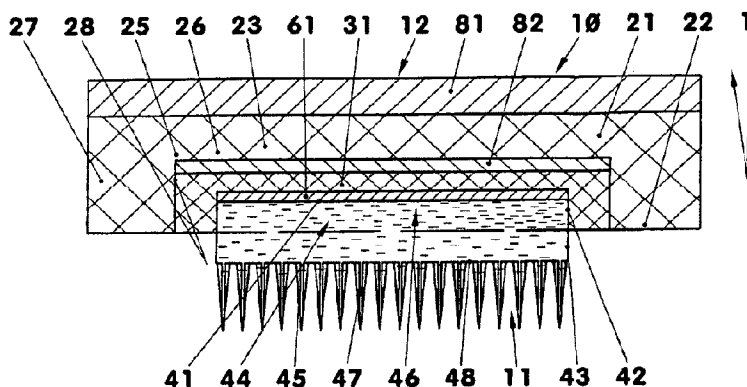




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(54) Title: TRANSDERMAL THERAPEUTIC SYSTEM WITH PRESSURE GENERATING DEVICE



(57) **Abrégé/Abstract:**

The invention relates to a transdermal therapeutic system with a system support, at least one advancing element which is embedded into the system support, and at least one active ingredient reservoir which can be elastically deformed at least in some regions and which is embedded into the advancing element. On the application side of the transdermal therapeutic system, the system support surrounds the advancing element, and the advancing element surrounds the active ingredient reservoir. The advancing element comprises a swelling body which can be expanded by means of a liquid intake. The system support is designed to be rigid at least in some regions. By means of the invention, a transdermal therapeutic system is developed which enhances the effect of the advancing element.

Abstract

The invention relates to a transdermal therapeutic system with a system support, at least one advancing element which is embedded into the system support, and at least one active ingredient reservoir which can be elastically deformed at least in some regions and which is embedded into the advancing element. On the application side of the transdermal therapeutic system, the system support surrounds the advancing element, and the advancing element surrounds the active ingredient reservoir. The advancing element comprises a swelling body which can be expanded by means of a liquid intake. The system support is designed to be rigid at least in some regions. By means of the invention, a transdermal therapeutic system is developed which enhances the effect of the advancing element.

LTS Lohmann Therapie-Systeme AG

Transdermal therapeutic system with pressure generating device**5 Description:**

The invention relates to a transdermal therapeutic system with a system support, at least one advancing element which is embedded into the system support, and at least one active substance
10 reservoir which is elastically deformable at least in some regions and which is embedded into the advancing element, wherein the system support has a bearing surface on the application side of the transdermal therapeutic system that can be made to face the skin of the patient, wherein the system support is
15 constructed as a concave body which bounds an interior space of the system support on five sides, wherein the advancing element that can be brought into contact with the skin of the patient is arranged in the interior space, wherein the active substance reservoir protrudes out of the advancing element beyond the
20 bearing surface and wherein the advancing element comprises a swelling body which can be expanded by means of liquid uptake.

A system of this kind is known from the post-published EP 12 158 740.6.

25

US 5,848,991 A and US 6,611,707 81 disclose reusable devices with a housing, wherein the housing encloses on all sides an active substance reservoir, a water reservoir and a salt-containing swelling body. The three containers are arranged one on top of
30 the other. The swelling takes place on the basis of osmosis of the water through a semipermeable wall into the swelling body.

The problem addressed by the present invention is that of enhancing the effect of the advancing element.

This problem is solved by the features the system support is designed to be deformation-resistant at least in some regions.

Some embodiments disclosed herein provide a transdermal therapeutic system having a system support, having at least one
5 advancing element which is embedded in the system support and having at least one active substance reservoir which is elastically deformable in at least some regions and which is embedded in the at least one advancing element, wherein the system support comprises a bearing surface on an application side
10 of the transdermal therapeutic system which is faceable towards the skin, wherein the system support is configured as a concave body which delimits an interior of the system support on five sides, wherein the at least one advancing element which can come into contact with the skin of the patient is disposed in the
15 interior, wherein the at least one active substance reservoir protrudes out of the at least one advancing element from the bearing surface and wherein the at least one advancing element comprises a swelling body which is expandable by liquid uptake, wherein the system support is configured so as to be resistant to
20 deformation at least in some regions.

Further details of the invention will become clear from the following descriptions of schematically depicted illustrative
25 embodiments.

Figure 1 shows the transdermal therapeutic system;

Figure 2 shows the system after it has been placed onto the skin;

30 Figure 3 shows the system during delivery of the active substance into the skin;

Figure 4 shows the system with hollow needles on the advancing element;

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Figure 5 shows the system with a flexurally and torsionally rigid pressure plate;

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Figure 3 shows the system during delivery of the active substance into the skin;

Figure 4 shows the system with hollow needles on the
5 advancing element;

Figure 5 shows the system with a flexurally and torsionally rigid pressure plate;

10 Figure 6 shows the system with hollow needles penetrating the active substance reservoir;

Figure 7 shows the system as in Figure 6 with hollow needles and semipermeable membrane;
15

Figure 8 shows the system with integrated water reservoir;

Figure 9 shows the system according to Figure 8 after
20 the water reservoir has been opened.

Figures 1-3 show a transdermal therapeutic system (10). Systems (10) of this kind are used to introduce liquid or liquefiable substances into the skin (2) of a
25 patient. It has an application side (11) that can face toward the skin (2) of the patient, and a handling side (12) facing away therefrom.

The transdermal therapeutic system (10) comprises a
30 system support (21) which can be secured on the skin (2) of the patient, for example, by means of an adhesive layer (22). This adhesive layer (22) can be free of active substances. On the bearing surface (24) facing toward the skin (2), it can be applied to a
35 support part (23) of the system support (21). However, it is also conceivable to construct the entire system support (21) from the material of the adhesive layer (22).

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In the illustrative embodiment, the side of the system support (21) facing away from the skin (2) carries a covering layer (81). In a design of the system support
5 (21) made from the material of the adhesive layer (22), the covering layer (81) is glued to the system support (21).

The system support (21) is constructed as a concave
10 body. It comprises a cover part (26) and wall parts (27) adjoining the latter. In the illustrative embodiment, the wall parts (27) are twice as thick as the cover part (26). In the illustrative embodiment, the thickness of the cover part (26) is more than one
15 third of the height of the transdermal therapeutic system (10) above the bearing surface (24). The system support (21) thus has a high resistance moment against bulging of the cover part (26). In the illustrative embodiment, an additional protective layer (82) is
20 arranged on the inner face of the cover part (26). The height of the wall parts (27) in a direction perpendicular to the bearing surface (24) is greater than two thirds of the overall height of the transdermal therapeutic system (10) above the bearing
25 surface (24). The system support (21) thus has a high resistance moment against bending and also against torsion. The system support (21) is thus deformation-resistant, taking into consideration the flexibility that is required for wearing comfort.

30 The wall parts (27) and the cover part (26) form a shell (25) and delimit on five sides an interior (28) of the system support (21). The join of the wall parts (27) to the cover part (26) can be at right angles.
35 Hollow fillets can be formed in the area of this join. However, the interior (28) can also be open in a funnel shape in the direction of the application side (11). The angle enclosed by a wall part (27) and a vertical

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plane is, for example, smaller than or equal to 45 degrees.

An advancing element (31) is arranged in the interior
5 (28). In the installed state, this advancing element
(31) is flush with the bearing surface (24), or it
protrudes from the bearing surface (24) in the
direction of the skin (2). In the illustrative
embodiment, the advancing element (31) is composed of
10 an elastically and/or plastically deformable material.
The basic materials of the advancing element (31) are,
for example, crosslinked polymers that contain the
sodium salt of acrylic acid. The use of sodium
polyacrylate or crosslinked polyacryl amides is also
15 conceivable. These materials are hydrophilic. Depending
on the composition and nature of the liquid, they are
able to take up 30 times to 800 times their weight of
liquid. For example, the absorbency is determined by
the electrical potential difference of the material and
20 of the liquid to be absorbed. In the illustrative
embodiment, the liquid used is water. The latter can be
distilled or demineralized.

The volume of the advancing element (31) increases as
25 liquid is absorbed. For example, the increase in volume
is proportional to the volume of the absorbed liquid.
The advancing element (31) is therefore also designated
below as a swelling body (31).

30 An active substance reservoir (41) is embedded in the
advancing element (31). It protrudes therefrom above
the bearing surface (24). The active substance
reservoir (41) is bag-shaped and contains one or more
active substance formulations. It is produced from an
35 elastically deformable material.

Instead of a single active substance reservoir (41), it
is also possible for several active substance

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reservoirs (41) to be embedded in the advancing element (31). They can be arranged alongside one another or over one another. For example, the walls (42) of the active substance reservoir (41) are semipermeable or
5 are equipped in such a way that, for example, individual active substances are mixed together directly before being applied.

10 An intermediate layer (61) can be arranged between the advancing element (31) and the active substance reservoir (41). This intermediate layer (61) can be designed, for example, as a pressure plate (61) and/or a water-absorbing layer (61), or the active substance-containing layer (41) is, for example, separated from
15 the advancing element (31) by a film (e.g. PET).

A needle carrier (43) with a multiplicity of needles (45) is also secured on the active substance reservoir (41). The needle carrier (43) and the needles (45)
20 protrude from the bearing surface (24) on the side facing away from the system support (21). For example, the needle support (43) comprises a distributor channel (48) and connects the interior (46) of the active substance reservoir (41), filled with active substance
25 (44), to the needles (45). The active substance reservoir (41) can also be designed without a distributor channel (48). The needle carrier (43) then forms a boundary of the interior (46) of the active substance reservoir (41).

30 The individual needle (45) has a length of between 10 micrometers and one millimetre. Its external diameter is between ten micrometers and 500 micrometers. In the illustrative embodiment, all the needles (45) are
35 designed as hollow needles. The diameter of the through-bore (47) is between 3 micrometers and 80 micrometers. The needles (45) secured on the application side (11) on the needle support (43) can

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also be designed as porous needles (45) or as soluble needles (45). The needles (45) shown with a conical shape in the figures can also have a cylindrical shaft and a conical tip. The needles (45) thus connect the
5 interior (46) of the active substance reservoir (41) to the environment (1).

It is also conceivable to arrange needles (33) on the advancing element (31) (cf. Figure 4). These have, for
10 example, the same internal and external dimensions as micro-needles (45). The needles (33) can also be secured on the needle support (43) outside the distributor channel (48).

15 During use of the transdermal therapeutic system (10), the latter is placed with the needles (45) onto the skin (2) of the patient and is pressed on until the bearing surface (24) bears on the skin (2) of the patient (cf. Figure 2). The adhesive layer (22) affixes
20 the skin (2) to the transdermal therapeutic system (10). The advancing element (31) can contact the skin (2) of the patient. The needles (45) are pushed into the skin (2) of the patient. On account of their short length, they pierce substantially the outer layer of
25 skin (stratum corneum) and end outside the nerve endings of the deeper skin layers, such that the patient feels no appreciable pain during the application.

30 The advancing element (31) takes up moisture from the skin (2). The volume of the swelling body (31) increases (cf. Figure 3). If appropriate, liquid can be taken up from the area below the stratum corneum, as is shown in Figure 4. Since the system support (21)
35 prevents or at least greatly reduces the free deformation of the swelling body (31), the swelling body (31) can expand substantially only in the direction of the active substance reservoir (41). The

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elastically deformable active substance reservoir (41) is deformed and compressed. Active substance (44) is thus forced out of the interior (46) of the active substance reservoir (41) into the needle support (43) and into the needles (45). From the needles (45), the active substance (44) is conveyed into the skin (2) of the patient. As more liquid is taken up, the active substance reservoir (41) is further deformed. In this way, active substance (44) is increasingly forced into the skin (2) of the patient. During the uptake of liquid, the liquid is stored in the swelling body (31) and not released.

The delivery of active substance is ended when either the swelling body (31) is expanded to its maximum volume or when all the active substance (44) has been forced out of the active substance reservoir (41) in the direction of the skin (2).

In the embodiment in Figure 5, the system support (21) protrudes with a stamp (29) into the interior (28). This stamp has a square cross section, for example, and delimits the advancing element (31) laterally adjoining it. In this illustrative embodiment, the for example mat-shaped advancing element (31) has a central recess (32) which engages around the stamp (29). In the view in Figure 5, the pressure plate (61) is arranged above the active substance reservoir (41). The pressure plate (61) comprises a plate (62) with a reinforcing edge (63). In the illustrative embodiment, diagonal ribs (64) are also arranged on the top face of the plate (62) and intersect in the middle of the top face of the pressure plate (61). The pressure plate (61) thus has a torsionally rigid and flexurally rigid design. If appropriate, the pressure plate (61) can additionally be guided in a for example vertically arranged guide bolt.

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During use of the transdermal therapeutic system (10), in this illustrative embodiment too, liquid is taken up from the skin surface or from the skin (2) by means of the advancing element (31). The swelling body (31) expanding as a result of the uptake of liquid presses the pressure plate (61) downward in the view in Figure 5. The swelling body (31) is in this case guided on the system support (21) and on the stamp (29). The pressure plate (61) is moved at least approximately parallel and compresses the active substance reservoir (41). In the case of a pressure plate (61) guided, for example, by means of a guide pin, the guiding additionally prevents jamming. The active substance (44) is forced substantially uniformly out of the interior (46) into the needles (45) and into the skin (2).

Figure 6 shows a transdermal therapeutic system (10) with additional hollow needles (34). These hollow needles (34) are arranged parallel to the needles (45) that convey the active substance (44) into the skin (2). For example, the number of the hollow needles (34) is a fifth of the number of the needles (45) carrying the active substance. The hollow needles (34), of which the tips (39) in the illustrative embodiment have the same dimensions as the needles (45) carrying the active substance, pass through active substance reservoir (41), e.g. in sealed passages (49). The hollow needles (34) pass through the advancing element (31) and, in the view in Figure 6, bear on the protective layer (82) in the system support (21). In the area of the advancing element (31), the hollow needles (34) have passages (35) extending through their circumferential surface. In this way, the central area of the advancing element (31) is connected to the environment (1) by means of the hollow needles (34). The distance of the passage (35) from the needle tip (39) is smaller than the reciprocal value of the diameter of the cavity (37) in millimetres, multiplied by an area of 25 square

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millimetres. For example, if the cavity (37) has a diameter of 0.5 millimeter, the maximum distance is 50 millimeters.

5 During the use of the transdermal therapeutic system (10), the liquid from the skin (2) ascends through the hollow needles (34), for example by the capillary effect, and reaches the advancing element (31). The liquid entering the latter causes an additional
10 swelling of the swelling body (31) in the areas adjoining the hollow needles (34). For example, the central portion of the active substance reservoir (41) can be compressed earlier than in the embodiment according to Figures 1-3.

15 In the view in Figure 7, the hollow needle (34) passes through the system support (21). On the outside of the covering layer (81), for example, a semipermeable membrane (36) is arranged which closes the cavity (37)
20 of the hollow needle (34) on the handling side (12). This semipermeable membrane (36) allows gas and/or liquid to pass from the cavity (37) to the environment (1). However, the movement of these substances from the environment (1) into the cavity (37) is blocked.
25 Instead of the semipermeable membrane (36), a nonreturn valve, etc., can also be provided.

The function of the transdermal therapeutic system (10) shown in Figure 7 is similar to the function of the
30 system (10) shown in Figure 6. The air displaced during the ascent of the liquid from the capillary (37) can here escape through the semipermeable membrane (36) into the environment (1).

Figures 8 and 9 show a transdermal therapeutic system (10) with an integrated liquid reservoir (71), e.g. a water reservoir (71). The water reservoir (71) is arranged in the interior (28) of the system support (21) between the advancing element (31) and the system support (21). It comprises a jacket (72), which can be torn open, for example. In the views in Figures 8 and 9, a lattice (73) is arranged between the water reservoir (71) and the advancing element (31). This lattice (73) is, for example, anchored in the system support (21).

On the side facing toward the water reservoir (71), the advancing element (31) carries tearing spikes (38), which are initially spaced apart from the water reservoir (71), for example by a few tenths of a millimetre.

When the transdermal therapeutic system (10) is placed onto the skin (2), the needles (45) and the active substance reservoir (41) are moved toward the system support (21). The advancing element (31) guided in the system support (21) is moved in the direction of the water reservoir (71) by the active substance reservoir (41). In doing so, the tearing spikes (38) contact the jacket (72) of the water reservoir (71) and tear the jacket (72) of the water reservoir (71) open (cf. Figure 9). The water (75) leaving the water reservoir (71) enters the advancing element (31) and causes the latter to swell. If appropriate, the water (75) can spray into the advancing element (31). The lattice (73) here prevents an expansion of the swelling body (31) in the direction of the system support (21). The swelling body (31) compresses the active substance reservoir (41). The active substance (44) is forced out of the active substance reservoir (41) and through the needles (45) into the skin (2).

It is also conceivable to arrange tubular capillaries in the advancing element (31). Here, in addition to the conveying effect of the material of the advancing element (31), liquid can be

conveyed into the central area of the advancing element (31). It is also conceivable for liquid to be guided by means of the intermediate layer (61). If appropriate, the swelling of the swelling body (31) can thus be controlled.

5

Of course, it is also conceivable for the various embodiments mentioned to be combined with one another.

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List of reference signs:

- 1 environment
- 2 skin
- 10 transdermal therapeutic system
- 11 application side
- 12 handling side
- 21 system support
- 22 adhesive layer
- 23 support part
- 24 bearing surface
- 25 shell
- 26 cover part
- 27 wall parts
- 28 interior
- 29 stamp
- 31 advancing element, swelling body
- 32 recess
- 33 needles, hollow needle
- 34 hollow needles
- 35 passages
- 36 semipermeable membrane, nonreturn valve
- 37 cavity, capillary
- 38 tear-open spikes
- 39 needle tip
- 41 active substance reservoir
- 42 walls
- 43 needle support
- 44 active substance, active substance formulation
- 45 needles, micro-needles
- 46 interior
- 47 through-bore
- 48 distributor channel

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- 49 passages
- 61 pressure plate, intermediate layer, water-
absorbing layer
- 62 plate
- 63 reinforcing edge
- 64 diagonal ribs
- 71 liquid reservoir, water reservoir
- 72 jacket
- 73 lattice
- 75 water
- 81 covering layer
- 82 protective layer

CLAIMS:

1. A transdermal therapeutic system having a system support,
having at least one advancing element which is embedded in
5 the system support and having at least one active substance
reservoir which is elastically deformable in at least some
regions and which is embedded in the at least one advancing
element, wherein the system support comprises a bearing
surface on an application side of the transdermal
10 therapeutic system which is faceable towards the skin,
wherein the system support is configured as a concave body
which delimits an interior of the system support on five
sides, wherein the at least one advancing element which can
come into contact with the skin of the patient is disposed
15 in the interior, wherein the at least one active substance
reservoir protrudes out of the at least one advancing
element from the bearing surface and wherein the at least
one advancing element comprises a swelling body which is
expandable by liquid uptake, wherein the system support is
20 configured so as to be resistant to deformation at least in
some regions.
2. The transdermal therapeutic system as claimed in claim 1,
wherein the at least one active substance reservoir
25 comprises hollow micro-needles which connect the interior
of the at least one active substance reservoir to the
environment on the application side.
3. The transdermal therapeutic system as claimed in claim 2,
30 wherein the micro-needles are at least one of porous and
swellable in configuration.
4. The transdermal therapeutic system as claimed in claim 1,
wherein the system support comprises an adhesive layer on
35 at least the application side.

5. The transdermal therapeutic system as claimed in claim 1, wherein the at least one active substance reservoir comprises a liquid or liquefiable active substance formulation.

5

6. The transdermal therapeutic system as claimed in claim 1, wherein an intermediate layer is disposed between the swelling body and the at least one active substance reservoir.

10

7. The transdermal therapeutic system as claimed in claim 1, wherein at least one hollow needle connects the swelling body to the environment on the application side.

15

8. The transdermal therapeutic system as claimed in claim 7, wherein a semipermeable membrane closes the at least one hollow needle on a handling side facing away from the application side.

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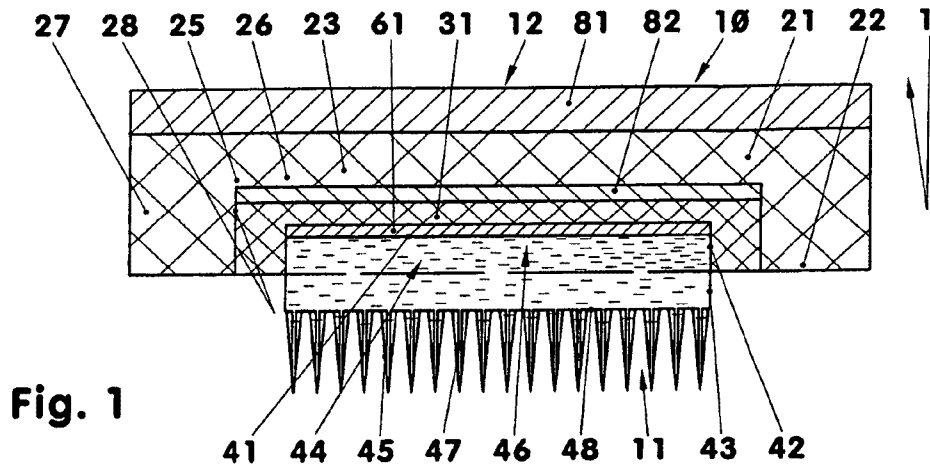


Fig. 1

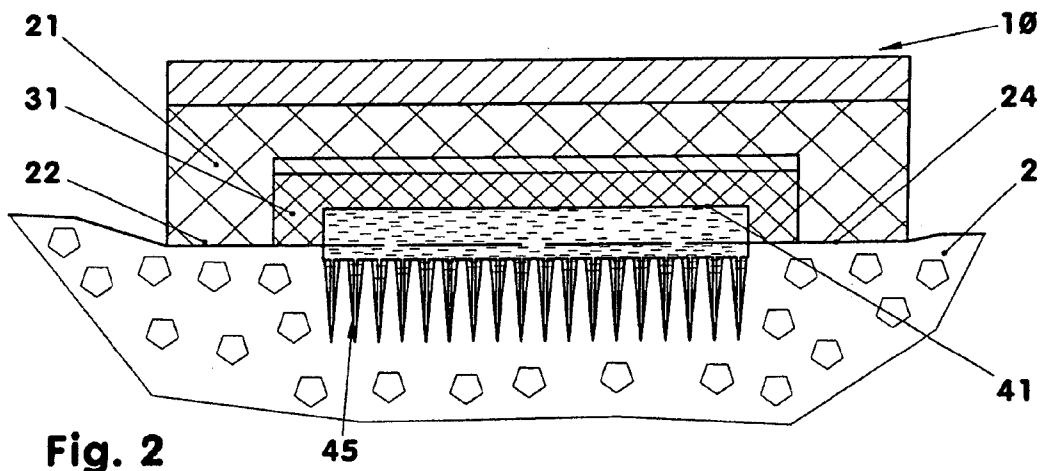


Fig. 2

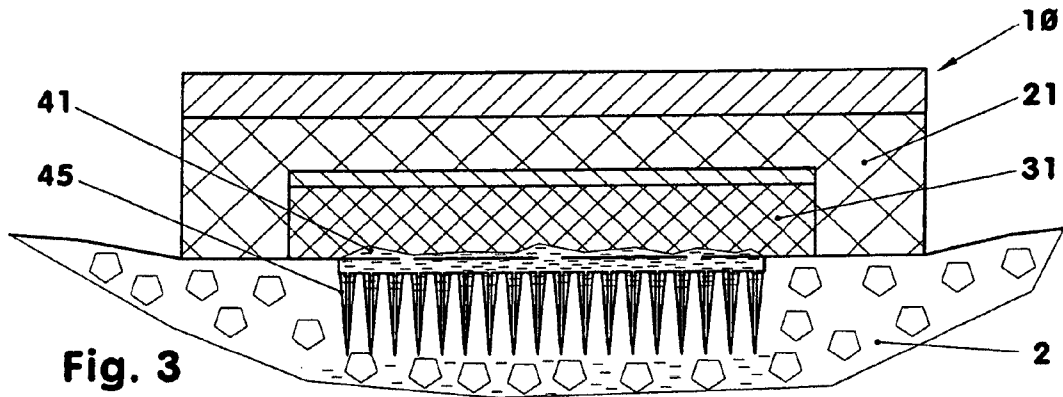


Fig. 3

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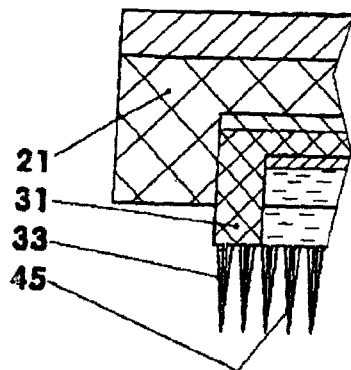


Fig. 4

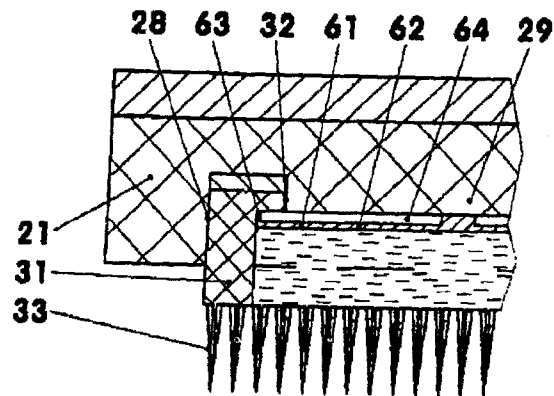


Fig. 5

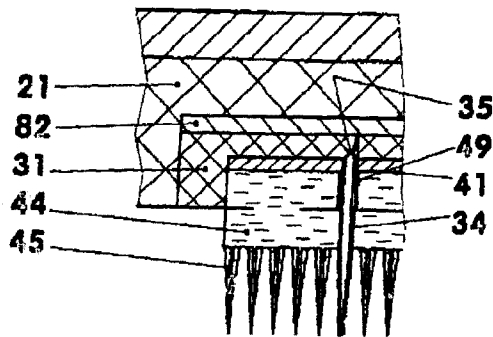


Fig. 6

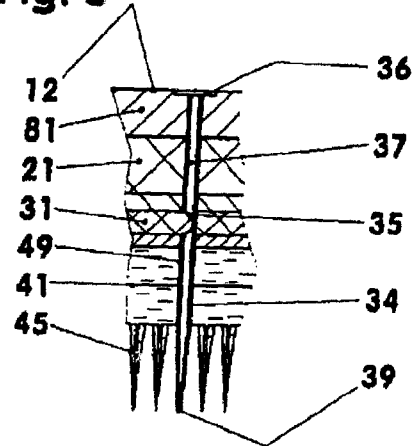


Fig. 7

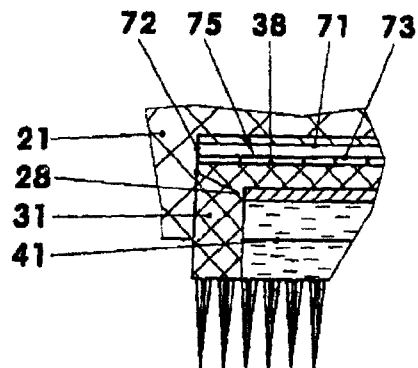


Fig. 8

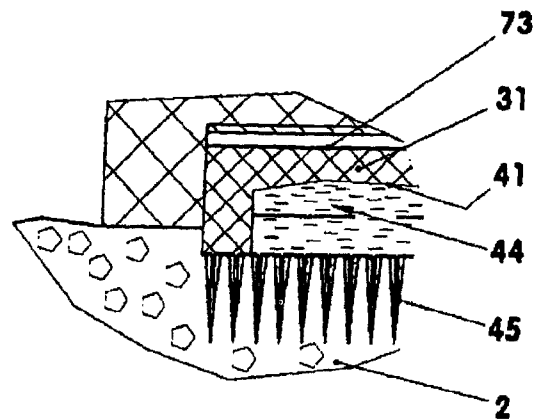


Fig. 9

