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Method for preventing the misuse of a transdermal therapeutic system

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<p>(21) Internationales Aktenzeichen: PCT/EP98/05955 (22) Internationales Anmeldedatum: 18. September 1998 (18.09.98) (30) Prioritätsdaten: 197 43 484.3 1. Oktober 1997 (01.10.97) DE AG (71) Anmelder (für alle Bestimmungsstaaten ausser/US): LTS LOHMANN THERAPIE-SYSTEME GMBH [DE/DE]; Ir- licherstrasse 55, D-56567 Neuwied (DE). Lohmannsstraße 2 D-56626 Andernach (72) Erfinder; und (75) Erfinder/Anmelder (nur für US): BECHER, Frank [DE/DE]; Keltenstrasse 84, D-56072 Koblenz (DE). KLINK, Ann-Katrin [DE/DE]; Birkenweg 18, D-56323 Waldesch (DE). (74) Anwalt: FLACCUS, Rolf-Dieter, Bussardweg 10, D-50389 Wesseling (DE).</p>		<p>(81) Bestimmungsstaaten: AU, CA, CZ, HU, ID, IL, JP, KR, MX, NO, NZ, PL, SG, SI, SK, TR, US, europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Veröffentlicht <i>Mit internationalem Recherchenbericht. Vor Ablauf der für Änderungen der Ansprüche zugelassenen Frist; Veröffentlichung wird wiederholt falls Änderungen eintreffen.</i></p> 
<p>(54) Title: METHOD FOR PREVENTING THE MISUSE OF A TRANSDERMAL THERAPEUTIC SYSTEM (54) Bezeichnung: VERFAHREN ZUR VERMEIDUNG DES MISSBRAUCHS EINES TRANSDERMALEN THERAPEUTISCHEN SYSTEMS (57) Abstract According to the invention, denaturing agents are added to a transdermal therapeutic system to prevent misuse in the form of unauthorised oral application. (57) Zusammenfassung Zur Verhinderung einer unzulässigen oralen Applikation werden einem transdermalen therapeutischen System Vergällungsstoffe zugesetzt.</p>		

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Process for the protection of a person against
contamination as a result of improper, i.e. oral,
application of toxic components of a transdermal
therapeutic system, as well as transdermal therapeutic
systems containing a denaturant

The invention relates to a process for the protection of a person against contamination as a result of improper, i.e. oral, application of toxic components of a transdermal therapeutic system (TTS), comprising at least one active substance-containing, especially pressure-sensitive adhesive layer and at least one further, active substance-impermeable backing layer, as well as a TTS containing a denaturant.

A series of TTS present an acute danger of undesired side effects if administered orally by a person in order to extract a soluble active agent - either from a new system or a used one. Infants, for example, have a tendency to stick anything interesting into their mouth and to at least suck or chew on it. This cannot be avoided especially if children happen to attain access to such systems by chance, especially systems without a release liner.

Such incidents have not yet been known to occur, but the pharmaceutical authorities increasingly fear that they might and have therefore, in various instances, demanded childproof packages. Such childproof packages have, in fact, been developed in various embodiments. However, they do not protect a child from putting a TTS in its mouth once the package has been opened or if the child somehow gets hold of a used patch. Especially in the case of TTS with active substances such as anesthetics, analgesics, tranquilizers or psychopharmacological agents, an oral use can lead to serious health impairments. On the other



hand, addicts could be tempted to extract such active agents from transdermal therapeutic systems by means of sucking or chewing.

It is known that drinkable ethyl alcohol can be denatured and then put on the market as methylated spirit. A denaturing of pharmaceutical active agents, on the other hand, has not yet been published.

There is a need in the art to develop a process for the protection of a person against contamination as a result of improper, i.e., oral application of toxic components of a TTS in a way that makes an oral abuse of the kind mentioned above impossible, at the same time, however, avoiding a disadvantageous change in the system's therapeutic active agent and also ruling out an impairment of health in the case of improper, i.e. oral, application.

The process according to the invention proposes the addition of a denaturant which, as used herein, is a therapeutically neutral, non-interacting substance which has a disgusting taste. Because this substance causes extremely unpleasant and unexpected experiences with respect to taste, a first oral contact with the TTS according to the invention or with one of its denatured layers is sufficient for achieving a spontaneous reaction with the effect of immediately spitting out the corresponding patch and thus for preventing children or drug addicts from an improper, i.e. oral, application of the active substance contained in the patch.

Thus, in accordance with the present invention there is provided transdermal therapeutic system (TTS), comprising



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at least one active substance-containing adhesive layer, and
at least one further, active substance-impermeable backing
layer, characterized in that the active substance-containing
adhesive layer is denatured with a denaturant which has a
5 disgusting taste.

In accordance with another aspect of the present invention
there is provided process for the protection of a person
against contamination as a result of improper oral
10 application of a TTS comprising toxic components, which
comprises denaturing at least the active substance-
containing adhesive layer of said TTS with a denaturant,
said TTS comprising at least one active substance-containing
adhesive layer and at least one further active substance-
15 impermeable backing layer.

One embodiment provides that a substance is used for the
denaturation of a TTS which causes nausea and thus spoils
the temptation of oral application for the person concerned.

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with a disgusting taste for the denaturation of at least one layer of a TSS.

For the implementation of one embodiment of the process, the invention provides for the incorporation of the substances used for denaturation in a film layer with which the active substance-containing layer and, depending on the case, also the backing layer are coated. An especially advantageous solution provides for the use of a film layer soluble in saliva.

The process is uncomplicated and effective and protects children and/or addicts against improper, i.e. oral, application of toxic components of a transdermal therapeutic system. Thus, the process and the TTS according to the invention present an ideal means of achieving the object as mentioned above.

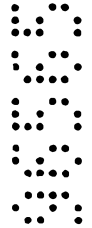
Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or group of integers or steps but not the exclusion of any other integer or group of integers or steps.

The reference to any prior art in this specification is not, and should not be taken as, an acknowledgement or any form of suggestion that the prior art forms part of the common general knowledge in Australia.



The claims defining the invention are as follows:

1. Transdermal therapeutic system (TTS), comprising at least one active substance-containing adhesive layer, and at least one further active substance-impermeable backing layer, characterized in that the active substance-containing adhesive layer is denatured with a denaturant which has a disgusting taste.
2. TTS according to claim 1, characterized in that the denaturant is also incorporated in a film layer with which the active substance-containing adhesive layer and, optionally the backing layer are coated.
3. TTS according to claim 2, characterized in that the film layer is soluble in saliva.
4. TTS according to anyone of claims 1 to 3, characterized in that said denaturant causes nausea.
5. TTS according to claim 1, characterized in that said denaturant is applied on top of the active substance-containing adhesive layer in a separate, extremely thin layer which does not prevent the permeation of the active substance.
6. TTS according to claim 5, characterized in that said denaturant is applied to the backing layer in the form of an additional separate, extremely thin layer.
7. TTS according to claim 5 or claim 6, characterized in that the separate substance layer is applied in a



thickness of between 10 and 100 μm and preferably between 5 and 20 μm .

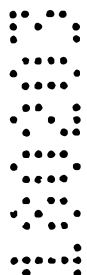
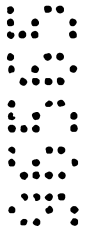
5 8. TTS according to anyone of claims 1 to 7, characterized in that the substance which causes a disgusting taste is a substance which causes an irritation such as burning of the oral mucosa and the tongue.

10 9. TTS according to anyone of claims 1 to 8, characterized in that the substance which causes a disgusting taste is a substance which causes an intensely bitter taste and especially aftertaste.

15 10. TTS according to anyone of claims 1 to 9, characterized in that the denaturant comprises gallic acid, quinine, tannin, angoustura, (pure) caffeine, lobeline, tea tree oil, hyphomycete cultures, denatured or coagulated substances, turpentine or ammonia as amaroids or substances with a disgusting taste.

20 11. Process for the protection of a person against contamination as a result of improper oral application of a TTS comprising toxic components, which comprises denaturing at least the active substance-containing adhesive layer of said TTS with a denaturant, said TTS comprising at least one active substance-containing adhesive layer and at least one further active substance-impermeable backing layer.

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12. A TTS or processes comprising same, substantially as
hereinbefore described.

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