarchonanthus camphoratus E.O.	5%	
Sorbitan monoleate 20 (OE)	13%	
Demineralized water	q.s.	to 100%

EXAMPLE N. 5

Anti-edema gel

Carboxyvinyl polymer (Carbomer 940)	0.76%	
Glycerine	3%	
Sorbitan 20 (OE) monolaurate	0.4%	
Tarchonanthus camphoratus E.O.	0.1%	
Preservatives (antibacterial/antimould)	q.s.	
Triethanolamine	0.5%	
Demineralized water	q.s.	to 100%

EXAMPLE N. 6

Anti-irritating, soothing gel

Carboxyvinyl polymer (Carbomer 940)	0.76%	
Glycerine	3%	
Sorbitan 20 (OE) monolaurate	0.2%	
Tarchonanthus camphoratus E.O.	0.05%	
Preservatives (antibacterial/antimould)	q. s.	
Triethanolamine	0.5%	
Demineralized water	q.s.	to 100%

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EXAMPLE N. 7

Anti-irritating gel pre/after shave/depilation

5	Carboxyvinyl polymer (Carbomer 940)	0.5%
	Glycerine	3%
	Sorbitan 20 (E.O.) monolaurate	0.2%
	Tarchonanthus camphoratus E.O.	0.04%
	Preservatives (antibacterial/antimould)	q.s.
10	Triethanolamine	0.3%
	Demineralized water	q.s. to 100%

EXAMPLE N. 8

After sun gel

15	Carboxyvinyl polymer (Carbomer 940)	0.76%
	Glycerine	3%
	Sorbitan 20 (OE) monolaurate	0.4%
	Tarchonanthus camphoratus E.O.	0.1%
	Preservatives (antibacterial/antimould)	q.s.
20	Triethanolamine	0.5%
	Demineralized water	q.s. to 100%

EXAMPLE N. 9

30 Anti-edema gel

30	Carboxyvinyl Polymer (Carbomer 940)	0.70%
	Glycerine	3%
	Sorbitan 20 (OE) monolaurate	1.2%
	Tarchonanthus camphoratus E.O.	0.3%
35	Preservatives (antibacterial/antimould)	q.s.
	Triethanolamine	0.45%
	Demineralized water	q.s. to 100%

EXAMPLE N. 10

Anti-edema alcoholic gel

45	Carboxyvinyl polymer (Carbomer 940)	0.5%
	Alcohol type D	40%
	Glycerine	5%
	Peg 40 Hydrogenated Castor Oil	3%
	Tarchonanthus camphoratus E.O.	1%
50	Preservatives (antibacterial/antimould)	q.s.
	Triethanolamine	0.3%
	Demineralized water	q.s. to 100%

EXAMPLE N. 11

Soothing/refreshing alcoholic gel

60	Carboxyvinyl polymer (Carbomer 940)	0.5%
	Alcohol type D	40%
	Glycerine	5%
	Peg 40 Hydrogenated Castor Oil	2.5%
	Tarchonanthus camphoratus E.O.	0.8%
	Preservatives (antibacterial/antimould)	q.s.
65	Triethanolamine	0.3%
	Demineralized water	q.s. to 100%

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EXAMPLE N. 12

Alcoholic solution for pimply skins

Alcohol type C	40%	5
Glycerine	2%	
Sorbitan 20 (OE) monolaurate	2%	
Tarchonanthus camphoratus E.O.	0.1%	
Lavender e.o.	0.4%	
Demineralized water	q.s.	to 100%

EXAMPLE N. 13

Anti-irritating fluid emulsion

Carboxyvinyl polymer (Carbomer 940)	0.30%	
Glycerine	6%	
Tarchonanthus camphoratus E.O.	0.1%	
Triethanolamine	0.2%	
Acetylated Lanoline	1%	
Dimethylpolyxyloxane	1%	20
Myristil lactate	2%	
Decyle oleate	2%	
Preservatives (antibacterial/antimould)	q.s.	
Demineralized water	q.s.	to 100%

EXAMPLE N. 14

Anti-irritating/decongestant fluid emulsion

Carboxyvinyl polymer (Carbomer 940)	0.30%	
Glycerine	6%	
Tarchonanthus camphoratus E.O.	0.1%	
Allantoine	1%	
Tocopheryl acetate	0.5%	
Triethanolamine	0.2%	35
Acetylated lanoline	1%	
Dimethylpolyxiloxane	1%	
Myristil lactate	2%	
Decyl oleate	2%	
Preservatives (antibacterial/antimould)	q.s.	
Demineralized water	q.s.	to 100%

EXAMPLE N. 15

Gum toothpaste

Potassium sorbate	0.2%
Glycerine	11%

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Sorbitan 20 (OE) monolaurate	0.8%
Tarchonanthus camphoratus E.O.	0.2%
Carboxyvinyl cellulose medium density	1.5%
Dicalcium phosphate di-hydrate	48%
Sorbitol 70%	11%
Sodium laurylether sulphate	2%
Acesulfame Hoechst (sweetener)	0.2%
Preservatives (antibacterial/antimould)	q.s.
Demineralized water	q.s. to 100%

EXAMPLE N. 16

Idroalcoholic mouthwash

Alcohol type E	15%
Glycerine	4%
Glycyrrhizinate ammonium	0.1%
Tarchonanthus infusion at cold state grinded fresh leaves at slow stirring for 7 days in demin. water preserved	20%
Demineralized water	q.s. to 100%

EXAMPLE N. 17

Mosquito fumigant

A convenient quantity of dried leaves, belonging to a plant picked up by no more than 30 days, was grounded small.

30% of it was mixed up with arabic gum (10%), pit-coal (50%) potassium nitrate (10%), worked in water, spiral shaped and dried in a heater at 35° C. for 24 hrs.

The same examples can be formulated with extracts and soaked in the proper concentrations.

We claim:

1. A method for repelling insects, and alleviating edema, congestion and skin irritation symptoms which comprises applying to the cutis of an individual a pharmaceutical composition comprising as the principal active ingredient from 0.01-10% of the extract of *Tarchonanthus camphoratus* together with a pharmaceutically acceptable carrier.

2. A method for alleviating edema, congestion and skin irritation symptoms which comprises applying to the cutis of an individual a pharmaceutical composition comprising as the principal active ingredient from 0.03-0.5% of the extract of *Tarchonanthus camphoratus* together with a pharmaceutically acceptable carrier.

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