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(54) Benævnelse: **MEDICINSK VIRKSOMT PLASTER**

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Description

The present invention relates to a medical patch for administering to the skin pharmaceutical agents that are liquid at room temperature, in particular for administering the antiphlogistic agent etofenamate.

Medical patches for administering pharmaceutical agents to the skin are known *per se.* These patches usually consist of a top layer, a backing layer containing the pharmaceutical agent, and a peelable protective layer. It is difficult to manufacture a patch of this type, however, because the backing layer that comes into contact with the skin must ensure optimum transfer of the agent into the skin and at the same time adhere to the skin less firmly than to the top layer, so that the plaster can be easily and completely removed from the skin.

The backing layer should also contain the highest possible concentration of the agent so that it can be released from the patch in a pharmaceutically active concentration over a comparatively long period of time. This is difficult to achieve in agents that are liquid at room temperature, since liquid agents have to be embedded in the backing layer in a stable way and must be compatible with the material of the backing layer. The agent must also be released from the backing material at a sufficient rate over a longer period of time. Not only the type of the backing material but also the chemical structure of the agent plays an important role here.

A medically active patch is known from US 6,316,022, in which the backing layer containing the agent consists of a polyacrylate compound and the agent is dissolved in the backing layer. US 5 830 505 describes a medical patch in which an acrylate copolymer is used as the backing material, in which the agent is dissolved. US 2001/053383 relates to a medical patch in which the backing layer consists of a polyacrylate/ polysiloxane mixture and the agent is dissolved in the matrix. US 2006/263419 relates to a medical patch, in which the backing layer contains e.g. polyvinylpyrrolidone, a copolymer of vinylpyrrolidone and vinyl acetate or a copolymer of ethylene and vinyl acetate and the agent as solid particles. WO 2006/064576 describes a patch, in which the backing layer represents a mixture consisting of a non-adhesive synthetic rubber, an adhesive resin and a liquid paraffin. US 4,623,346 describes a similar patch, in which the backing layer consists of multiple components selected from a synthetic polymer, a flow promotor and an adhesive resin.

It has recently surprisingly been found that the antiphlogistic agent etofenamate, which generally dissolves poorly, can be stably embedded in a self-adhesive silicone matrix in a pure form with a uniformly fine distribution and that it forms a finely distributed dispersion therein, such that a matrix with very good adhesive properties is obtained, which releases the agent in an active concentration over a longer period of time and, according to the invention, can be used as a backing layer.

The present invention is defined in the patent claims. The present invention relates to a medical patch for administering the antiphlogistic agent etofenamate to the skin, wherein this patch has a structure consisting of a top layer (a), the carrier layer (c), the peelable protective layer (d) and optionally an intermediate layer (b), characterized in that:

- the top layer (a) consists of an inert material;
- the backing layer (c) consists of a self-adhesive polysiloxane as a backing material, which was obtained by condensing a dimethylpolysiloxane containing silanol groups with a silicate resin that is soluble in organic solvents and then reacting the remaining silanol groups with a reactive trimethylsilyl compound; and
- this self-adhesive polysiloxane optionally contains additives that are known *per se* for modifying the adhesive properties and optionally additives for reducing the viscosity of the self-adhesive polysiloxane, and into which the antiphlogistic agent is incorporated in the form of a dispersion, optionally with a substance that promotes permeation through the skin;
- the adhesive force of the backing layer (c) is in the range from 0.8 N/25 mm to 1.4 N/25 mm;
- the backing layer (c) contains the agent etofenamate in a concentration in the range from 1.0% to 25.0% by weight, based on the total weight of the backing layer (c);
- the backing layer (c) contains the agent in dispersed form in an average droplet size in the range from 0.1 µm to 500 µm;

- the backing layer (c) adheres directly to the top layer (a) or is optionally attached to it by the intermediate layer (b); and
- the peelable protective layer (d) consists of an inert material, adheres to the backing layer (c) and can be easily peeled off of it.

Preferably, a medical patch has a structure according to Figure 2 consisting of the top layer (a), the backing layer (c) and the peelable protective layer (d), characterized in that:

- the top layer consists of an inert material,
- the backing layer (c) consists of a self-adhesive polysiloxane, in which the antiphlogistic agent etofenamate is incorporated in the form of a dispersion, optionally with a substance that promotes permeation through the skin and optionally with further additives, and this backing layer (c) adheres directly to the top layer (a); and
- the peelable protective layer (d) consists of an inert material, adheres to the backing layer (c) and can be easily peeled off of it.

If the adhesive layer (b) is provided as an intermediate layer between the top layer (a) and the backing layer (c), then this adhesive layer (b) either contains an agent or is optionally loaded with agent in various amounts and has a comparably strong adhesive force, and so the adhesive layer (b) firmly adheres both to the top layer (a) and to the backing layer (c). The adhesive force of the adhesive layer (b) is largely independent of the backing layer (c) that contains the agent and is greater than the adhesive force of the carrier layer (c). The adhesive force of the carrier layer (c) is only strong enough that the patch is not prevented from being easily and completely removed from the skin.

If the adhesive layer (b) is loaded with agent, then preferably there is at least as much of the agent in the adhesive layer (b) as in the backing layer (c). Preferably, the adhesive layer (b) is loaded to the saturation point with the agent.

The present invention also relates to a method for producing the patch according to Figure 1 containing an adhesive layer (b), characterized in that the components of the adhesive layer (b) are applied, in liquefied form, i.e. as a “hot melt” without the addition of a solvent, or dissolved in a suitable organic solvent, to the top layer (a) and then rid of the optionally present organic solvent and dried; the components of the backing layer (c) are subsequently applied, in liquefied form, i.e. as a "hot melt" without the addition of a solvent, or dissolved in a suitable organic solvent, to the adhesive layer (b) and then rid of any organic solvent that may be present and dried; and the peelable protective layer (d) is applied to the dried backing layer (c).

Thus the adhesive layer (b) can optionally also contain the agent, as described above.

The present invention also relates to a method for producing the patch according to Figure 2, characterized in that the components of the backing layer (c) are applied, in liquefied form, i.e. as a "hot melt" without the addition of a solvent, or dissolved in a suitable organic solvent, to the top layer (a) and then rid of the optionally present organic solvent and dried; and the peelable protective layer (d) is applied to the dried backing layer (c).

When producing the claimed patch, it is also possible to begin with the peelable protective layer (d). In that case, the method for producing the patch, e.g. according to Figure 1, is characterized in that the components of the backing layer (c) are applied, in liquefied form, i.e. as a "hot melt" without the addition of a solvent, or dissolved in a suitable organic solvent, to the peelable protective layer (d) and then rid of the optionally present organic solvent and dried; in a separate step, the components of the adhesive layer (b), in liquefied form, i.e. as a "hot melt" without the addition of a solvent, or dissolved in a suitable organic solvent, are applied to the top layer (a) and then rid of any organic solvent that may be present and dried; and the backing layer (c) is then laminated with the top layer (a), which already contains the adhesive layer (b).

Similarly, the method for producing the patch, e.g. according to Figure 2, is characterized in that the components of the backing layer (c) are applied, in liquefied form, i.e. as a "hot melt" without the addition of a solvent, or dissolved in a suitable organic solvent, to the peelable protective layer (d) and then rid of the optionally present organic solvent and dried; and the top layer (a) is applied to the dried backing layer (c).

Preferably, the adhesive later (b) and the backing layer (c) are dried immediately after they are applied, if they contain solvents. However, it is also possible to apply all of the layers in succession and to dry them only at the end. The backing layer is preferably processed as a "hot melt". For this purpose, the constituents of the backing layer (c) are mixed intensively in the liquefied state by introducing the agent without addition of a solvent, or dissolved in a suitable organic solvent, optionally together with a substance which promotes permeation through the skin and optionally further additives. The components are preferably mixed at a temperature in the range of 80°C-190°C, preferably in the range of 140°C-180°C in particular in the range of 160°C-180°C, until the desired dispersion of the agent has formed in the matrix. The mixture is then permitted to cool to the laminating temperature, i.e. to a temperature in the range of 120°C-140°C, preferably in the range of 80°C-120°C and in particular to approximately 100°C, wherein the dispersion is applied to and laminated on the desired substrate at this temperature in the form of a "hot melt," and is processed to form the backing layer (c). At the lamination temperature, the dispersion is preferably free of solvents or is subsequently, before or after the lamination, freed from any organic solvent that may be present. Polysiloxanes that can be applied without any solvents and polysiloxanes that are preferably applied from a solvent, with the solvent subsequently being removed, are known *per se*.

The top layer (a) consists of an elastic textile fabric, which is coated with a polymer material. A textile fabric made e.g. of cotton and coated with polyethylene terephthalate (PET), for example, can be used as the textile material. Said textile fabric can also consist e.g. of PET, PVC, PUR and further polymeric plastics or can be manufactured in a non-woven form. Materials of this type are known *per se* and commercially available.
The adhesive layer (b) consists of an organic polymer with good adhesive properties that is known *per se* and is preferably soluble in an organic solvent. Suitable adhesive materials include polymers of isoprene or copolymers of isoprene with a styrene such as styrene-isoprene-styrene (SIS); poly (alkyl acrylates) produced e.g. from amyl, butyl, hexyl, heptyl, octyl, nonyl, 2-ethyl

hexyl or 2- methoxyethyl acrylate or copolymers of this type of alkyl acrylates with acrylic acid, methacrylic acid, methyl or ethyl acrylate, hydroxyethyl acrylate or hydroxypropyl acrylate. Styrene-butadiene-styrene copolymers (SBS) or polyisobutylene and copolymers thereof are also suitable.

Especially preferred for the preparation of the adhesive layer (b) are copolymers produced from 2-ethylhexyl acrylate and methyl acrylate, such as from approximately 19.9% by weight 2-ethylhexyl acrylate and approximately 79.3% by weight methyl acrylate, with an average molecular weight in the range from 350,000 to 550,000 daltons, preferably approximately 400,000 to 500,000 daltons, and polymerized e.g. in the presence of azobisisobutyronitrile.

The aforementioned acrylate polymers are preferably also used in combination with SBS polymers, wherein the ratio can be optimized by a person skilled in the art. For instance, the weight ratio of the acrylate polymers to SBS can lie in the range from 2:1 to 1:2, preferably in the range from 5:3 to 3:5.

Preferably for the preparation of the adhesive layer (b) are also styrene-butadiene-styrene block copolymers (SBS), styrene-butadiene block copolymers (SB) and mixtures of these copolymers with a glass transition temperature (T_G) preferably less than -22°C [T_g<(-22°C)]. These polymers can contain additives such as the glycerol ester of hydrogenated rosin or polyterpenes. A preferred composition contains e.g. 17.0% by weight SB, 11.3% by weight SBS, 70.8% by weight glycerol ester of rosin and 0.9% by weight of an antioxidant. Examples of preferred solvents for these adhesive materials include saturated and aromatic hydrocarbons such as hexane, heptane, octane, benzene or toluene.

To produce the adhesive layer (b), the polymers and/or copolymers are preferably dissolved in a suitable solvent. If the adhesive layer (b) contains the agent, then the agent is preferably dissolved in advance in the desired amount in a suitable solvent and then mixed in the dissolved form with the polymer and/or copolymer of the adhesive layer (b). The solvent of the adhesive layer (b) is applied to the top layer (a) and the solvent is removed. Suitable solvents include ethyl acetate, propyl acetate, saturated and aromatic hydrocarbons, such as hexane, heptane, octane benzene and toluene.

Numerous polymers that are suitable for the production of the adhesive layer (b) can also be applied in liquefied form, without the addition of a solvent, as a “hot melt”.

Polymers and copolymers such as this, which can be used to produce the adhesive layer (b), are known *per se* and are commercially available. For instance, coated fabrics can be obtained as Scotchpak® from the 3M Company. The top layer is coated with approximately 40 g/m^2 SBS (as an adhesive layer), for example. Scotchpak is used e.g. as a protective layer (e.g. Scotchpak 1022 by the 3M company). Whether the adhesive layer (b) is applied to the top layer (a) from a solvent or without a solvent is not essential, according to the invention. Preferably, the claimed patch does not contain an adhesive layer (b).
According to the invention, the backing layer (c) consists of a self-adhesive polysiloxane. Self-adhesive polysiloxanes are known *per se* and are produced and sold commercially in various compositions e.g. by the Dow Corning company under the trade name BIO-PSA® Amine-Compatible Silicone Adhesives. Silicone polymers such as these can be utilized in the manner according to the invention. To optimize their adhesive properties, these silicone polymers can further contain additives that are known *per se* for modifying adhesive properties, such as rosin compounds, e.g. dehydrated or hydrogenated rosin, glycerol ester of rosin, terpene resins, polyterpene resins, of alpha- or beta-pinene or a mixture of these compounds, or low-viscosity silicones or polysiloxanes having terminal silanol groups, or polydimethylsolixoanes such as dimethiconol.
Self-adhesive polysiloxanes, which are suitable for the production of the backing layer (c) without the addition of a solvent as a “hot melt,” are commercially available, e.g. as BIO-PSA® 7-4560 Silicone Adhesive by the Dow Corning company. Siloxane compounds of this type are known e.g. under CAS number 68440-70-0 and CAS number 63148-62-9, and the mixtures of these compounds, e.g. compounds of CAS number 68440-70-0 in a concentration of at least 60% by weight with compounds of CAS number 63148-62-9 in a concentration of 10.0 to 30.0% by weight

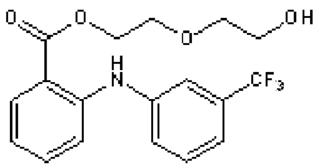
Self-adhesive polysiloxanes, which are suitable for the production of the backing layer (c) with the addition of a solvent, are commercially available, e.g. as BIO-PSA® 7-4603 or BIO-PSA® 7-4201 by the Dow Corning company. A person skilled in the art can readily select suitable polysiloxanes for the production of the backing layer (c).
Suitable self-adhesive polysiloxanes are obtained, for example, by condensing a dimethylpolysiloxane that contains silanol groups with a silicate resin that is soluble in organic solvents and then reacting the remaining silanol groups with a reactive trimethylsilyl compound. This type of polysiloxane is soluble in organic solvents, such as in ethyl acetate, propyl acetate, saturated and aromatic hydrocarbons, such as hexane, heptane, octane benzene and toluene.

A preferred embodiment consists in that the self-adhesive polysiloxane of the backing layer (c) contains a compound or a mixture of compounds which reduce the viscosity of the self-adhesive polysiloxane that contains the agent, without thereby negatively influencing the other properties of the self-adhesive polysiloxane. Such compounds are preferably glycerol and/or ester compounds of a medium-chain fatty acid with a monovalent or multivalent alcohol. Preferred ester compounds of a medium-chain fatty acid with a monovalent alcohol are e.g. ester of propyl alcohol, isopropyl alcohol, butyl alcohol or isopropyl alcohol with a (C_{10}-C_{16}) fatty acid, preferably with medium-chain (C_{12}-C_{16}) fatty acids, preferably with lauric acid, myristic acid or palmitic acid, such as isopropyl myristate. Examples of ester compounds of medium-chain fatty acids with multivalent alcohols are mono-, di- or triesters of glycerol with medium-chain (C_{10}-C_{16}) fatty acids, preferably mono-, di- or triesters of glycerol with medium-chain (C_{12}-C_{16}) fatty acids as well as natural oils, preferably olive oil or castor oil.

Liquid paraffin, polysorbates (i.e. polyoxyethylene sorbitan fatty acid compounds), such as Tween®60 (polyoxyethylene sorbitan monostearate) or Tween®80 (polyoxyethylene sorbitan monooleate), polyethylene glycols, such as polyethylene glycol 400, propylene glycol and polypropylene glycols, esters of multivalent acids with alcohols, such as triethyl citrate, and mixtures of these compounds can also be used as compounds that similarly reduce the viscosity of the self-adhesive polysiloxane containing the agent. The self-adhesive polysiloxanes used in the invention preferably contain approximately 2-15% by weight, preferably ca. 5-10% by weight, of these compounds based on the total weight of the backing layer (c). The stated compounds can occasionally also function as permeation accelerators.

The backing layer (c) that contains the agent and the adhesive layer (b), which can optionally also contain the agent, optionally contain the agent together with a substance that promotes permeation through the skin. The presence of a substance that promotes permeation through the skin is not critical, though. The agent can additionally be mixed with further agents and can also contain e.g. stabilizers and perfumes.

Preferred is etofenamate, which corresponds to the chemical formula



i.e. 2-(2-hydroxyethoxy)-ethyl-(a,a,a-trifluoro-m-tolyl)- anthranilate (etofenamate).

The backing layer (c) contains the agent, preferably etofenamate, preferably in a concentration in the range from approximately 1.0% by weight to approximately 25.0% by weight, preferably 2.0% by weight to 20% by weight, and preferably 2.5% by weight to 15% by weight, preferably in a concentration of approximately 5% by weight to approximately 10% by weight, based on the total weight of the backing layer.

A method for producing the dispersion that can be used as a carrier layer (c), containing at least one self-adhesive polysiloxane as well as the agent, preferably etofenamate, optionally together with a substance that fosters permeation through the skin and optionally further additives, is characterized in that the self-adhesive polysiloxane that forms the backing layer (c) is heated together with the agent, optionally together with a substance that fosters permeation through the skin and optionally further additives, to a temperature in the range of 80°C-200°C, preferably in the range of 140°C-190°C and especially in the range of 160°C- 190°C, and stirred vigorously until the desired dispersion has formed. This dispersion can be further processed without solvents in the temperature range indicated, but preferably in the range of 120°C-140°C, preferably in the range of 80°C-120°C and especially at approximately 100°C, and can be applied to the provided substrate as a thin layer in the desired amount.

A further method for producing the dispersion that can be used as the backing layer (c), containing at least one self-adhesive polysiloxane and the agent, preferably etofenamate, optionally with a substance that promotes permeation through the skin and optionally further additives, is characterized in that the self-adhesive polysiloxane that forms the carrier layer (c) is heated together with the agent and optionally further additives in the presence of a solvent at an elevated temperature, preferably in the range of 40°C-90°C, preferably in the range of the boiling point of the solvent, and stirred vigorously until the desired dispersion has formed.

Preferably, enough solvent is employed that the dispersion thus obtained can be processed into a patch at room temperature, i.e. the obtained dispersion can be applied to the provided substrate as a thin layer in the desired amount at room temperature.
Alternatively, the solvent can be largely or completely removed from the dispersion that has been formed [in order to create the backing layer (c)] and the dispersion formed in this manner can be further processed at an elevated temperature largely or completely without a solvent and can be applied as a thin layer in the desired amount to the provided substrate.
Solvents utilized for this purpose are preferably an organic solvent, such as e.g. ethyl acetate, propyl acetate and saturated and/or aromatic hydrocarbons, such

as hexane, heptane, octane, benzene or toluene. The solvent is preferably evaporated at a temperature in the range of 50°C to 90°C, depending on the boiling point of the solvent, preferably at a temperature of approximately 60°C to 70°C, during a period of approximately 30 minutes to 60 minutes, either from the dispersion obtained or from the layer applied in the patch.

The backing layer (c) contains the agent in a highly dispersed distribution with an average droplet size in the range from 0.1 gm to 500 gm, preferably from 1.0 gm to 100 gm. The surface of the adhesive layer (b) and the backing layer (c) are both covered in the range from 30 g/m^2 to 300 g/m^2, preferably in the range from approximately 40 g/m^2 to 200 g/m^2 and especially in the range from approximately 40 g/m^2 to 100 g/m^2.

The adhesive force of the adhesive layer (b) is preferably in the range from 0.8 N/25 mm to 2.0 N/25 mm, preferably in the range from 9 N/25 mm to 1.7 N/25 mm. The adhesive force of the backing layer (c) is preferably in the range from 0.8 N/25 mm to 1.4 N/25 mm.

Compounds that promote permeation through the skin (permeation enhancers) are additives that foster the administration of the agent through the skin and the penetration of the stratum corneum. Such compounds are known *per se*, even for use in patches of this type. Naturally occurring substances are preferred, like natural oils and fats or fatty acids and higher fatty alcohols and esters thereof as well as glycerol and mixtures of these compounds. The weight ratio of agent: permeation enhancers preferably lies in the range of 98 : 2 to 2 : 8, preferably in the range from 9 : 1 to 3 : 7, preferably approximately 1 : 2.

Natural oils and fats are especially mono-, di- and triglycerides, which represent glyceride esters with saturated and/or unsaturated fatty acids, e.g. esters of fatty acids with preferably 4 to 22 carbon atoms. Fatty acids of this type are preferably butyric, caproic, capric, myristic, palmitic, stearic, arachidic, palmitoleic, oleic (oil) acid, ricinoleic, linoleic, linolenic and arachidonic acid. This type of fatty acids with preferably 4 to 22 carbon atoms can also be employed by themselves as accelerators.

Alcohols are understood to be the corresponding alcohols and fatty alcohols with 4 to 22 carbon atoms, preferably n-, iso-, sec-butyl alcohol; n-, iso-, tert.-

amyl alcohol; n-hexyl alcohol, cyclohexyl alcohol; octyl alcohol, capryl alcohol (octanol-2), n-decyl alcohol, lauryl alcohol, myristyl alcohol, cetyl alcohol and stearyl alcohol.

Also suitable are synthetic fatty acid esters of the aforementioned fatty acids with lower or higher alcohols, such as ethyl stearate, cetyl palmitate, isopropyl myristate, isopropyl palmitate or mixtures of these kinds of compounds. Isopropyl myristate is preferred.

Natural oils also include castor oil, olive oil, peanut oil, corn oil, hazelnut oil, jojoba oil and wheat germ oil.

The peelable protective layer (d) consists of an inert material that -adheres to the backing layer (c) and can easily be peeled off of it. Materials of this type are known in the form of thin films and are commercially available, for example, from 3M under the brand name Scotchpak®. The following examples illustrate the invention without restricting it.

Example 1

5.0 parts pure ethyl acetate are added to 5.0 parts pure etofenamate in a round-bottom glass flask and mixed intensively on a magnetic stirrer plate. 85 parts of a self-adhesive polysiloxane dissolved in ethyl acetate (respectively, BIO-PSA® 7-4603, and BIO-PSA® 7-4560 by the Dow Corning company) are then admixed and stirred intensively for 2.5 hours at room temperature. Optionally, 10 parts isopropyl myristate (IPM) are added to the mixture. From the mixture obtained in this way, a coating apparatus is used to create a laminate that has a basis weight of 100 g/m^2, 75 g/m^2 and 40 g/m^2 [= backing layer (c) on a peelable layer (d)] and which is dried in the drying cabinet at a temperature of 60°C for 60 minutes until all of the solvent is removed. After drying, the laminate that is obtained is laminated with a top layer (a) consisting of PET fabric provided with an adhesive layer (b) (Duro-Tak® 87-6173 by the company National Starch), wherein the adhesive layer has basis weight of 40 g/m^2. The additional examples in Table 1 were produced in a similar way.

Table 1

Etofenamate	Bio PSA 7-4603	IPM	area mass
5%	95%	-	40 g/m^2
5%	95%	-	75 g/m^2
10%	90%	-	40 g/m^2
10%	90%	-	75 g/m^2
5%	85%	10%	100 g/m^2
10%	80%	10%	100 g/m^2

Example 2

5.0 parts pure etofenamate are intensively stirred with 10 parts isopropyl myristate (IPM) and 85 parts of a self-adhesive polysiloxane (BIO-PSA® 4560 by the Dow Corning company) in a Becomix brand high-speed mixer at a temperature of 190°C for 2.5 hours. The mixture or dispersion obtained in this way is allowed to cool, and a coating apparatus by the company Hofmann & Schwabe is used at a lamination temperature of 100°C to create a laminate that has a basis weight of 100 g/m^2, 75 g/m^2 and 40 g/m^2 [= backing layer (c) on the top layer (a), consisting of PET fabric] and which is cooled down to room temperature. The laminate obtained in this way is then laminated with a protective layer (d) (Scotchpack®, a removable film that is coated with a fluoropolymer, produced by the 3M Company).

Patentkrav

1. Medicinsk plaster til administration på huden af det betændelseshæmmende middel etofenamat, som er flydende ved stuetemperatur, hvilket plaster har en struktur, der består af et toplag (a), et bærelag (c), et afriveligt beskyttelseslag (d) og eventuelt et mellemliggende lag (b), kendetegnet ved, at:

- toplaget (a) består af et inert materiale;
- bærelaget (c) består af en selvklæbende polysiloxan som bæremateriale, der er opnået ved at kondensere en dimethylpolysiloxanholdig silanolgruppe med en silicatharpiks, som er opløselig i organiske opløsningsmidler, og derpå at omsætte de resterende silanolgrupper med en reaktiv trimethylsilylforbindelse; og at
- denne selvklæbende polysiloxan eventuelt indeholder additiver, som er kendte til modifikation af klæbende egenskaber, og eventuelt indeholder tilsætningsstoffer til reduktion af viskositeten af den selvklæbende polysiloxan, og i hvilken det betændelseshæmmende middel er inkorporeret i form af en dispersion, eventuelt sammen med et middel, der fremmer permeation gennem huden;
- bærelagets klæbende kraft (c) ligger i området på fra 0,8 N/25 mm til 1,4 N/25 mm;
- bærelaget (c) indeholder midlet etofenamat i en koncentration i området på fra 1,0 til 25,0 vægt-%, baseret på totalvægten af bærelaget (c);
- bærelaget (c) indeholder midlet i dispergeret form i en gennemsnitlig dråbestørrelse i området på fra 0,1 µm til 500 µm;
- bærelaget (c) klæber direkte til toplaget (a) eller eventuelt er fastgjort til dette over mellemlaget (b); og
- det afrivelige beskyttende lag (d) består af et inert materiale, der klæber til bærelaget (c) og let kan fjernes fra dette.

2. Plaster ifølge krav 1, som har en struktur, der består af toplaget (a), bærelaget (c) og det afrivelige beskyttelseslag (d), kendetegnet ved at:

- toplaget (a) består af et inert materiale;

- bærelaget (c) består af en selvklæbende polysiloxan, hvori det betændelseshæmmende middel er inkorporeret i form af en dispersion, eventuelt sammen med et middel, som fremmer permeation gennem huden, og eventuelt med yderligere additiver, og hvilket bærelag (c) klæber direkte til toplaget (a); og
- det afrivelige beskyttende lag (d) består af et inert materiale, der klæber til bærelaget (c) og let kan fjernes fra dette.

3. Plaster ifølge krav 1, kendetegnet ved, at et mellemlag (b) er til stede mellem toplaget (a) og bærelaget (c), hvilket klæbemiddellag (b) enten ikke indeholder noget af midlet eller er fyldt med en anden mængde af midlet, og klæbemiddellagets klæbekraft (b) er stærkere end bærelagets (c) klæbende kraft, hvor klæbemidlets (c) klæbemiddelkraft kun er stærk nok til, at plastret kan fjernes let og fuldstændigt fra huden.

4. Plasteret ifølge krav 3, kendetegnet ved, at klæbemiddellaget (b) er fyldt med middel, og der er mindst lige så meget af midlet i klæbelaget (b) som i bærelaget (c), hvor klæbemiddellaget (b) fortrinsvis er fyldt til mætningspunktet med midlet.

5. Plaster ifølge krav 1-4, kendetegnet ved, at toplaget (a) består af et elastisk tekstilstof, som er belagt med et polymermateriale.

6. Plaster ifølge krav 1 eller krav 3-5, kendetegnet ved, at klæbemiddellaget (b) består af en organisk polymer, som er kendt som sådan, og som fortrinsvis er opløselig i et organisk opløsningsmiddel og har gode klæbende egenskaber, og som fortrinsvis er udvalgt fra gruppen, der indeholder følgende: 2-ethylhexylacrylat, methylacrylat, SBS-polymerer, styren-butadien-styren-blokcopolymerer (SBS), styren-butadien-blokcopolymerer (SB) og blandinger af disse copolymerer med en glasovergangstemperatur (Tg), der fortrinsvis er lavere end -22 °C [TG<(-22 °C)], og hvilke polymerer eventuelt indeholder additiver, fortrinsvis glycerolesteren af hydrogeneret kolofonium eller

polyterpener.

7. Plasteret ifølge krav 6, kendetegnet ved, at klæbemiddellaget (b) består primært af 2-ethylhexylacrylat og methylacrylat, fortrinsvis ca. 19,9 vægt-% 2-ethylhexylacrylat og ca. 79,3 vægt-% methylacrylat, med en gennemsnitlig molekylvægt i området på fra 350.000 til 550.000 dalton, fortrinsvis ca. 400.000 til 500.000 dalton.

8. Plasteret ifølge krav 6, kendetegnet ved, at klæbemiddellaget (b) består af 17,0 vægt-% SB, 11,3 vægt-% SBS, 70,8 vægt-% kolofonium-glycerolester og 0,9 vægt-% antioxidant.

9. Plaster ifølge et af kravene 1-8, kendetegnet ved, at bærelaget (c) består af en selvklæbende polysiloxan, der er valgt fra selvklæbende polysiloxaner, som er registreret som Dow Corning® BIO-PSA® 7-4201, Dow Corning® BIO-PSA 7-4560 og Dow Corning® BIO- PSA 7-4603.

10. Plaster ifølge et af kravene 1-9, kendetegnet ved, at additiverne til modifikation af de klæbende egenskaber er valgt blandt kolofoniumforbindelser, fortrinsvis dehydrogeneret eller hydrogeneret kolofonium, kolofonium-glycerolester, terpenharpikser, polyterpenharpikser, alfa- eller beta-pinen eller en blanding af disse forbindelser eller af lavviskositetssilikoner eller polysiloxaner, der har terminale silanolgrupper.

11. Plasteret ifølge krav 10, kendetegnet ved, at bærelaget (c) består af en selvklæbende polysiloxan, der kan anvendes uden tilsætning af et opløsningsmiddel og som kan påføres underlaget under produktionen af plasteret.

12. Plaster ifølge et af kravene 1-11, kendetegnet ved, at den selvklæbende polysiloxan af bærelaget (c) indeholder mindst en forbindelse til reduktion af viskositeten af den selvklæbende polysiloxan, hvilken forbindelse er valgt fra gruppen, der indeholder glycerol og/eller en esterforbindelse af en middelkædet

fedtsyre med en monovalent alkohol, fortrinsvis en ester af propylalkohol, isopropylalkohol, butylalkohol eller isopropylalkohol med en (C_{10}-C_{16})-fedtsyre, fortrinsvis med en middelkædet (C_{12}-C_{16})-fedtsyre, fortrinsvis med laurinsyre, myristinsyre eller palmitinsyre, fortrinsvis isopropylmyristat, hvor fortrinsvis ca. 2-15 vægt-%, fortrinsvis ca. 5-10 vægt-% af disse forbindelser er til stede, baseret på den samlede vægt af bærelaget (c).

13. Plaster ifølge et af kravene 1-11, kendetegnet ved, at den selvklæbende polysiloxan af bærelaget (c) indeholder mindst en forbindelse til reduktion af viskositeten af det selvklæbende polysiloxan, hvilken forbindelse er valgt fra gruppen, der indeholder esterforbindelser af en middelkædet fedtsyre med en multivalent alkohol, fortrinsvis mono-, di- eller triestere af glycerol med middelkædet (C_{10}-C_{16})-fedtsyrer, fortrinsvis mono-, di- eller triestere af glycerol med middelkædet (C_{12}-C_{16})-Fedtsyrer og/eller naturlige olier, fortrinsvis olivenolie eller ricinusolie, hvor fortrinsvis ca. 2-15 vægt-%, fortrinsvis ca. 5-10 vægt-% af forbindelserne er til stede, baseret på den samlede vægt af bærelaget (c).

14. Plaster ifølge et af kravene 1-11, kendetegnet ved, at den selvklæbende polysiloxan af bærelaget (c) indeholder mindst én forbindelse til reduktion af viskositeten af det selvklæbende polysiloxan, hvilken forbindelse er valgt fra gruppen, der indeholder flydende paraffin, polyoxyethylensorbitanfedtsyreesterforbindelser, fortrinsvis polyoxyethylensorbitanmonostearat, polyoxyethylensorbitanmonooleat, polyethylenglycol, fortrinsvis polyethylenglycol 400, propylenglycol, polypropylenglycol, estere af multivalente syrer med alkoholer, fortrinsvis triethylcitrat og blandinger af forbindelserne, hvor fortrinsvis ca. 2-15 vægt-%, fortrinsvis ca. 5-10 vægt-% af forbindelserne er til stede, baseret på den samlede vægt af bærelaget (c).

15. Plaster ifølge et af kravene 1-14, kendetegnet ved, at bærelaget (c) indeholder mindst en forbindelse til at fremme permeation gennem huden og

eventuelt yderligere stabilisatorer og duftstoffer.

16. Plasteret ifølge krav 15, kendetegnet ved, at forbindelsen, der fremmer gennemtrængning gennem huden (permeationsforstærkeren) er valgt blandt naturligt forekommende stoffer, fortrinsvis fra naturlige olier og fedtstoffer eller fra fedtsyrer og højere fedtalkoholer og estere deraf såvel som fra glycerol og blandinger af de nævnte forbindelser, hvor vægtforholdet mellem middel og permeationsforstærker er fortrinsvis i området på fra 98 : 2 til 2 : 8, fortrinsvis i området på fra 9 : 1 til 3 : 7, fortrinsvis ca. 1 : 2.

17. Plaster ifølge et af kravene 1-16, kendetegnet ved, at bærelaget (c) indeholder midlet etofenamat i en koncentration i området på fra 2,0 vægt-% til 20 vægt-% og fortrinsvis 2,5 vægt-% til 15 vægt-%, fortrinsvis i en koncentration på ca. 5 vægt-% til ca. 10 vægt-%, baseret på den samlede vægt af bærelaget (c).

18. Plaster ifølge et af kravene 1-17, kendetegnet ved, at bærelaget (c) indeholder midlet i dispergeret form med en gennemsnitlig dråbestørrelse i området på fra 1,0 µm til 100 µm.

19. Plaster ifølge et af kravene 1-18, kendetegnet ved, at overtrækket af overflade til underlaget (c) ligger i området på fra 30 g/m^2 til 300 g/m^2, fortrinsvis i området på fra 40 g/m^2 til 200 g/m^2, fortrinsvis i området på fra 40 g/m^2 til 100 g/m^2.

20. Fremgangsmåde til fremstilling af en dispersion, der kan anvendes som et bærelag (c) ifølge et af kravene 1-19, kendetegnet ved, at den selvklæbende polysiloxan, som danner bærelaget (c), blandes sammen med midlet, eventuelt med et stof, der fremmer gennemtrængning gennem huden, og eventuelt yderligere additiver, ved en temperatur i området på fra 80 °C til 190 °C, fortrinsvis i området på fra 140 °C til 180 °C og især i området på fra 160 °C til 180 °C, indtil den ønskede dispersion af midlet er dannet i matrixen, og efterfølgende at lade afkøle til en temperatur i området på fra 120 °C til 140 °C,

fortrinsvis i intervallet på fra 80 °C til 120 °C og især til ca. 100 °C, og anvende dispersionen på det ønskede substrat ved denne temperatur i form af en "varm smelte" og bearbejde den til bærelaget (c), og eventuelt fjerne, før eller efter laminering, ethvert organisk opløsningsmiddel, som stadig kan være til stede.

21. Fremgangsmåde til fremstilling af dispersionen, der kan anvendes som et bærelag (c) ifølge et af kravene 1-19, kendetegnet ved, at den selvklæbende polysiloxan, der danner bærelaget (c), opvarmes sammen med midlet, eventuelt med et stof, som fremmer permeation gennem huden, og eventuelt yderligere additiver, i nærvær af tilstrækkeligt opløsningsmiddel ved en forhøjet temperatur, fortrinsvis i området på fra 40 °C til 90 °C, fortrinsvis i området af opløsningsmidlets kogepunkt, og omrøres kraftigt, indtil den ønskede dispersion er dannet, og opløsningsmidlet fjernes efterfølgende i det væsentlige eller fuldstændigt fra den dannede dispersion.

22. Fremgangsmåde til fremstilling af plaster ifølge krav 1, kendetegnet ved, at bestanddelene af klæbemiddellaget (b) anvendes på toplaget (a) enten i flydende form eller opløst i et egnet organisk opløsningsmiddel og efterfølgende fjernes det organiske opløsningsmiddel, der kan være til stede, henholdsvis tørres; dispersionen af bærelaget (c), der er fremstillet ifølge et af kravene 19 og 20, anvendes derefter på klæbemiddellaget (b) og ethvert organisk opløsningsmiddel, der kan være til stede, fjernes, og derefter tørres; og det afrivelige beskyttende lag (d) påføres på det tørrede bærelag (c).

23. Fremgangsmåde til fremstilling af plaster ifølge krav 2, kendetegnet ved, at dispersionen af bærelaget (c), der er fremstillet ifølge et af kravene 19 og 20, anvendes på toplaget (a) og derefter fjernes ethvert organisk opløsningsmiddel, der kan være til stede, henholdsvis tørres; og det afrivelige beskyttende lag (d) påføres på det tørrede lag (c).

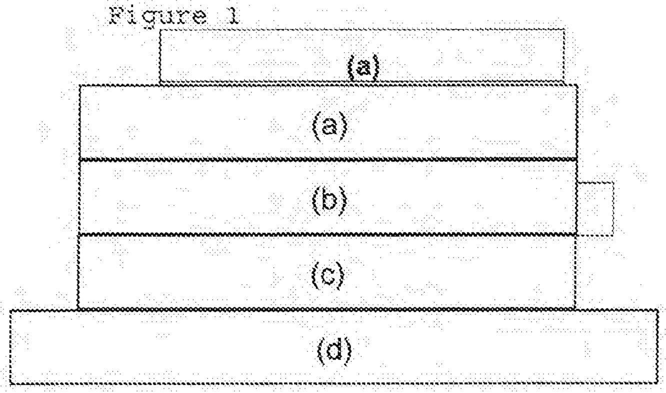
24. Fremgangsmåde til fremstilling af plaster ifølge krav 1, kendetegnet ved, at dispersionen af bærelaget (c), der er fremstillet ifølge et af kravene 20 og 21, anvendes på det afrivelige beskyttelseslag (d) og efterfølgende fjernes ethvert

organisk opløsningsmiddel, der kan være til stede, og derefter tørres; i et separat trin anvendes klæbemiddellagets (b) bestanddele på toplaget (a) enten i flydende form eller opløst i et egnet organisk opløsningsmiddel, og derefter fjernes ethvert organisk opløsningsmiddel, der eventuelt kan være til stede, henholdsvis tørres; og bærelaget (c) lamineres derefter med toplaget (a), som allerede indeholder klæbemiddellaget (b).

25. Fremgangsmåde til fremstilling af plaster ifølge krav 2, kendetegnet ved, at dispersionen af bærelaget (c), der er fremstillet ifølge et af kravene 20 og 21 anvendes på det afrivelige beskyttende lag (d) og efterfølgende fjernes ethvert organisk opløsningsmiddel, der eventuelt kan være til stede, henholdsvis tørres; og toplaget (a) påføres på det tørrede bærelag (c).

26. Fremgangsmåde ifølge et af kravene 22-25, kendetegnet ved, at dispersionen af bærelaget (c) anvendes uden opløsningsmiddel ved en temperatur i området på fra 120 °C til 140 °C, fortrinsvis i området på fra 80 °C til 120 °C og især ved ca. 100 °C.

Figure 1



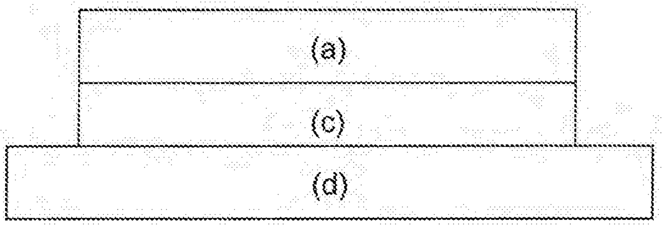
(a) = Top layer

(b) = Adhesive layer

(c) = Backing layer

(d) = Peelable protective layer

Figure 2



(a) = Top layer Adhesive layer

(c) = Backing layer

(d) = Peelable protective layer