The invention relates to a medicinal composition for the treatment and protection of injured, excoriated and irritated skin. The inventive composition comprises at least one substance for sensorial deterrence selected from the group containing pungent constituents, bitter constituents and odorant constituents, and at least one therapeutic substance selected from the group of substances with antiseptic properties and substances with wound healing properties. The use for the manufacturing of a medicament for treatment and protection of injured, excoriated and irritated skin is provided. The invention is of particular use for the treatment of animals.
MEDICINAL COMPOSITION FOR TREATING ANIMAL SKIN COMPRISING A WOUND HEALING AGENT AND A DETERRENT

The present invention relates to a medicinal composition for treatment and protection of injured, excoriated and irritated animal skin according to claim 1 and its use for the manufacture of a medicament according to claim 10.

In a time period of about 10 days after an operation or a bite animals, especially dogs, are required to wear a collar, a sleeve or a muzzle. This is caused by the tendency of animals for postoperative self-mutilation independently of the operation method.

It is therefore necessary to prevent an animal to lick its wounds, since otherwise the danger of a wound haematoma or serom formation prevails. In the course of this process ichor is formed, causing the skin to be squeezed off from the underlying tissue. This leads to a lump containing reddish aqueous liquid which needs to be punctured.

In order to prevent animals from licking their wounds several proposals have been made. One such proposal is described in EP 1015418 B1.

The use of denatonium capsaicinate (denatonium nonyl vanylamide) as a synthetic derivative of the hot, spicy, pungent flavour capsaicin as an animal repellent, antifoulant and irritant is disclosed. The capsaicin derivative can be added to paints, lacquers or coating compositions which might be used to coat a layer or film on an electric or optic cable, a pipe, a wall or outdoor furniture to deter animals from gnawing on or destroying it.

Denatonium capsaicinate may also be added to medical dressings such as bandages, to salves, creams, lotions or ointments in order to prevent animals from removing these materials by biting, gnawing, chewing or licking after procedures by the veterinarian.

Although this approach may deter animals to lick their wounds it does not promote or improves the healing process itself.

It is therefore an objective of the present invention to provide an alternative solution in preventing animals, especially dogs, of licking or pawing their wounds in combination with an improved wound healing effect.
This objective is solved by providing a medicinal composition according to claim 1.

The present medicinal composition for treatment and protection of injured, excoriated and irritated animal skin comprises

- at least one deterrent substance for sensorial deterrence selected from the group containing pungent constituents, bitter constituents and odorants, and

- at least one therapeutic substance selected from the group of constituents with antiseptic properties and constituents with wound healing properties.

The composition according to the invention enables the formation of a thin protective film on the wound as well as a flavour and odour barrier preventing the animal from touching or licking the wound. Furthermore, the antiseptic and curing substances promote the wound healing process.

The pungent or bitter constituents of the present composition deter the animal specifically from licking the open wound by providing a pungent or bitter taste. The odorant constituents provide preferably a bad smell, thus making it unpleasant for an animal to draw nearer to the open wound.

The pungent constituents, bitter constituents, odorant constituents, antiseptic and wound healing constituents are present at a concentration between 0 and 5 % [m/m], whereby % [m/m] relates to mass percentage.

Preferably, the pungent substances are present at a concentration between 0,001 % [m/m] and 0,1 % [m/m]. The bitter constituents are preferably present in form of extracts at a concentration between 0,05 %[m/m] and 3 %[m/m]. The odorant constituents are preferably present at a concentration between 0 % [m/m] and 1 % [m/m]. The aseptic constituents as therapeutic substances are preferably present at a concentration between 0,05 %[m/m] and 1 %[m/m]. The wound healing constituents are preferably present at a concentration between 0 % [m/m] and 5 % [m/m].

The pungent constituent is preferably selected from the group containing (E)-N- (4-hydroxy-3-methoxybenzyl)-8-methylnon-6-enamide (capsaicine), 1-[5-(1,3-Benzodioxol-5-yl)-1-oxo-2,4-pentadienyl]pipedhine (piperine), 5-hydroxy-1 - (4-hydroxy-3-methoxy-phenyl) -decan-3-one (gingerol), 4-(4-hydroxy-3-methoxyphenyl)-
2-butanone (zingerone), 5-allyl-1-methoxy-2,3-methylenedioxybenzene (myristicin) 2-propene-1-sulfinothioic acid S-2-propenyl ester (allicin) and mustard oil.

The bitter constituent is preferably selected from the group comprising a flavonoide as dihydrochalcone, glycosides present in gentian extract, yarrow extract or centaury extract, isoprenoides present in hops, absinth, calamus, angelica, dandelion, hemlock, limonoids, carлинаoxide from carline thistle and (2-ethenyl-4-azabicyclo[2.2.2]oct-5-yl)-(6-methoxyquinolin-4-yl)-methanol (quinine). In one preferred embodiment, at least one of these constituents is combined with the bitter tasting substances glycercyl caprylate and/or polyglyceryl 10-laurate.

According to an alternative embodiment of the present invention, the bitter constituent comprises glycercyl caprylate and/or polyglyceryl 10-laurate.

The odorants is preferably selected from the group of containing aromatic substances, preferably essential oils from lemon balm, *Melissae folium*, *Menthae arvensis* and *Methae piperitae*.

The therapeutic substance with antiseptic and wound healing properties is preferably selected form the group comprising *Myroxylum balsamum* (Peru ageratum), chlorohexidine, colloidal silver (argent), silver nanoparticles, 5-chloro-2-(2,4-dichlorophenoxy)-phenol (triclosan), ethacridine lactate, extracts from Centella asiatica, willow bark, birch, olive leaves, tea-tree, Aloe vera, calendula, passion flower, hamamelis, camomile, bearberry, licorice, 18β-glycyrrhetine acid or mixtures thereof, polysaccharides as lichenine, isolichenine and lichen acid from *Lichen islandicus, Plantaginis lanceolatae folium*, *Uvae ursi folium*, *Myrrha*, *Arnicae flos* and *Equiseti herba*.

Advantageously, the present composition comprises also at least one astringent constituent, preferably selected from the group comprising tannins such as tannins from *Quercus robur* or *Syzygium cumini*, flavanoides such as epigallocatechin-3-gallate, proanthocyanidines, flavonoles such as quercitine glycosides in *Gossypium*, quinine as 5-Hydroxy-1,4-naphthalindion (juglon) from *Carya ovata*, aluminium compounds such as aluminium chlorohydrate, aluminium alkali sulphate, aluminium hydroxid acetate hydrate, ammoniumchlohide, colloidal silver, extract from blackberry leaves, extracts from green tea, black tea, *Krameria triandra* and *Rhizoma tormentillae*.
The astringent constituents are preferably present in form of extracts at a concentration between 0.5%[m/m] and 5%[m/m].

The present composition might be applied directly onto the wound or the wound edge in form of emulsion, emulsifying gel, semisolid or liquid formulation, salves, medical dressings, plaster, compress, gauze, film forming polymeric solution or another polymer carrier. The composition may also be sprayed onto the wound in form of a liquid vehicle.

An emulsifying gel preferably comprises

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<th>[0.1 - 0.001 % m/m]</th>
<th>capsaicin</th>
<th>((4-hydroxy-3-methoxybenzyl)-8-methylnon-6-enamide)</th>
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<tr>
<td>[0 - 20.0 % m/m]</td>
<td>middle chain triglycerides</td>
<td></td>
</tr>
<tr>
<td>[0 - 1.0 % m/m]</td>
<td>lemon balm oil</td>
<td></td>
</tr>
<tr>
<td>[0 - 5.0 % m/m]</td>
<td>silicone oil</td>
<td></td>
</tr>
<tr>
<td>[0.1 - 5 % m/m]</td>
<td>Cremophor RH 40</td>
<td></td>
</tr>
<tr>
<td>[5 - 20 % m/m]</td>
<td>propylene glycol</td>
<td></td>
</tr>
<tr>
<td>[0 - 10.0 % m/m]</td>
<td>glycerol</td>
<td></td>
</tr>
<tr>
<td>[0.1 - 2.0 % m/m]</td>
<td>polymer carrier (polyacrylate as Ultrez 10 or Carbopol 980)</td>
<td></td>
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<tr>
<td>[0.05 - 1.0 % m/m]</td>
<td>Triclosan</td>
<td></td>
</tr>
<tr>
<td>[0.5 - 5.0 % m/m]</td>
<td>tannin</td>
<td></td>
</tr>
</tbody>
</table>

A film forming polymer composition preferably comprises

| [0 - 25 % m/m]  | Ethanol                                               |
| [0.05 - 1.0 % m/m] | Chlorhexidindigluconat                             |
| [0.05 - 3.0 % m/m] | Oleum Absinthii                                     |
| [0 - 10 % m/m]  | *Plantaginis lanceolatae folium* (ribwort extract).  |
| [5 - 15 % m/m]  | silicon gum, SGM, Dow Corning S.A.                   |
| [40 - 80 % m/m] | Q7-91 80 Fluid (Hexamethyldisiloxane / Octamethylthsiloxane), Dow Corning S.A. |
| [1 - 20 % m/m]  | 193 Fluid (Alkylmethylsiloxane copolyol), Dow Corning S.A. |
The medicinal composition according to the invention is also used for the manufacture of a medicament for the treatment of wounds, excoriated or irritated skin of animals, especially of dogs.

In order to point out more fully the nature of the present invention, the following specific examples are given as an illustrative embodiment.

**Example 1** describes an emulsifying gel for application on the wound edge.

**Ingredients per 100 g gel:**

- 0,008 g capsaicin ((4-hydroxy-3-methoxybenzyl)-8-methylnon-6-enamide))
- 4,5 g middle chain triglycerides
- 0,1 g lemon balm oil
- 2,0 g silicone oil
- 1,5 g Cremophor RH 40
- 15,0 g propylene glycol
- 1,0 g glycerol
- 1,0 g polymer carrier (polyacrylate as Ultrez 10 or Carbopol 980)
- 0,3 g Tholosan
- 2,0 g tannin
- ca. 6 g 5% NaOH solution, pH 5-6
- add up to 100 g water (Aqua Purificata)

**Manufacturing process for 1000 g:**

a) Water phase:

1. A mixing vessel is filled with 650 g Aqua Purificata. 20 g Tannin is added to the water. The mixture is stirred at a temperature of 25°C ± 5°C till a clear yellow solution is formed.

b) Capsaicin solution:

0,08 g Capsaicin and 3 g Triclosan are weight into a beaker. 150 g Propylene glycol is added and dissolved under stirring at a temperature of 25°C ± 5°C.
c) Lipid phase:

A beaker is filled with 45 g MCT, 1 g lemon balm oil, 15 g Cremophor RH40 and mixed at a temperature of 25°C ± 5°C.

d) Combining the phases:

The Capsaicin solution is added to the water phase while stirring. Then, the lipid phase is mixed into the water phase. The obtained mixture is homogenized at a vacuum of -0.8 bar at a temperature of 25°C ± 5°C. After 5 minutes the mixture is aerated carefully.

e) Gel manufacturing:

10 g Polyacrylic acid (for example Ultrez 10 or Carbopol 980) is added to the above mixture while vigorous stirring for a time period of 5 min. The pH value is adjusted to 5-6 by adding 60 g of a 5% NaOH solution under vigorous stirring. The obtained mixture is homogenized at a vacuum of -0.8 bar at a temperature of 25°C ± 5°C. After 2 minutes the mixture is carefully aerated and water is added up to total weight of 940 g of the mixture while maintaining the pH.

Finally, 10 g silicon oil (for instance 350) and 10 g glycerol (85%) are added under stirring to the mixture. The mixture is homogenized for 2 min at a vacuum of -0.6 bar at a temperature of 25°C ± 5°C.

**Example 2** describes a film forming polymer composition for application onto the wound.

**Ingredients per 100 g gel:**

10,0 % [m/m]  silicon gum, SGM, Dow Corning S.A.
15,0 % [m/m]  Ethanol
61,5 % [m/m]  Q7-91 80 Fluid (Hexamethyldisiloxane / Octamethyltrisiloxane), Dow Corning S.A.
8,5 % [m/m]  193 Fluid (Alkylmethylsiloxane copolyol), Dow Corning S.A.
0,2 % [m/m]  Chlorhexidindigluconat
1,0 % [m/m]  Oleum Absinthii
3,8 % [m/m]  *Plantaginis lanceolatae folium* (ribwort extract)
Manufacturing process:

Chlorhexidindigluconate, Oleum Absinthii and ribwort extract are dissolved in ethanol. In a further beaker the silicon gum is dissolved in Q7-91 80 fluid and 193 Fluid. In the following both solutions are unified under constant stirring. The amount of ethanol can be adapted to the solubility of the plant extracts in the silicon media. The composition can be applied with a brush or a spray applicator. Within minutes a flexible, dry film is formed on the animal skin.

Example 3 describes further recipes for medicinal compositions according to the present invention that can be obtained according to the principles outlined above.

Example 3 A

0.08 g lemon balm oil (oleum melissae indicum, cymbopogon winterhanus)
0.90 g glyceryl caprylate
0.15 g absinthe oil (oleum absinthii, artemisia absinthicum)
2.0 g polyglyceryl 10-laurate
5-10 g solvent: propylene glycol and/or ethylalcohol (and/or up to 15 g aqua purificata), if necessary for solubilisation
0.10 g Chlorhexidin-bis(D-gluconate)
10.0 g SGM 36
2 - 8.5 g 193 Fluid (Alkylmethysiloxane copolyol), depending on solvent cone.
ad 100 g Q7-9180 (Hexamethyldisiloxane / Octamethylthsiloxane) depending on solvent cone.

Example 3 B

0.05 g camelia sinensis extract (green tea extract, polyphenols >80%)
1.5 g glyceryl caprylate
3.0 g polyglyceryl 10-laurate
5-10 g solvent: propylene glycol and/or ethylalcohol (and/or up to 15 g aqua purificata), if necessary for solubilisation
10.0 g SGM 36
2 - 8.5 g 193 Fluid depending on solvent cone.
ad 100 g Q7-9180 depending on solvent cone.
Example 3 C

0.02 g 5-hydroxy-1-(4-hydroxy-3-methoxy-phenyl)-decan-3-one (gingerol) or
0.250 g ginger root extract (Zingiber officinale)
5.0 g gentian extract
5-10 g solvent: propylene glycol and/or ethylalcohol (and/or up to 15 g aqua
puhficata), if necessary for solubilisation
10.0 g SGM 36
2 - 8.5 g 193 Fluid depending on solvent cone.
ad 100 g Q7-9180 depending on solvent cone.
Claims

1. Composition for treatment and protection of damaged animal skin, especially injured, excoriated and/or irritated animal skin comprising

- at least one deterrent substance for sensorial deterrence selected from the group comprising pungent constituents, bitter constituents and odorants, and
- at least one therapeutic substance selected from the group comprising constituents with antiseptic properties and constituents with wound healing properties.

2. Composition according to claim 1 comprising at least one astringent constituent.

3. Composition according to any of the preceding claims characterized in that pungent constituents, bitter constituents, odorant constituents, antiseptic and wound healing constituents are present at a concentration between 0 and 5%.

4. Composition according to any of the preceding claims characterized in that the at least one deterrent substance comprises:

- at least one pungent constituent selected from the group containing (E)-N-(4-hydroxy-3-methoxybenzyl)-8-methylnon-6-enamide (capsaicine), 1-[5-(1,3-Benzodioxol-5-yl)-1-oxo-2,4-pentadienyl]piperdine (piperine), 5-hydroxy-1-(4-hydroxy-3-methoxy-phenyl)-3-decan-3-one (gingerol), 4-(4-hydroxy-3-methoxyphenyl)-2-butane (zingerone), 5-allyl-1-methoxy-2,3-methylene dioxybenzene (myristicin) 2-propene-1-sulfinothioic acid S-2-propenyl ester (allicin) and mustard oil, and/or

- at least one bitter constituent selected from the group containing a flavonoid as dihydrochalcone, glycosides present in gentian extract, yarrow extract or centaury extract, isoprenoides present in hops, absinth, calamus, angelica, dandelion, hemlock, limonoids, carlineoxide from carline thistle and (2-ethenyl-4-azabicyclo[2.2.2]oct-5-yl)-(6-methoxyquinolin-4-yl)-methanol (quinine).

5. Composition according to any of the preceding claims comprising glyceryl caprylate and/or polyglyceryl 10-laurate.
6. Composition according to any of the preceding claims comprising at least one odorant constituent selected from the group of compounds contained in the essential oils from lemon balm, *Melissae folium*, *Menthae arvensis* and *Methae piperatae*.

7. Composition according to any of the preceding claims 26, characterized in that the at least one astringent constituent is selected from the group comprising tannins from *Quercus robur*, tannins from *Syzygium cumini*, flavanoids such as epigallocatechin-3-gallate, proanthocyanidines, flavonoles such as querctine glycosides in Gossypium, quinine as 5-Hydroxy-1,4-naphthalindion (juglon) from Carya ovata, aluminium compounds such as aluminium chlorohydrate, aluminium hydroxid acetate hydrate, ammoniumchlohde, colloidal silver, extract from blackberry leaves, extracts from green tea, black tea, *Krameña triandra* and *Rhizoma tormentillae*.

8. Composition according to any of the preceding claims characterized in that the at least one therapeutic substance selected from the group comprising *Myroxylum balsamum* (Peru ageratum), chlorhexidine, colloidal silver (argent), silver nanoparticles, 5-chloro-2-(2,4-dichlorophenoxy)-phenol (thlosan), ethacridine lactate, extracts from Centella asiatica, willow bark, birch, olive leafs, tea-tree, *Aloe vera*, calendula, passion flower, hamamelis, camomile, bearberry, licorice, 18β-glycyrhetine acid or mixtures thereof, polysaccharides as lichenine, isolichenine and lichen acid from *Lichen islandicus*, *Plantaginis lanceolatae folium*, *Uvae ursi folium*, *Myrrha*, *Arnicae flos* and *Equiseti herba*.

9. Use of the composition according to any of the preceding claims for the manufacture of a medicament for the treatment of wounds, excoriated or irritated skin of mammals.

10. Use according to claim 9, characterized in that the mammal is a dog or a cat.

11. Use according to claim 9, characterized in that the mammal is a human being.

12. Use of the composition according to at least one of the claims 1 to 8 as an ointment, w/o or o/w emulsion, semisolid or liquid formulation, salves, medical dressings, plaster, compress, gauze, film forming polymeric solution.
13. Ointment, w/o or o/w emulsion, semisolid or liquid formulation, salves, medical dressings, plaster, compress, gauze, film forming polymeric solution for the treatment of damaged animal skin comprising a composition according to at least one of the claims 1 to 8.
### A. CLASSIFICATION OF SUBJECT MATTER

According to International Patent Classification (IPC) onto both national classification and IPC:

**INV. A61K45/06**

### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

- **A61K**

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

- Electronic database consulted during the international search (name of database and, where practical, search terms used)

**EPO-Internal, WPI Data, BIOSIS, EMBASE**

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim</th>
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### D. Further documents are listed in the continuation of Box C

- See patent family annex

**Notes:**
- **A** - document defining the general state of the art which is not considered to be of particular relevance
- **E** - earlier document 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 applicant 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
- **S** - document member of the same patent family

**D. Date of the actual completion of the international search**

- 30 May 2008

**D. Date of mailing of the international search report**

- 10/06/2008

**D. Name and mailing address of the ISA/Authorized officer**

- European Patent Office, P B 5818 Patentlaan 2 NL - 2280 HV Rijswijk
- Tel (+31-70) 340-2040, Tx 31 651 epo nl
- Fax (+31-70) 340-3016

- Engl, Brigitte
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Form PCT/ISA/210 (patent family annex) (April 2005)