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(57) Zusammenfassung: Die Erfindung betrifft die Aufzucht von Insekten, insbesondere für die therapeutische Applikation des Sekrets von Fliegenlarven (Maggots). Die Eier der Fliegen werden unter der Weiterentwicklung der Eier beindustriert und/oder transportiert. Für die Applikation werden die Eier aus diesen entwicklungsbeeinträchtigenden Bedingungen in Behälter gehalten und/oder transportiert. So kann die Applikation des Sekrets in der Entwicklung von Fliegenlarven (Maggots) genutzt werden.

(54) Bezeichnung: Verfahren und Vorrichtung zur Aufzucht von Insekten, insbesondere für die Gewinnung des Sekrets von Fliegenlarven für die therapeutische Anwendung

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Description

A method and a device for rearing insects, especially for obtaining a secretion from fly larvae for therapeutic application.

The invention relates to a method and a device for rearing insects, especially for obtaining a secretion from fly larvae (maggots) for therapeutic application.

In order to treat wound infections and wounds containing dead tissue, e.g., in the therapy of diabetic gangrene, fly larvae, or maggots, are employed, especially dipteran larvae of the families Muscidae, Sarcophagidae, and Calliphoridae (for example, Lucilla, the bluebottle). The maggots are placed for a certain period of time, for example approximately three days, into the wound that is resistant to treatment. As it turned out, within this period the maggots remove dead tissue from the wound, eliminate bacterial inflammations and stimulate wound healing. This effect is caused in particular by the digestive secretion discharged by the maggots. Through this secretion the dead tissue is liquefied so that it can be taken up by the maggots as food. In addition, the secretion has a potent bactericidal effect and promotes wound healing.

For this method of treatment it is essential to have live maggots available that will be applied to the wound and
discharge the curative secretion. This creates a considerable logistic problem for the application of the method. As the period of the active larval stage, during which the curative secretion is discharged, is relatively short and lasts only for a few days, it is essential that the maggots are transported from the producer, where the maggots are reared, to the user immediately prior to application. This requires exact planning of the time schedule. Furthermore, the maggots are relatively sensitive and must be supplied with air and nutrients during transport. Due to these difficulties, therapy with fly larvae is limited regarding its possible applications and does not gain the acceptance one would hope for.

The object of the invention is the task of providing a method and a device through which the rearing of insects can be done in a controlled manner and which especially simplifies and facilitates the therapeutic application of the secretion obtained from fly larvae.

According to the invention, this task has been accomplished by providing a method for treating wounds using the secretions of fly larvae, the method including

- enclosing fly eggs in a container,
- maintaining the container under a first controlled condition to inhibit the development of the fly eggs to permit their storage and subsequent transportation,
- maintaining the container under a second controlled condition to develop the fly eggs into fly larvae until they secrete a therapeutically active secretion,
- applying the therapeutically active secretion to the wound.

The invention also provides a device for preparing fly larvae secretions with which to treat wounds, the device including

- a container for enclosing fly eggs,
- means for maintaining the container at a first controlled condition to inhibit the development of the fly eggs to permit their storage and subsequent transportation,
- means for maintaining the container at a second controlled condition to develop the fly eggs into fly larvae until they secrete a therapeutically active secretion,
means for removing the therapeutically active secretion from the container for subsequent application of the secretion to the wound. Advantageous embodiments of the invention are described in the reflexive sub-claims.

The essential point of the invention is to carry out the rearing of insects in a self-contained biotope under exactly defined environmental conditions through which the developmental cycle can be specifically influenced. This makes it possible to study the development and
behaviour of the insects under specifically altered physical, chemical, biochemical and biological conditions and to influence these for medical/therapeutic and pharmaceutical exploitation. While doing so, the course of the developmental cycle can be controlled, that is, either delayed or accelerated, by changing the conditions. Furthermore, quality and yield can be increased by applying a specific influence.

When using the method for obtaining the secretion of fly larvae for therapeutic application, an important aspect is to arrest the development of the fly larvae in the egg stage and to store and/or transport the eggs under conditions inhibiting development. At the producer who rears the flies, the fly eggs are separated and preferably disinfected to make them sufficiently sterile. The sterile eggs are locked into a self-contained biotope, for example, a container, where the conditions inhibiting further development of the eggs can be created or maintained. Such conditions may include that the eggs are cooled and/or stored in a dehumidified atmosphere. Furthermore, the eggs may be stored in an oxygen-depleted atmosphere, for example, by evacuating the container or by filling it with an inert gas. Reversible chemical/biochemical influences (for example, Neb-TMOP) that lead to oostasis for a defined period of time are also possible. These measures may be applied individually or in combination. Under such development-inhibiting conditions, the resistant eggs may be kept viable over long periods of time. This makes it possible to keep the eggs in storage at the producer for a certain period of time. Furthermore, the eggs can be easily transported to the user under these conditions without being damaged.
The user, for example in a hospital, can also keep a certain amount of eggs in reserve for a certain period of time so that the actual need can be covered.

When the maggot secretion is about to be applied, the development of eggs into the larval stage is initiated by the user. For this purpose, the development-inhibiting conditions are terminated and the eggs are exposed to incubation conditions so that they will continue development and maggots will hatch within a short period of time. As the eggs had been made aseptic by the producer, the hatching maggots are aseptic as well and can be applied without any problems.

It is also possible to colonize the artificially created, microbiologically self-contained biotope with specific microorganisms in order to increase or change the effectiveness of the maggots and their microbiologically modified secretion.

The maggots can be directly placed into the wound in the usual way but must be removed from the wound after a certain period of action. As a modification, the maggots are introduced into the wound while inside an application container. Such an application container has a fluid-permeable wall, which is, nevertheless, impenetrable to the maggots locked up in the application container. For example, the application container may be a flexible bag with a net-like wall. The secretion discharged by the maggots can pass through the wall of the application container and reach the wound. Likewise, the wound tissue dissolved by the secretion can pass through the wall of the application container and can be taken up by the
maggots. Such an application container has the advantage that the maggots, and therefore also the secretion they discharge, can be applied in a more targeted, localized manner. In addition, the maggots can be simply removed from the wound together with their application container.

Finally, it is also possible to bring the maggots into contact with a porous wound pad, which absorbs the secretion discharged by the maggots. In this case, the wound pad saturated with the secretion is applied to the wound. This has the advantage that the wound pad can be applied temporally and locally separated from the maggots, which simplifies the use and avoids the dislike toward live maggots that patients occasionally have.

Preferably, incubation of the eggs is done in an incubation container until the maggots have hatched. The eggs are introduced into this incubation container and incubated at a temperature of 20 to 40°C. The incubation container is supplied with sufficient nutrients and air for the hatching larvae so that these can develop into the larval stage in which they discharge the therapeutically acting secretion. This incubation container is preferably manufactured as a bag made of plastic foil and contains already, if necessary, an absorbent material for taking up, under sterile or microbiologically controlled conditions, the active substances produced.

In an expedient embodiment, the eggs enclosed in the application container can be placed into the incubator container. The small eggs are retained inside the application container by the incubation container so that
they do not fall through the net-like wall. When the larvae hatch from the eggs, they can take up the nutrients from the incubation container and grow up in the application container until they reach the size at which they discharge the therapeutically acting secretion. When of this size, they can no longer slip through the net-like wall of the application container. The application container may now be taken out of the incubation container, or the incubation container may be removed from the application container, so that the maggots with the application container can be directly placed into the wound or brought into contact with a porous wound pad.

In an embodiment that is particularly simple for the user, the eggs are already placed in the incubation containers by the producer and kept for some time in the incubation containers for storage and transport under development-inhibiting conditions. For this purpose, the incubation containers are evacuated or filled with a dehumidified inert gas or manipulated chemically/biochemically to maintain oostasis. The incubation containers may also - or, if necessary, additionally - be placed into a cooling container and chilled for storage and transport.

Once the maggots are to be applied, conditions of incubation are created in the incubation containers. For this purpose, the incubation containers with the eggs are brought into a warm environment. The incubation containers receive oxygenated air, the nutrient solution required for the hatching larvae and, if applicable, activating chemical or biochemical factors (for example,
peptidases). For supplying oxygen, the wall of the incubation container may be punctured with a needle or it may possess a port. If applicable, the required nutrient solution and, if applicable, the substances deactivating the oostatic effects may be placed in the incubation container in this way. One possibility that makes it particularly easy for the user is that the producer already stores air, nutrient solution and other substances inside the incubation container in sealed bags or sealed vials, which will then be destroyed by the user so that air and nutrient solution and, if applicable, chemical, biochemical and microbiological components enter the incubation container, promote hatching and are taken up by the hatched maggots.

If the flies are transported to the user in the egg stage so that the maggots for application of the secretion hatch at the user's location, the maggots are usually destroyed once they are removed from the wound or have discharged their secretion onto the wound pad.

At the producer, the complete developmental cycle is carried out, preferably with part of the insect stock, in a biotope that can be temporally modified and controlled.

After hatching of the maggots, these are used for obtaining the secretion, if required, which is then provided in applicable form to the user or used for the production of pharmaceutical preparations. At the end of the larval stage, the environmental conditions required for pupation are created in the biotope, for example, dry air. The maggots then enter the chrysalis stage so that a new generation of insects will hatch which, in turn, can be used for the laying of eggs under sterile conditions.
Rearing the insects from egg to emerged fly under conditions that can be regulated and controlled temporally gives the producer the opportunity to adjust the production of maggots or maggot secretion to market demands in terms of time and quantity. In addition, the insect strains can be influenced through breeding in order to yield increased production and quality. Finally, it is possible to exert a specific microbiological effect on the self-contained biotope so that a therapeutic synergistic effect, for example, of the specific bacteria added and the secretion discharged by the maggots, can be achieved.
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method for treating wounds using the secretions of fly larvae, the method including

5 enclosing fly eggs in a container,

maintaining the container under a first controlled condition to inhibit the development of the fly eggs to permit their storage and subsequent transportation,

10 maintaining the container under a second controlled condition to develop the fly eggs into fly larvae until they secrete a therapeutically active secretion,

applying the therapeutically active secretion to the wound.

15 2. A method as claimed in claim 1 wherein the therapeutically active secretion is collected from the container and applied directly to the wound.

3. A method as claimed in claim 1 wherein the container has walls which are permeable to the therapeutically active secretion but impermeable to fly larvae and the wound is contacted with the container such that the secretions are applied to the wound.

20 4. A method as claimed in claim 1 wherein the therapeutically active secretion is absorbed by a porous wound pad which is subsequently applied to the wound.

25 5. The method as claimed in any one of claims 1 to 4 wherein the container is enclosed within an incubation container such that the fly eggs are exposed to incubation conditions.

6. The method as claimed in any one of claims 1 to 5 wherein the first controlled condition to retard the development of the fly eggs involves cooling
and/or dehumidification and/or evacuation and/or inert gas atmosphere and/or chemical or biochemical inhibitors, either individually or in combination.

7. A device for preparing fly larvae secretions with which to treat wounds, the device including

a container for enclosing fly eggs,

means for maintaining the container at a first controlled condition to inhibit the development of the fly eggs to permit their storage and subsequent transportation,

means for maintaining the container at a second controlled condition to develop the fly eggs into fly larvae until they secrete a therapeutically active secretion,

means for removing the therapeutically active secretion from the container for subsequent application of the secretion to the wound.

8. A device as claimed in claim 1 wherein the container is enclosed within an incubation container such that the fly eggs are exposed to incubation conditions.

9. A device as claimed in claim 8 wherein the incubation container is a plastic foil bag.

10. A device as claimed in any one of claims 7 to 9 wherein the walls of the container are permeable to the therapeutically active secretion but impermeable to fly larvae.

11. A device as claimed in claim 10 wherein the container has a flexible, net-like wall.

12. A device as claimed in any one of claims 8 to 11 wherein one or more incubation containers are placed in a further container in which the development-inhibiting conditions are maintained.
13. A device as claimed in any one of claims 8 to 12 wherein the development-inhibiting conditions in the incubation containers can initially be created and maintained and can be changed on demand into incubation and nutritional conditions.

14. A device as claimed in any one of claims 8 to 13 wherein air and/or nutritive solution and/or chemical/biological/microbiological components can be added through the wall of the incubation container.

15. A device as claimed in claim 14 wherein the air and/or nutritive solution and/or chemical/biological/microbiological components can be added through the wall of the incubation container by means of a cannula.

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