"GETTER DEVICE FOR ACTIVE SYSTEMS FOR THE TRANSDERMAL RELEASE OF DRUGS"

The present invention relates to a getter device for active systems for the transdermal release of drugs.

System for the transdermal release of drugs are used in the treatment of conditions, dysfunctions or diseases requiring a regular administration of drugs to a patient, such as post-operative aches, cardiovascular diseases or diabetes. These systems essentially consist of an envelope of polymeric material having at the inside the drug to be dispensed, generally in form of suspension in a gel. A portion of the envelope surface is made of a plastic material permeable to the drug; by causing this portion of the envelope to adhere to the patient's skin (e.g. on an arm), the drug is released onto and absorbed by the skin itself, then entering the blood stream.

The first transdermal systems, appeared at the beginning of '90s, were of the so-called passive type, wherein the drug release was determined only by the velocity of absorption by the skin. These systems have a number of drawbacks, such as the fact that it is impossible to control the drug flow (and consequently its dosing in the time unit), as well as that it is impossible to have intermittent administrations, only for prefixed durations of time and at prefixed intervals or only upon the patient's request, which on the contrary are the more appropriate administration modes in some cases.

Therefore, more recently active systems for releasing drugs have been introduced which are based on the ionophoresis, i.e. transportation of drugs in ionic form under the effect of electrical fields. An example of this kind of apparatus is schematically shown in Fig. 1: the system T is formed of an envelope P at the inside of which there is a gel, H, wherein the drug is dispersed; the system also comprises a microcomputer MC, being fed by a battery B, that controls the polarity of two electrodes E and E'; the battery is preferably of the lithium type. When the electrodes are not fed, there is no flow towards the skin of ions corresponding to the drug, whereas when the microcomputer feeds the electrodes, ions F^+, corresponding to the drug, are forced to pass through the permeable parts of the envelope towards the skin; at the second electrode there is a passage of sodium ions, Na^+, from the skin towards a container of

saline solution, in order to keep the system neutral. The figure refers to the case that the ion corresponding to the drug is positively charged, but the system operates with ions with negative charge, F^-, as well, in this case being balanced through the transportation of chlorine ions, Cl^- from the skin to the transdermal system. The microcomputer can be programmed for a timed release of the drug; the system can also comprise a push-bottom for releasing the drug upon the patient's request (not shown in the drawing).

The problem that has been observed with active transdermal systems is that the battery releases dimethoxyethane (also indicated in the following as DME), an essential component of the process of manufacturing the batteries, which is kept partly trapped at the inside thereof. This compound together with water, always present in these systems, forms corrosive solutions attacking the electrical parts, thus leading in time to the loss of functionality of the system. Other acid components can be released by the polymeric material itself forming the envelope; for example, a material commonly employed to make the envelope is Surlyn (Surlyn is a registered trademark of the company Du Pont of Wilmington, Delaware, USA), a mixture of copolymer ethylene/(meth)acrylic acid, other polymers such as polyesters or nylon and including charges of metallic salts; it has been observed that in the working conditions of transdermal systems, Surlyn releases small quantities of acetic acid which in any case contribute to the problem of corrosion of the electrical parts.

The problem of organic components being released by the batteries in general (not necessarily in field of the the present application) is known e.g. from patent application EP 1.115.168 A1; according to the teaching of this document, the problem can be solved by introducing at the inside of the battery a material for the sorption of organic compounds, such as silica, alumina, titanium oxide, or porous solid particles of polymers. The problem of this solution is that first of all the battery manufacturing is complicated; in addition, in order not to have a continuous removal of organic components of the electrolyte, such as DME or the like (necessary for the battery operation), the sorbing material in this case is coated with a layer of material impermeable to the organic compound which dissolves only in consequence of malfunctions of the battery causing its overheating. Thereby this solution is inefficient to absorb the DME quantities, however small, which are released by the battery under

normal operating conditions, i.e. when the temperature of the battery does not exceed the foreseen values; consequently a battery of the type described in the mentioned patent application would not solve the above-described problems of active systems for the transdermal release of drugs.

Object of the present invention is that of providing a solution to the above-mentioned problems.

This one and other objects are achieved according to the present invention with a getter device for active systems for the transdermal release of drugs, consisting of activated charcoals and at least a first wall, permeable to organic molecules but capable of retaining solid particles, said first wall being coupled to a second wall capable of retaining solid particles so that the assembly resulting by the connection of said first wall and said second wall is suitable to contain the activated charcoals.

The invention will be illustrated in the following with reference to the drawings wherein:

Figure 1 schematically shows an active system for the transdermal release of drugs according to the prior art;

Figure 2 shows a broken apart view of a possible getter device according to the present invention;

Figure 3 shows a system similar to that of figure 1, including the getter device of the invention of figure 2; and

Figure 4 shows a transdermal system comprising an alternative embodiment of getter device of the invention.

Figure 1 has been already described with reference to the prior art.

Figure 2 shows a first possible embodiment of the getter device according to the invention. In this embodiment the device 20 consists in an envelope 21 formed of two sheets, the first one forming the first wall 22 permeable to the organic molecules but capable of retaining particles, the second one forming the second wall, 23. The two sheets are mutually coupled at the peripheral zone 24 identified in the figure as hatched area; the activated charcoals 25 are contained within the envelope. The two sheets can be continuous polymers having a sufficient permeability with respect to small organic molecules such as dimethoxiethane or organic acids. Preferably however said sheets are

made with a fabric, either normal or nonwoven, of polymeric fibers; for example it is possible to use two sheets of nonwoven fabric made with polyolefin fibers (e.g. polyethylene or polypropylene), of polyesters such as PET, or Teflon (Teflon is a registered trademark of the company Du Pont). The joining of the two walls 22 and 23 in zone 24 can be obtained by glues, but preferably is obtained by heat sealing: in this case to favor their welding the two sheets are preferably made of the same material.

In an alternative embodiment (not shown in the drawings) the envelope can be formed by joining a wall permeable to the organic molecules (e.g. a sheet similar to that of wall 22 as described above) and an impermeable wall which can be a polymeric sheet of greater thickness than that of the permeable wall or a metallic sheet, such as of aluminum; in this case the impermeable wall can be formed as a cup for housing the activated charcoals.

The activated charcoals useful for the present invention are the simple ones, not impregnated with additional substances; charcoals of this type are sold e.g. by the company C*Chem of Lafayette, Colorado, USA, under the name Chemsorb 1000, or by the company Chemviron Carbon of Feluy, Belgium.

The amount of activated charcoals contained in the device depends upon the required life length of the transdermal system; for example, in order to ensure to the system a life of about 3 years, including the store time between the production and the actual use, it has been observed with accelerated tests that at least 50 mg of activated charcoals are required.

The getter device of the invention can be located at any position inside the envelope of the transdermal system. However the getter device is preferably fixed to the system envelope in a region remote from those parts wherein the ionic flow occurs from and toward the skin. Figure 3 shows this preferred embodiment: the transdermal system 30 comprises an envelope 31 having at the inside gel 32 in which the drug is suspended, and electronic parts, as already described with reference to figure 1; in addition the system includes the getter device 20, adhering to a portion of the internal surface of envelope 31 being remote from the electrodes for the ionic species transportation, with at least wall 22 permeable to organic molecules in contact with gel 32.

In view of manufacturing the system of figure 3, the getter device 20 is caused to

adhere to the internal wall of envelope 31 preferably by heat sealing; in this case, at least the sheet designed to be fixed to the internal wall of the envelope, among those forming envelope 21, is made of a material chosen in function of the heat sealability with envelope 31: for example, if envelope 31 is made with a Surlyn containing a copolymer with ethylene, the sheet of wall 23 can be made with a polyolefin.

In an alternative embodiment of the transdermal system, shown in figure 4, the getter device is not a discrete component, but is integrated in the system itself and is manufactured in a production step of the final system. In this embodiment of the transdermal system 40, the getter device 41 consists of a first wall 42, permeable to organic molecules but capable of retaining solid particles, the perimeter of which is directly fixed to the internal surface of the envelope 43 of system 40, so that in this case a portion of envelope 43 also forms the second wall of the getter device; in the pocket thus formed there are housed the activated charcoals 44.

This second embodiment can be manufactured for example by placing powders of activated charcoals on a small portion of the polymeric sheet intended to form the envelope 43 and by fixing the perimeter of a sheet designed to form wall 42, having the required features described above, along a closed line completely encircling the area where the activated charcoals are present. In alternative it is possible to use a support (e.g. metallic) having in its top portion a recess of similar shape and size as those of the final getter device; to lay and cause to adhere the sheet which will form wall 42 within said recess; to pour the desired quantity of activated charcoals onto said sheet, in an area corresponding to the recess; to cause the peripheral portion of said sheet to adhere to a polymeric sheet intended to form the envelope 43, fixing the two sheets by glueing or heat sealing; and finally, to remove said support. Other successions of operations for obtaining the system shown in figure 4 will be clear to those skilled in the art. The envelope 43 with an "integrated" getter device thus obtained is then employed for the subsequent steps of production of the transdermal system. Also in this case the coupling between the sheet intended to form wall 42 and envelope 43 is preferably performed by heat sealing, and consequently the materials for envelope 43 and the sheet forming wall 42 will be chosen in a way suitable to the purpose, as described above.

CLAIMS

1. A getter device (20; 41) for active systems for the transdermal release of drugs (30; 40), consisting of activated charcoals (25; 44) ad at least a first wall (22; 42), permeable to organic molecules but capable of retaining solid particles, said first wall being coupled to a second wall (23; 43) capable of retaining solid particles so that the assembly resulting by the connection of said first wall and second wall is suitable to contain the activated charcoals.

2. A getter device according to claim 1, wherein said first wall is made of a continuous polymeric sheet.

3. A getter device according to claim 1, wherein said first wall is formed of a woven fabric or a nonwoven fabric of polymeric fibers.

4. A getter device according to one of claims 2 or 3, wherein the material for making said first wall is chosen among sheets or fibers of polyolefin, polyester or Teflon.

5. A getter device according to claim 1, wherein said first and second wall are mutually fixed by heat sealing.

6. A getter device (20) according to claim 1, wherein said second wall (23) is formed as a continuous polymeric sheet, fabrics, or nonwoven fabric.

7. A getter device (41) according to claim 1, wherein said second wall is a portion of the internal surface of the envelope (43) of the system for the transdermal release of drugs.

8. A process for manufacturing a getter device according to claim 7, comprising the step of: placing powders of activated charcoals (44) on a portion of a polymeric sheet intended to form the envelope (43) of the system for the transdermal release of drugs; and fixing along a closed line encircling completely the area wherein the activated charcoals are present a sheet permeable to organic molecules but capable of retaining particles, this latter forming the first wall (42) of the getter device.

9. A process for manufacturing a getter device of claim 7, comprising the steps of: arranging a support having in its upper portion a recess of similar shape and size as those of the final getter device; within said recess laying and causing to adhere a sheet

permeable to organic molecules but capable of retaining particles, designed to form the first wall (42) of the getter device; pouring the desired quantity of activated charcoals (44) onto said sheet being permeable to the organic molecules but capable of retaining particles, in the area corresponding to the recess; fixing said sheet permeable to the organic molecules but capable of retaining particles to a polymeric sheet intended to form the envelope (43) along a closed line completely encircling the area wherein the activated charcoals are present; and removing said support.