THE INVENTION RELATES TO AN ELECTRICALLY TREATED OR AFFECTED COMPOSITION CAPABLE OF BEING USED IN A METHOD FOR THERAPEUTIC TREATMENT OF A HUMAN BEING OR AN ANIMAL. THE ELECTRICALLY TREATED COMPOSITION IS PARTICULARLY USEFUL IN SUPPRESSING THE SECRETION OF HISTAMINE FROM MAST CELLS AND, THEREFORE, REPRESENTS A NEW FORM OF ASTHMA TREATMENT.
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ELECTRICALLY TREATED COMPOSITION AND USE THEREOF

Technical field

The invention relates to an electrically treated or affected composition capable of
being used in a method for therapeutic treatment of a human being or an animal.

The electrically treated composition is particularly useful in suppressing the
secretion of histamine from mast cells and, thus, represents a new form of asthma
treatment.

Background of the invention

A composition such as a liquid optionally comprising positive and/or negative
charged ions can be subjected to a current or an electrical treatment by for example
contacting the liquid with a positive and a negative electrode and connecting the
electrodes to a power source, which connection provides a migration of charged
particles, preferably ions, in the said liquid. The electrically treated composition has
a number of different uses, for example within the field of cell biology.

Mast cells are present in connected tissue and epithelia in particularly lungs, the gut
and skin. Mast cells are natural components in the immunity defence of the body
along with for example macrophages, neutrophile, eosinofile and basofile leukocytes
along with B lymphocytes and T lymphocytes.

These cells are recruited in the normal reaction towards an infection in the body.

Mast cells contain a cell nucleus surrounded by various organelles and exist as
single cells in a mammal organism such as a human being or an animal.

What is particular about the mast cell is the presence of a very large number of
small and closely packed granula in the cytoplasm of the cell. When the mast cell is
stimulated, these granula are secreted by exocytosis. The influence of the mast cell
on the inflammation reactions is thought to be due to their ability to form and secrete a number of biologically active compounds which together are termed mediators.

Mast cells secrete the mediator histamine under for example an allergic reaction. Histamine provides for example contractions in the airways and lungs under an asthma attack. Histamine is one of the only compounds which are common for all types of mast cells. When the mast cell is secreting histamine, the result is among other things an increase in the intracellular pH, a change in the membrane potential and a changes ion transport, such as for example an increase in the \( \text{Na}^+\text{K}^+ \) pump activity.

Histamine is synthesised from histidine and is stored in the granula of the mast cell in a complex comprising proteoglycans (Warner & Kroegel, 1994). Histamine exerts its effect via \( H_1 \), \( H_2 \) and \( H_3 \) receptors. Stimulation of \( H_1 \) receptors leads to an increased permeability in veins, contraction of smooth muscles, kemotaxis of neutrophiles and eosinophiles as well an increased production of prostaglandines. \( H_2 \) recepto-stimulation results in stomach acid secretion, increased vein permeability, increased T-cell suppresser function, inhibition of \( \text{IgE} \)-mediated basofil histamine secretion, and decreasing neutrofil and eosinofil chemotaxis.

\( H_3 \) receptors are present in the central nerve system and in the lungs, and it is believed that \( H_3 \) receptors participate in controlling histamine formation and secretion via negative feedback (Rothe et al., 1990).

In some individuals, the mast cell "over-react" which provide asthma and allergies (Redington et al., 1995). The mast cell is, thus, involved in anaphylactic shock which comprises secretion of substantial amounts of heparin and histamine to the serum. It is known that these and other biological active compounds which are contained in the granula of the mast cells to a certain degree is responsible to the symptoms that are observed in allergic reactions.

Asthma is used herein as defined as an airway suffering characterised by an increased bronchial activity from a stimulus resulting in spasm and/or inflammation of the bronchial wall and a subsequent reduced access of air to the lungs. Bronchitis is
used herein as defined as an acute or chronic inflammation of any part of the bronchus or the bronchial airways.

Allergy is used herein is defined as any way of reacting towards an allergen, typically hypersensitivity, after antigen exposure. Hypersensitivity comprises a significant increased histamine secretion after exposure to an antigen. Type 1 allergy is characterised by degranulation of the mast cell in response to a cross binding between a suitable allergen and immunoglobulin molecules of the E type (IgE), which are present on receptors on the surface of the mast cell.

Traditional medical treatment of asthma has comprised the use of steroids and a number of beta-agonists, however, this use in therapeutic treatment leads to a number of unwanted side-effects. The treatment with bronchodilating beta-agonists alone has for example been criticised as giving rise to the so-called “asthma-paradox” characterised by recruitment of for example macrophages and a following state of chronic inflammation. This state of inflammation is not treated with beta-agonists alone. Steroid treatment is preventive for asthma, but the steroids, particularly when given in large doses, has a number of unwanted side-effects on the organism.

Consequently, a need exists for a natural form of treatment, alleviation and/or elimination of the unpleasant side-effects due to the histamine secretion related to for example allergic attack and asthma, said treatment, alleviation and/or elimination not being connected with onset of the known and unwanted side-effects.

Several techniques for determining intra-cellular pH, herein termed pHi, have been described in the literature. A detailed description is provided by Boron (1992). One method concerns measuring distribution of radio actively labelled weak acid or base over the plasma membrane. This method is relatively sensitive to volume changes, and there will in addition be a certain compartmentalisation of the tracer. Furthermore, this method is less well suited for following pH changes over time. Nuclear Magnetic Resonance (NMR) is another method for measuring intracellular pH. An inorganic phosphate signal is used since it is easy to observe the $^{31}$P spectrum, and because this frequency is particularly sensitive to pH in the neutral area.
A further method comprises use of pH sensitive micro electrodes, which penetrates the plasmamembrane, which allows monitoring pH changes over time. By using this method, compartmentalisation of the tracer is not a problem. However, one does risk that the cells become damaged when the electrode is introduced through the plasma membrane. The method is, therefore less well-suited for small cells.

Fluorescent compounds with pH dependent fluorescent in the physiological area are very useful for examination of regulatory mechanisms and measuring intracellular pH. One preferred probe is 2',7'-bis(2-carboxyethyl)-5-carboxyfluorescein acetoxymethylster (BCECF-AM). BCECF-AM is introduced in the cell as a liquid soluble ester, which is cleaved by esterases in the cytoplasm (Rink et al., 1982; Moolenaar et al., 1983). The fluorescent can be monitored over time and it is, therefore, possible to monitor pH changes over time.

The three most important pHi regulatory mechanisms are i) a Na⁺/H⁺ transporter, ii) a Na⁺-dependent Cl⁻/HCO₃⁻ transporter, which are both activated by low pH and are acid secretion mechanisms under physiological conditions, along with iii) a Na⁺ independent Cl⁻/HCO₃⁻ transporter, which is activated by high pH and at physiological ion gradients will lead to a reduction of intracellular pH (Thomas, 1989). All three ion transport mechanisms may occur in one and the same cell (Redon & Batlle, 1994).

According to the known technique, cells in a HEPES buffer without bicarbonate will dominantly regulate their pH via a Na⁺/H⁺ transporter (Green, 1994). If bicarbonate on the other hand is present, the steady-state pH will also be regulated by up to three additional, secondary transport systems. The term secondary means that these ion transport systems are driven by other ion gradients capable of being maintained under consumption of ATP energy against their electro-chemical gradients.

According to one presently preferred hypothesis, the electrical treatment or affect of a fluid, water-based composition, such as a aqueous solution will result in cell-stabilising affect and in a preferred embodiment provide a cell characterised by having a predetermined resting membrane potential or a predetermined resting pH.
and/or a predetermined steady-state resting membrane potential or a predetermined steady-state resting pH, or a cell capable of entering a condition characterised by maintaining a characteristic resting membrane potential for the respective cell and/or a resting pH or a characteristic steady-state resting membrane potential for the respective cell and/or steady-state resting pH.

According to another presently preferred hypothesis, the properties of the electrically treated or affected fluid composition is achieved when a reaction between the fluid composition and the electrodes with which the composition is contacted sets in. The reaction preferably occurs, however, not limited to occur, when the electrodes are having an electric potential. According to the hypothesis, the electrodes having the electric potential will result in a current of charged particles, preferably ions, migrating in the fluid composition, reducing or increasing the amount of gasses in said composition, or reducing or increasing the solubility of the respective gasses or the amount of dissolved gas in the liquid. It is also possible that the concentration of ions or the concentration or presence of certain species of ions in the composition is changed as a consequence of the fluid composition being contacted by a current of charged particles, preferably ions.

According to the present invention, it is possible by electrically treating a fluid composition, such as an aqueous composition or any other liquids to change not only the concentration of salt, but also the concentration of a gas in a liquid. Increasing concentrations of CO₂ have for example turned out to inhibit the compound 48/80 mediated secretion of histamine independent of pH. The same effect is observed if a cell liquid is subjected to a current of about 1.5 µA and subsequently supplemented with mast cells. Compound 48/80 mediated secretion of histamine from the mast cells is also in this case reduced significantly. The reduction, according to a presently preferred hypothesis, is due to cell stabilising effect that provides cells capable of easier or more rapidly entering a condition characterised by maintenance of a characteristic resting membrane potential for the respective cell and/or a resting pH or a characteristic steady-state resting membrane potential for the respective cell and/or steady state resting pH.
Summary of the invention

It is novel to treat and/or alleviate for example asthma, bronchitis or an allergic reaction with a composition, which has been treated with an electrical current or subjected to a ionisation. It has now very surprisingly and unexpectedly turned out that a composition, such as for example liquid, which has been subjected to an electrical current or a ion treatment, is an effective means for treatment of an individual suffering from for example asthma, bronchitis and/or an allergy.

In a first aspect, the invention relates to an electrically treated composition for use as a medicament. In a further aspect, the invention relates to an electrically treated composition for use in a method for therapeutic or surgical treatment, or a method of diagnostics, of a human being or an animal. There is also provided the use of an electrically treated composition in the manufacture of a medicament for treating a suffering of a human being or an animal. In a further aspect of the invention relates to the use of an electrically treated composition or such a composition for use in method for therapeutic or surgical treatment, or for use in a method of diagnostics, of a human being or an animal.

There is, furthermore, provided a method of producing a composition according to the invention, said method comprising contacting the composition with a ion generated by a ion generator or an electrical current of charged particles, preferably ions, generated by electrodes connected to a power source. In further aspect, there is provided a composition obtainable by this method.

When the mast cell is secreting histamine, the result is among other things an increasing intracellular pH, a change in the membrane potential, and a increase in Na⁺/K⁺ pump activity. The electrically treated composition according to the invention is, thus, capable of i) reducing the amount of secreted histamine and/or ii) reducing the increase in intracellular pH associated with the secretion of histamine and/or iii) reducing the increase in the Na⁺/K⁺ pump activity associated with the secretion of histamine. The composition is, furthermore, capable of counter-acting changes in the membrane potential in a cell during the secretion of histamine.
In a further aspect, the invention provides an anti microbial means, preferably, but not limited to, an anti bacterial means, effective in eliminating bacteria, preferably, but not limited to, pathogenic bacteria, or capable of inhibiting the growth of such bacteria in an environment wherein they occur.

**Detailed description of the invention**

With the experiments described herein, the efficiency of the technique is demonstrated by documenting the exerted effects on mast cells in the experimental solutions. When the principles of the idea are to be applied on human beings a similar approach may not be directly possible. Instead we have to rely on experimental results. It appears that there may be only a minor beneficial effect of the application of an electrical current through electrodes fixed to limited well-defined areas of the body. It is now the claim, which is supported by many practical experiences, that the best effect is obtained when the current is directed to the area to be treated by the way of a flow of unipolar, ionized air. A ground-connection is applied to a suitable part of the body, like the wrists, and the ionized air is directed to the area to be treated, like the soles of the feet. It is now the theory that the current, carried by the ions, will dissipate an effect to the body fluid similar to what was found with the experimental solutions. It is also claimed that it is important that the current to the body is independent of the relative position of the body and the ionizer. As a consequence a device has been developed by means of which it is possible via an electronic feedback to secure that the ion current to the exposed area of the body is independent of the position of the ionizing device.

**Treatment of liquids by an electrical current**

In this patent application it is demonstrated that the passing of a current through certain liquids has a desirable effect and provides a predetermined property to said liquid. It is the assumption that the effect is caused either by the charge passing a certain area or by the energy dissipated in a certain volume. These questions are most adequately described by the use of the current density, i.e. the current through a unit area perpendicular to the current as described herein below.
If the current density is \( j \) (unit A\cdot m^{-2}) then a charge equal to \( j \) is passing through each unit area per unit time. In a time \( t \) the charge \( q_1 \) passing through a unit area is then given by

\[
q_1 = j \cdot t
\]  

(1)

At the same time a power \( w_1 \) (unit J\cdot s^{-1}\cdot m^3 = W\cdot m^3 = \text{watts per meter cube}) is dissipated in each unit of volume per unit time given by

\[
w_1 = \rho \cdot j^2
\]  

(2)

where \( \rho \) (unit \( \Omega \cdot m \)) is the resistivity of the liquid. In a time \( t \) the total energy \( W_1 \) (unit J\cdot m^3) dissipated per unit volume is given by

\[
W_1 = \rho \cdot j^2 \cdot t
\]  

(3)

When comparing results from experiments with different experimental set-ups we should compare the values of \( q_1 \) and \( W_1 \). With the experiments described in the application a set-up like the one shown in Fig. 1 was used. In an insulating cylindrical vessel A is on the bottom placed an electrode C with the same radius \( r \) as the container. On the surface of the liquid to be treated is placed another electrode B with the same radius.

From a voltage supply \( V \) a current \( I \) is sent through the liquid causing a uniform current density

\[
j = \frac{I}{\pi r^2}
\]

It appears that the current density is independent of the height \( h \) of the liquid in the experimental vessel. In a following series of experiments the experimental arrangement shown in Fig. 2 will be used. The experimental chamber is a metallic cylindrical container A with an inner radius \( R \). A cylindrical electrode B with the radius \( r \) is placed in the axis of A and submerged in the liquid to be treated. The length of B in the liquid is \( h \) and it is assumed that the distance from the end of B to the bottom of A is much smaller than \( h \).
From a voltage supply \( V \) a current \( I \) is sent through the liquid causing a current density \( j_x \) at a distance \( x \) from the axis which by a good approximation is given by

\[
 j_x = \frac{I}{2\pi h x}
\]

We see that the current density changes throughout the liquid, and it is now the assumption that in order to compare the results obtained with the cylindrical electrodes, Fig. 2, to the results with plane electrodes, Fig. 1, we should for the same time exposure, achieve to have the same mean value \( j_m \) of the current density, when we consider the effect of the charge passed, or the mean value \( j^2_m \) of the square of the current density when we consider the effect of the energy dissipated in the liquid.

The mean value of the current density with cylindrical electrodes is given by

\[
 j_m = \frac{1}{R - r} \int_r^R j_x \, dx = \frac{I}{2\pi h (R - r)} \ln \frac{R}{r}
\]

(6)

\[
 I = \frac{2\pi h (R - r)}{\ln \frac{R}{r}} \cdot j_m
\]

(7)

The relationship between the mean value of the square of the current density and the current is obtained by the following consideration.

The total energy dissipated in the liquid per unit time (the power) is given by

\[
 w = \int_r^R \rho \cdot j_x^2 \cdot 2\pi x h \, dx
\]

(8)

The power \( w \), dissipated per unit volume is then

\[
 w_1 = \frac{w}{h \pi (R^2 - r^2)} = \frac{\rho I^2}{2 \pi^2 h^2 (R^2 - r^2)} \cdot \ln \frac{R}{r} = \rho (j^2)_m
\]

(9)
or

\[ I = \frac{\sqrt{2\pi h}\sqrt{R^2 - r^2}}{\ln \frac{R}{r}} \cdot \sqrt{(j^2)_m} \]

**Experimental Values.**

With the experiments described in the application using plane electrodes the parameters were \( r = 3.6125 \) cm and \( I = 1.5 \times 10^{-6} \) A.

According to eq. (4) this corresponds to a current density

\[ j = \frac{1.5 \times 10^{-6}}{\pi \cdot (3.1625 \cdot 10^{-2})^2} = 3.63 \times 10^{-4} \text{ A.m}^{-2} = 36.3 \text{ mA.m}^{-2} \]

When using the cylindrical set-up, Fig. 2, we will then, when studying the effect of the charge, use a current (eq. (7)) giving a mean density of

\[ j_m = 3.63 \times 10^{-4} \text{ A.m}^{-2} \]

and when studying the effect of the charge dissipated a current which in the cylindrical geometry has a mean value (eq. 9) of the square of the density \((j^2)_m\) satisfying eq. (10) where

\[ \sqrt{(j^2)_m} = 3.63 \times 10^{-4} \text{ A.m}^{-2} \]

With the experiments with cylindrical electrodes the parameters are \( R = 8 \times 10^{-2} \) m, \( r = 2.5 \times 10^{-3} \) m, and \( h = 0.12 \) m. Introducing these figures in eq. (7) we find

\[ I = \frac{2\pi \cdot 0.12 \cdot (0.08 - 0.0025)}{\ln \frac{0.08}{0.0025}} \cdot 3.63 \times 10^{-4} = 6.12 \times 10^{-6} \text{ A} \]

\[ I = \frac{\sqrt{2\pi \cdot 0.12 \cdot 0.08^2 - 0.0025^2}}{\ln \frac{0.08}{0.0025}} \cdot 3.63 \times 10^{-4} = 8.34 \times 10^{-6} \text{ A} \]

valid for charge experiments, and from eq. (10), valid for energy experiments.
It should be emphasized that the above considerations are true only for the conditions considered, and that other experimental geometries will require separate evaluations. However, the above calculations are for illustrative purposes and they should not be considered as limiting the application of the invention.

In a first aspect of the invention there is provided a method of providing a composition with a predetermined property, said property being obtainable by contacting said composition with a charged particle, preferably an ion. The predetermined property is preferably essentially sustainable over time. In one preferred embodiment the composition is transiently contacted by said charged particle. It is also preferred that the predetermined property is essentially sustainable over time, and that the composition is transiently contacted by said charged particle. When the predetermined property remains associated with the composition for a period of time, the period is at least essentially the same as the period of time in which the composition is contacted by said charged particle. In one embodiment, the predetermined property is essentially sustainable over time irrespective of the period of time in which said composition is contacted by said charged particle. The predetermined property is preferably sustainable for at least one week, such as one month, for example six months, for example one year, such as two years, for example five years, such as ten years.

Where the contacting of said composition by a charged particle results in the passage of a current through said composition, said current corresponds to at least about 0.01 μA and preferably less than about 1.5 A. The current may also result in a charge being provided to said composition, said charge being at least about 0.01 mC and preferably less than 10000 mC. In one particularly preferred embodiment, the composition comprising said predetermined property is a medicament.

The composition according to the invention is obtainable by any of the methods described herein immediately above. The composition in one embodiment is for use as a medicament. There is also provided a composition for use in a method for treatment of the human body by surgery, a composition for use in a method for treatment
of the human body by therapy, and a composition for use in a diagnostic method practised on the human or animal body.

In another embodiment the composition according to the invention is for use in a method of prophylactically or therapeutically treating an allergic condition in an individual. The composition may also be used in a diagnostic method capable of diagnosing an allergic condition in an individual, preferably rhinitis, urticaria, allergic conjunctivitis, and an allergic condition occurring in the airways of said individual, such as asthma.

The composition may also be used in a method of prophylactically or therapeutically treating an infection in an individual, and it may be used in a diagnostic method capable of diagnosing an infection in an individual. The infection may reside anywhere, but treatment of infections occurring in the airways of said individual are responding particularly well to treatment. On such form of infection is an infection associated with an obstructive disease of the airways, said disease may be sporadically, periodically or chronically occurring. The infection may, prior to treatment, result in an increased mucous production. One such form of infection is bronchitis.

The composition according to the invention is also for use in a method of treatment of a human being or an animal, said method being capable of reducing or eliminating the secretion of histamin from mast cells. The composition in one embodiment is capable of controlling the intracellular pH value of a human or animal cell and/or capable of reducing the increase in the intracellular pH-value in a human or animal cell during an allergic attack.

The composition can also be used in a method of prophylactically treating in a human or an animal body a cell at risk of developing cancer, or for therapeutically treating a cancer cell, as well as prophylactically or therapeutically treating a cardiovascular disease in an individual. The composition is also useful in a method of diagnosing an immunodeficient condition in an individual, in a method of prophylactically or therapeutically treating a rheumatic condition in an individual, a method of prophylactically or therapeutically treating a lesion to the skin including burns in an individual, a method of prophylactically or therapeutically treating a disease to the skin in an individual, a method of prophylactically or therapeutically treating eczema,
a fungus infection, a bacterial infection, exanthema, or psoriasis in an individual, as well as being useful in a method of boosting the immune response of a human or animal cell.

In another aspect there is provided the use of the composition according to the invention in the manufacture of a medicament for the treatment of a condition or illness in a human or animal in need of said treatment. The treatment may comprise prophylactically or therapeutically treating an allergic condition in an individual, diagnosis of an allergic condition in an individual, prophylactically or therapeutically treating an infection in an individual, or diagnosing such an infection in an individual.

The use of said medicament may also be directed to prophylactically or therapeutically treating a cardiovascular disease in an individual, aimed at diagnosing an immunodeficient condition in an individual, prophylactically or therapeutically treating a rheumatic condition in an individual, prophylactically or therapeutically treating a lesion to the skin including burns in an individual, prophylactically or therapeutically treating a disease to the skin in an individual, prophylactically or therapeutically treating eczema, a fungus infection, a bacterial infection, exanthema, or psoriasis in an individual, as well as boosting the immune response of a human or animal cell.

An electrically treatment of a composition according to the invention, preferably a fluid composition, such as a liquid or a gas including an aerosol, such as a suspension of particles, may take place by contacting the composition with other atmospheric ions or with electrodes having an electrical potential. By doing this, the composition is provided with properties that are useful for example in connection with a therapeutic treatment of a human being or an animal. In particular embodiment, the composition may also be a compound in powder form or a solid matter inclusive an amorphous material. The composition comprises at least one chemical compound and a carrier, preferably a physiologically and/or pharmaceutically acceptable carrier. The useful effect and the nature of this is not yet known in all details. There is, furthermore, provided a number of uses outside the therapeutic, diagnostic and surgical areas, such as it is described in the following.
The method of treating a composition in order to obtain the useful effects described herein can advantageously be used to show the effect on for example secretion of histamine in mast cells and monitor the development in the intracellular pH value under for example an allergic attack in a human being or an animal. The method according to the invention also relates to a method of manufacturing any composition capable of being subjected to an electrical treatment and subsequently shown to have a useful effect, i.e. an effect capable of reducing the secretion of histamine from mast cells under conditions comparable to an allergic or an asthma attack.

Under an allergic or an asthma attack, the mast cells are provoked to secrete histamine, and it is possible by means of chemically manufactured secretory active compound, called compound 48/80, to simulate the secretory process that take place in the body, when a mast cell is secreting histamine. By adding different concentrations of compound 48/80, it is possible to affect mast cells from rats to secret histamine in various amounts. This provides an opportunity for examining the connection between the form of treatment and histamine secretion.

It is possible with a suitable electrical treatment of a composition such as a liquid, which is subsequently used for incubating mast cells, or which is mixed with another liquid containing mast cells, to reduce the histamine secretion in the mast cells that are in contact with the liquid treated in this way.

The parameters indicated herein below are for guidance only and are not a condition for achieving the results described herein. The parameters may vary from for example very small units to very large vessels and tanks. The electrical current, electrical potential and time indicated herein below are not a condition for achieving described results. The electrical current, electrical potential and time may be varied and it is possible to achieve different effects. The person skilled in the art will know how electrical current, electrical potential and time may be varied in consideration of the terms described herein and in the examples.

In one preferred embodiment of the invention, a plastic bowl is used having an internal diameter of 7.25 cm and a height of 3.75 cm. In the bottom of the bowl, a copper plate (diameter 7.25 cm) is placed, which is connected to a neutral electrode.
via a sensitive electrical measuring instrument so that the total electrical current through the liquid can be measured. 32 ml of a composition is applied to the bowl and the content of the bowl is treated with an electrical current or with atmospheric ions.

Treatment with atmospheric ions involves providing a ion generator, optionally in combination with a blower, above the liquid, and indicated in Fig. 3. The ion generator is supplied with a neutral connection. Ions generated by the ion generator will hit the surface of the liquid and cause an electrical current in the liquid. The electrical current can be measured by an electrometer. In one embodiment, by treatment with an electrical current, a copper electrode (7.25 cm in diameter) is placed in contact with the surface of the liquid. This electrode is connected to one terminal of a generator providing a constant current. Said second terminal of said generator being connected to neutral, cf. Fig. 4. Also in this case, the electrometer will monitor the electrical current in the composition. In a particularly preferred embodiment, the composition, such as a liquid, is subjected to an electrical current of about 1.5 µA in 1 hour, so that a total amount of charge of about 5.4 mC is transferred. Alternatively, the composition is subjected to an electrical current of essentially the same intensity from the ion generator.

According to the invention, there is provided an electrically treated composition for use as an medicament and a electrically treated composition for use in a method of therapeutic or surgical treatment or a method of diagnostics of the human being or an animal. The method preferably comprises a prophylactic or therapeutic treatment, or diagnostic, of an allergic condition, preferably an allergic condition occurring in the airways, such as for example asthma. The method also comprises prophylactic or therapeutic treatment, or diagnostic, of a condition of infection in the airways, such as an obstructive airways disease. The allergic and/or infective condition may either be sporadically or periodically or chronically occurring and optionally also connected with or may lead to an increased mucoid mucous production. In one particular case, the condition is bronchitis.

There is also provided a composition for use in a method capable of effectively reducing or eliminating secretion of histamine from mast cells. The method in one preferred embodiment is, furthermore, effective in controlling the intracellular pH
value in a cell and preferably also effective in reducing the increase in the intracellular pH value in a cell during a allergic attack.

In another embodiment of the invention a composition is provided for use in a method for prophylactic or therapeutic treatment, or for diagnostics, of a cancer cell, of a cardio vascular disease, of an immunodeficient condition, of rheumatic sufferings, muscle sufferings and tendon sufferings and for therapeutic treatment of skin lesions such as burns.

There is also provided a composition for use in a method for prophylactically or therapeutically treating, or for diagnosing, stressed and/or sick cells. The composition according to the invention is also capable of being used in a method for prophylactically or therapeutically treating, or diagnosing, skin disease, and there is also provided a composition for use in a method for prophylactically or therapeutically treating eczema, fungus infection, bacteria infection, a rash or psoriasis. The composition according to the invention can also be used in a method of increasing the ability of a cell to counter act a bacterial or viral infection of the cell.

The composition according to the invention is, furthermore, in one particular preferred embodiment capable of controlling cellular activities mediated by H₁, H₂ and H₃ receptors. The composition is, thus, capable of controlling a H₁ receptor mediated permeability of veins and/or a H₁ receptor mediated contraction of smooth muscles and/or a H₁ receptor mediated kemotaxis of neutrofiles and eosinofiles and/or H₁ receptor mediated production of prostaglandines.

The composition is also capable of controlling a H₂ receptor mediated stimulation of secretion of stomach acid and/or a H₂ receptor mediated H₂ receptor permeability of veins and/or a H₂ mediated T-cell suppresser function and/or a H₂ receptor mediated inhibition of IgE mediated basofil histamine secretion and/or a H₂ receptor mediated neutrophilic and/or eosinophilic chemotaxis.

The composition in one particularly preferred embodiment is also capable of controlling a H₃ receptor mediated formation of histamine and secretion thereof in the airways or lungs.
In a further embodiment of the invention, the electrically treated composition is suitable for controlling the pH homeostasis of a cell. The pH homeostasis of a cell as used herein is defined as the mobile equilibrium condition in the intracellular pH, which provides the cell with an ability to sustain external changes. According, there exists a connection between intracellular pH and the mechanisms mediating the transport of ions across the cell membrane.

It will be known to the person skilled in the art how to determine intracellular pH and/or changes therein within a cell. The person skilled in the art will preferably measure intracellular pH and/or changes therein in a cell under physiological conditions. Alternatively, the person skilled in the art will consult recommended textbooks or scientific articles in order to orient himself of the characteristic intracellular pH value of a cell, for example a resting pH, and/or a characteristic membrane potential of a cell, for example a resting membrane potential, under physiological conditions.

Physiological conditions as used herein is defined as the conditions that must be present before a cell can enter homeostasis defined as the movable equilibrium condition of the cell, when it is in a natural environment under maintenance of the for the respective cell characteristic resting membrane potential and/or resting pH or a for the respective cell characteristic steady-state resting membrane potential and/or steady-state resting pH.

A natural environment as used herein is defined as the environment surrounding the cell when this is present in an intracellular solution or in an extra-cellular solution, preferably an extra-cellular solution selected from the group consisting of an interstitial solution, a plasma solution and a trans-cellular solution. These solutions preferably have a composition as indicated in Mainz (1997): Biokemi (Munksgaard, Copenhagen).

It is not required that the respective cell always will be able to enter into a condition characterised by maintenance of a for the respective cell characteristic resting membrane potential and/or resting pH or a for the respective cell characteristic steady-state resting membrane potential and/or steady-state resting pH. For example when a non-healthy cell, such as a cancer cell, or a cell infected by a
foreign body, such as a virulent virus, or a hyper-secreting mast cell is examined, these cells will in one embodiment of the invention be capable of being examined under physiological conditions as described above without this necessarily leading to entry into the above-mentioned characteristic resting membrane potential and/or resting pH\text{Hi} or a steady-state thereof.

If a cell, thus, enters the condition of homeostasis defined as a movable equilibrium that enables a cell to maintain — under physiological conditions as defined herein above — a for the respective cell characteristic resting membrane potential and/or resting pH\text{Hi}, or a for the respective cell characteristic steady-state resting membrane potential and/or steady-state resting pH\text{Hi}, such a cell according to the invention will be a cell free from disease or a healthy cell.

According to one particular preferred embodiment of the invention, it is possible to administer the composition to an organism, preferably a human being or an animal, and subsequently promote the formation of or the maintenance of cells free from disease or healthy cells as defined herein above. According to one presently preferred hypothesis, cells free from disease or healthy cells are formed or maintained by control of a ion transport mechanism, which the composition according to the invention is capable of exerting.

Ion transport as used herein will preferably be understood as the transport of a ion over a biological membrane, preferably a cell membrane, such as for example a plasma membrane.

There is provided a composition according to the invention capable of controlling a Na\textsuperscript{+}/H\textsuperscript{+} transporter without exerting any influence on the membrane potential of the cell, said control resulting in the maintenance of and/or re-establishment of the pH\text{Hi} homeostasis of a cell. According to another presently preferred hypothesis, there is provided a composition according to the invention capable of controlling a Na\textsuperscript{+}/H\textsuperscript{+} transporter and a bicarbonate dependent transport mechanism, said control resulting in the maintenance of and/or re-establishment of the pH\text{Hi} homeostasis of a cell.
There is also provided a composition according to the invention capable of controlling a Na⁺ independent Cl⁻/HCO₃⁻ transporter, said control resulting in maintenance and/or re-establishment of the pH homeostasis of a cell.

There is also provided a composition according to the invention capable of controlling a Na⁺ dependent Cl⁻/HCO₃⁻ transporter, said control resulting in maintenance and/or re-establishment of the pH homeostasis of a cell.

There is also provided a composition according to the invention capable of controlling a Na⁺/[(HCO₃⁻)₃] cotransporter, said control resulting in maintenance and/or re-establishment of the pH homeostasis of a cell.

The invention is not limited to regulation of the herein above mentioned ion transport mechanisms. Other ion transport mechanisms, which does not directly transport acid or base, but are involved in a secondary way in the regulation of pH by adding or removing ions, and in doing so, are capable of altering ion gradients, are also comprised by the invention.

According to one particularly preferred embodiment of the invention, there is provided a composition capable of controlling a Na⁺/H⁺ transporter without affecting the cell membrane potential and/or a Na⁺/H⁺ transporter in combination with a bicarbonate dependent transport mechanism and/or a Na⁺ independent Cl⁻/HCO₃⁻ transporter, and/or a Na⁺ dependent Cl⁻/HCO₃⁻ transporter, and/or a Na⁺/[(HCO₃⁻)₃] cotransporter, said control resulting in maintenance and/or re-establishment of the pH homeostasis of a cell.

According to a particularly preferred embodiment of the invention, the use of the composition according to the invention will result in the maintenance or re-establishment of the pH homeostasis of a cell, which result in naturally occurring cells in a human being or an animal can remain essentially healthy under conditions, such as for example a pathogen infection, which would otherwise have resulted in the conversion of naturally occurring healthy cells or cells free from disease to unhealthy cells. The composition according to the invention will in one preferred embodiment result in a number of naturally occurring healthy cells in a human being or an animal, being maintained essentially unchanged or increased for example an
infection with a virus or a pathogen organism. The pathogen infection according to
the invention is preferably an infection caused by a micro-organism, preferably a
micro-organism selected from the group consisting of a filamentous fungus, a yeast,
a bacteria, and a virus. The unchanged or increased amount of naturally occurring
healthy cells will contribute considerably to the ability of the organism to resist
infection or cell changes.

In one particularly preferred embodiment according to the invention, there is
provided a composition according to the invention for use an anti-microbial means
and/or an anti-microbial means comprising an electrically treated composition, said
composition being provided by a method comprising the steps of contacting the
composition with ions generated by a ion generator or by an electrical current of
charged particles, preferably ions, generated by electrodes having an electrical
potential and in contact with a power source. In a further embodiment, there is
provided a method of eliminating unwanted micro-organisms, such as bacteria in a
medium, said method comprising treating the medium with charged particles,
preferably ions, such as an electrical current of charged particles, for example ions.

The composition is preferably a fluid composition, such as for example a liquid or an
aqueous solution, preferably, however, not limited to, water, such as corporation
water or ordinary tapped water, an aqueous salt solution, such as for example
physiological selin (0.9% NaCl), demineralised water, Millipore water, ion exchanged
water or water filtrated though a filter of for example active charcoal. The charged
particles, preferably ions, such as for example an electrical current, preferably
provides the fluid composition with a charge of from about 5.4 mC to about 23.8 mC
per about 32 ml of the fluid composition.

The anti-microbial means is in one embodiment effective as an anti-bacterial means,
since the means eliminate bacteria or inhibit the growth of bacteria, such as bacteria
capable of causing disease, including pathogen bacteria in a certain environment,
for example a human being or an animal, or an eatable or drinkable product for
human or animal consumption, said product optionally being processed or
conditioned prior to intake. In a particular embodiment, the product is a meat
product, such as for example meat from an ox, a calf, a pig, a chicken, a duck, a
turkey, an ostrich, a poultry product such as an egg, or a dairy product such as milk.
In a particularly preferred embodiment, the milk is treated or affected with a current of charged particles, preferably ions, generated for example by electrodes having an electrical potential, said treatment or affection having an anti-microbial effect including an anti-bacterial effect and improves the shelf-life and storage-stability of milk treated in accordance with the invention. This invention is particularly useful for eliminating or inhibiting the growth of unwanted bacteria in milk and dairy products. The method according to the invention is in one embodiment useful in the production of canned milk and may be used together with a traditional treatment, such as a heat treatment of raw-milk, condensed milk or milk powder, particularly a heat treatment comprising one or more treatments, such as low-pasteurisation, high-pasteurisation, UHT-treatment, sterilisation or evaporation. The method according to the invention is particular useful in the manufacturing of dry milk or milk powder.

Pathogen bacteria as used herein are defined as bacteria capable of expressing a pathogen determinant, such as a secondary metabolite such as for example a toxin or a gene-product which does not occur naturally in environment, for example the gut in the human organism or an animal where the pathogen determinant is produced an optionally secreted to the surrounding by the pathogen bacteria.

According to one presently preferred hypothesis, the fluid composition according to the invention is inhibiting or eliminating the production of the pathogen determinant. According to another hypothesis, the growth of the pathogen bacteria is inhibited or eliminated when it is contacted with the composition according to the invention. It is also possible that both growth and pathogen determinant production is inhibited or eliminated at the same time.

The anti-bacterial means is particularly useful in eliminating or inhibiting the growth of bacteria selected from the group of bacteria consisting of Achromobacter xylosoxidans, Acinetobacter calcoaceticus, preferably A. anitratus, A. haemolyticus, A. alcaligenes, and A. Iwoffii, Actinomyces israelii, Aeromonas hydrophilia, Alcaligenes species, preferably A. faecalis, A. odorans and A. denitrificans, Arizona hinhshawii, Bacillus anthracis, Bacillus cereus, Bacteroides fragilis, Bacteroides melaninogenicus, Bordetella pertussis, Borrelia recurrentis, Brucella species, preferably B. abortus, B. suis, B. melitensis and B. canis, Calymmatobacterium granulomatis, Campylobacter fetus ssp. intestinalis, Campylobacter fetus ssp. jejuni,
Chlamydia species, preferably C. psittaci and C. trachomatis, Chromobacterium violaceum, Citrobacter species, preferably C. freundii and C. diversus, Clostridium botulinum, Clostridium perfringens, Clostridium difficile, Clostridium tetani, Corynebacterium diphtheriae, Corynebacterium, preferably C. ulcerans, C. haemolyticum and C. pseudotuberculosis, Coxiella burnetii, Edwardsiella tarda,

Eikenella corrodens, Enterobacter, preferably E. cloacae, E. aerogenes, E. hafniae (also named Hafnia alvei) and E. agglomerans, Erysipelothrix rhusiopathiae,

Escherichia coli, Flavobacterium meningosepticum, Francisella tularensis, Fusobacterium nucleatum, Gardnerella vaginalis, Haemophilus ducreyi,

Haemophilus influenzae, Helicobacter species, Klebsiella species, preferably K. pneumoniae, K. ozaenae and K. rhinoscleromatis, Legionella species, Leptospira interrogans, Listeria monocytogenes, Moraxella species, preferably M. lacunata and M. osloensis, Mycobacterium bovis, Mycobacterium leprae, Mycobacterium tuberculosis, Mycoplasma species, preferably M. pneumoniae, Neisseria gonorrhoeae, Neisseria meningitidis, Nocardia species, preferably N. asteroides and N. brasiliensis, Pasteurella multocida, Peptococcus magnus, Plesiomonas shigelloides, Proteus species, preferably P. mirabilis, P. vulgaris, P. rettgeri and P. morganii (also named Providencia rettgeri and Morganella morganii respectively), Providencia species, preferably P. alcalificiens, P. stuartii and P. rettgeri (also named Proteus rettgeri), Pseudomonas aeruginosa, Pseudomonas mallei,
Pseudomonas pseudomallei, Rickettsia, Salmonella species, preferably S. enteridis, S. typhi and S. derby, and most preferably Salmonella species of the type Salmonella DT104, Serratia species, preferably S. marcescens, Shigella dysenteriae, S. flexneri, S. boydii and S. sonnei, Spirillum minor, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus, Streptobacillus moniliiformis, Streptococcus, preferably S. faecalis, S. faecium and S. durans, Streptococcus agalactiae, Streptococcus pneumoniae, Streptococcus pyogenes, Treponema carateum, Treponema pallidum, Treponema pertenue, preferably T. pallidum, Ureaplasma urealyticum, Vibrio cholerae, Vibrio parahaemolyticus,

Yersinia enterocolitica, and Yersinia pestis.

There is also provided a means for eliminating or inhibiting the growth of lower eucaryots comprising for example yeast and fungide, preferably lower eucaryots selected from the group consisting of phycomycetes, ascomycets, basidiomycets,
deuteromycet and fungi imperfecti. Pathogenicity of lower eucaryots is defined as for bacteria herein above.

There is also provided a means for eliminating a virus, preferably a virus selected from the group consisting of Poxvirus, Herpesvirus, Adenovirus, Papovavirus, Parvovirus, Picornavirus, Togavirus, Myxovirus, Paramyxovirus, Reovirus, Rhabdovirus, Retrovirus, particularly Human Immunodeficient Virus (HIV) and Arenavirus.

According to the present invention, it is also possible to treat various conditions in a human being or and animal, said conditions being caused by microbial organisms. The treatment comprises contacting the respective microbial organisms with a composition according to the invention, preferably in the form of a fluid composition. The fluid composition is administered to a human being or an animal infected by a microbial organism, such as for example a pathogen bacteria or a lower eucaryot, such as for example a yeast or a fungi.

It is according to the invention possible to use the composition in the form of an antimicrobial means to prophylactically treat and/or alleviate and/or treat and/or cure diseases in a human being or an animal, said diseases being selected from the group consisting of Actinomycosis, Adenovirus-infections, Antrax, Bacterial dysentery, Botulisme, Brucellosis (Bang's disease), preferably caused by B. melitensis and B. suis, Candidiasis, Cellulitis, Chancroid, Kolera, Coccidioidomycosis, Acute afebril, Conjunctivitis, Cystitis, Dermatophytosis, Difteri, Bacteriel Endocarditis, Epiglottitis, Erysipelas, Erysipeloid, Gastroenteritis, Genital herpes, Glandulae, Gonorrhea, Viral Hepatitis, Histoplasmose, Impetigo, Mononucleosis, Influenza, Legionnaires disease, Spedalskhed, Leptospirosis, Lyme disease, Melioidosis, Meningitis, Fåresyge, Nocardiosis Nocardia asteroides, Nongonococcal urethritis, Pinta, Pest, Pneumococcal lungebetaendelse, Poliomyelitis, Primary lung infection, Pseudomembranøs enterocolitis, antibiotic-associated Puerperal sepsis, Rabies, Relapse- feber, Rheumatic fever, Rocky Mountain spotted-fever, Rubella, Rubeola, Nældefeber, Staphylococcal scalded skin syndrome, Streptococcal pharyngitis (strep throat), Syfilis, Tetanus, Toxic shock syndrome, Toxoplasmosis, Tuberculosis, Tularemia, Typhoid fever, Tyfus, Vaginitis, Varicella, verrucae, Pertussis, Framboesia (Yaws) and Yellow fever.
In a particularly preferred embodiment, there is provided a fluid composition according to the invention obtained by a method comprising the step of contacting water or a aqueous solution with a charged particle, preferably a ion, or an electrical current of charged particles, preferably ions, said charged particles or electrical current of charged particles being provided by an ion generator or electrodes having an electrical potential and being connected to a power source. The fluid composition in one preferred embodiment is contacted by charged particles in the form of an electrical current of from about 1.5 \( \mu \)A to about 6.6 \( \mu \)A in about 1 hour. The composition is obtainable in a preferred embodiment by provision of a total charge of from about 5.4 mC to about 23.8 mC per about 32 ml of the fluid composition.

The current may in one embodiment be varied from about 0.01 \( \mu \)A to about 150 \( \mu \)A, such as from about 0.05 \( \mu \)A to about 100 \( \mu \)A, for example from about 0.1 \( \mu \)A to about 50 \( \mu \)A, such as from about 0.2 \( \mu \)A to about 25 \( \mu \)A, for example from about 0.3 \( \mu \)A to about 20 \( \mu \)A, such as from about 0.4 \( \mu \)A to about 15 \( \mu \)A, for example from about 0.5 \( \mu \)A to about 12 \( \mu \)A, such as from about 0.6 \( \mu \)A to about 10 \( \mu \)A, for example from about 0.7 \( \mu \)A to about 8.0 \( \mu \)A, such as from about 0.8 \( \mu \)A to about 6.0 \( \mu \)A, for example from about 0.9 \( \mu \)A to about 4.0 \( \mu \)A, such as from about 1.0 \( \mu \)A to about 2.5 \( \mu \)A, for example from about 1.1 \( \mu \)A to about 2.2 \( \mu \)A, such as from about 1.2 \( \mu \)A to about 2.0 \( \mu \)A, such as from about 1.3 \( \mu \)A to about 1.8 \( \mu \)A, for example from about 1.4 \( \mu \)A to about 1.6 \( \mu \)A, such as about 1.5 \( \mu \)A.

The current in another embodiment may be varied from about 0.01 mA to about 150 mA, such as from about 0.05 mA to about 100 mA, for example from about 0.1 mA to about 50 mA, such as from about 0.2 mA to about 25 mA, for example from about 0.3 mA to about 20 mA, such as from about 0.4 mA to about 15 mA, for example from about 0.5 mA to about 12 mA, such as from about 0.6 mA to about 10 mA, for example from about 0.7 mA to about 8.0 mA, such as from about 0.8 mA to about 6.0 mA, for example from about 0.9 mA to about 4.0 mA, such as from about 1.0 mA to about 2.5 mA, for example from about 1.1 mA to about 2.2 mA, such as from about 1.2 mA to about 2.0 mA, such as from about 1.3 mA to about 1.8 mA, for example from about 1.4 mA to about 1.6 mA, such as about 1.5 mA.

In a further embodiment, the current may be varied from about 0.01 A to about 150 A, such as from about 0.05 A to about 100 A, for example from about 0.1 A to about
50 A, such as from about 0.2 A to about 25 A, for example from about 0.3 A to about 20 A, such as from about 0.4 A to about 15 A, for example from about 0.5 A to about 12 A, such as from about 0.6 A to about 10 A, for example from about 0.7 A to about 8.0 A, such as from about 0.8 A to about 6.0 A, for example from about 0.9 A to about 4.0 A, such as from about 1.0 A to about 2.5 A, for example from about 1.1 A to about 2.2 A, such as from about 1.2 A to about 2.0 A, such as from about 1.3 A to about 1.8 A, for example from about 1.4 A to about 1.6 A, such as 1.5 A.

The current may be provided in a period of hour from about 0.01 hour to about 5 hours, for example from about 0.05 hour to about 4.5 hours, such as from about 0.1 hour to about 4.0 hours, for example from about 0.2 hour to about 3.5 hours, such as from about 0.4 hour to about 3.0 hours, for example from about 0.5 hour to about 2.5 hours, such as from about 0.6 hour to about 2.0 hours, for example from about 0.7 hour to about 1.8 hours, such as from about 0.8 hour to about 1.6 hours, for example from about 0.85 hour to about 1.4 hours, such as from about 0.9 hour to about 1.2 hours, for example from about 0.95 hour to about 1.1 hours, such as about 1.0 hour.

The overall charge being provided to the composition according to the invention is from about 0.01 mC to about 10000 mC, such as from about 0.05 mC to about 8000 mC, for example from about 0.1 mC to about 4000 mC, such as from about 0.2 mC to about 2000 mC, for example from about 0.4 mC to about 1000 mC, such as from about 0.6 mC to about 800 mC, for example from about 0.8 mC to about 600 mC, such as from about 1.0 mC to about 300 mC, for example from about 1.2 mC to about 200 mC, such as from about 1.4 mC to about 100 mC, for example from about 1.6 mC to about 80 mC, such as from about 1.8 mC to about 60 mC, for example from about 2.0 mC to about 40 mC, such as from about 2.2 mC to about 30 mC, for example from about 2.4 mC to about 25 mC, such as from about 2.6 mC to about 20 mC, for example from about 2.8 mC to about 18 mC, such as from about 3.0 mC to about 16 mC, for example from about 3.2 mC to about 14 mC, such as from about 3.4 mC to about 12 mC, for example from about 3.6 mC to about 10 mC, such as from about 3.8 mC to about 8 mC, for example from about 4 mC to about 7 mC, para 6.5 mC to about 4.4 mC to about 6 mC, such as from about 4.6 mC to about 5.8 mC, for example from about 4.8 mC to about 5.7
mc, such as from about 5.0 mc to about 5.6 mc, for example from about 5.2 mc to about 5.5 mc, such as about 5.4 mc.

The fluid composition in a particularly preferred embodiment is provided according to the invention for use as a medicament and/or for use in a preventative, therapeutic or curative treatment of a condition in a human being or an animal. When the composition is used as medicament, it is preferably used in a pharmaceutically effective amount, which depends on the condition to be treated and the form of administration which is preferred for this treatment.

Furthermore, there is provided the use of an electrically treated composition in the manufacture of a medicament for treating a suffering in a human being or an animal. The treatment comprises using the medicament in a method for therapy or surgery, or a method of diagnostics and a particularly preferred embodiment, a method of prophylactically or therapeutically treating an allergic condition, preferably a treatment of the condition, when it is occurring in the airways, such as asthma.

There is also described the use of a composition in the manufacture of a medicament for prophylactically or therapeutically treating a condition of infection in the airways, such as an obstructive airways disease, which as the asthmatic condition described herein above, may occur sporadically or periodically or chronically. The condition may lead to an increased mucoid mucus production, such as it is the case in bronchitis.

In a further embodiment, there is provided the use of an electrically treated composition in the manufacture of a medicament, said medicament being effective in reducing or eliminating secretion of histamine from mast cells. The manufactured medicament is, furthermore, effective in controlling the intracellular pH value in a cell and preferably furthermore effective in reducing the increase in the intracellular pH value in a cell during an allergic attack.

Furthermore, there is provided an electrically treated composition in the manufacture of a medicament which is effective in prophylactically or therapeutically treating, or in diagnosing, a cancer cell, a cardiovascular disease, an Immunodeficient condition, stressed and/or sick cells as well as prophylactically or therapeutically
treating a skin disease, such as eczema, fungus, a bacteria infection or psoriasis. The use is also aimed at manufacturing a medicament that is effective in increasing the immune response of a cell during a bacterial or viral infection of said cell.

In a further embodiment, there is provided a method for treating a suffering in a human being or an animal, said method comprising contacting the suffering with the electrically treated composition according to the invention. The method comprises treating by prophylaxis, therapy or surgery and/or a method for diagnostics, such as a method for prophylactically or therapeutically treating an allergic condition, preferably a condition occurring in the airways such as asthma.

The method according to the invention is also aimed at a treatment comprising a method of prophylactically or therapeutically treating a condition of infection in the airways, preferably a condition comprising an obstructive airways disease, which just as the asthmatic condition is sporadically or periodically or chronically occurring. The condition may lead to an increased mucoid mucous production and is in preferred embodiment bronchitis.

In a particularly preferred embodiment, the method of treatment according to the invention is effective in reducing or eliminating secretion of histamine from mast cells, effective in controlling the intracellular pH value of a cell, and effective in reducing the increased value of the intracellular pH in a cell during an allergic attack.

The method of treatment is also effective in prophylactically or therapeutically treating, or in diagnosing, a cancer cell, a cardiovascular disease, an Immunodeficient condition, stressed and/or sick cells as well as prophylactically or therapeutically treating a skin disease, such as eczema, fungus, a bacteria infection or psoriasis. The method of treatment is also useful in increasing the immune response of a cell during a bacterial or viral infection of said cell.

There is also provided in further embodiments compositions according to the invention for use in methods – and the use of compositions in the methods – comprising for example washing of organ transplants and/or transplantation of skin or hair.
In another embodiment, there is provided a composition for use in oral or subcutaneous, such as intravenous administration of for example a medicament or for use as a dialysis solution.

It is according to one presently preferred hypothesis shown that the composition by transferring said composition to the skin of a human being or an animal suffering from internal bleeding, such as a hematome, is effective in treating the internal bleeding and effective in improving a curative process. The composition is also assumed to be effective in treatment of insect bites and snake bites.

The composition will according to one presently preferred hypothesis also be effective in treating an infection condition in a human being or an animal, as well as effective in treating skin being burned following scolding or sun burning.

According to one preferred embodiment within the field of hygiene, the compositions according to the invention are useful in a mouth hygienic treatment, said treatment comprising either a liquid mouth hygienic solution, contacting the teeth or the oral cavity, or by brushing the teeth. It is also possible to use the composition according to the invention in connection with bathing or washing a human being or an animal, said bathing or washing having a health improving effect on the human being or the animal.

Within the field of horticulture, it is according to one presently preferred hypothesis possible to use the composition according to the invention in order to promote the growth and health of plants.

There is also describe an embodiment of the invention, wherein the composition is effective in promoting the organoleptic qualities in beer, wine and alcoholic beverages in general. It is, thus, possible to provide the wine with a property that results in the contents of histamine in said wine being reduced, or that the taste of the wine or for example the colour of the wine is affected as well as the bouquet of said wine being improved.
According to yet another presently preferred hypothesis, it is possible to use the composition according to the invention in an improved treatment of waste water. In yet another embodiment, there is provided a method of providing sea water with such properties that are useful for fish-farming or useful in improving the quality of fish and the health of fish.

It is possible to dissolve a powdery material in a solution such as for example water and treat said dissolved powdery material by a current of for example atmospheric ions or a current provided by electrodes having an electrically potential and being connected to a power source. The treatment will provide the powdery material with properties that are useful in the production of for example chewing gum or lozenges, and it is possible to provide these products with properties that are promoting a healthy mouth hygiene. The treated powdery material can also be brought into contact with for example the skin of a human being or an animal and provide a curative effect or a pain alleviating effect. According to another embodiment, there is provided an powdery material being treated in accordance with invention, said material being brought into contact with crops and plants in a field and said contact providing a growth promoting effect or a prophylactically effect, an effect capable of reducing the occurrence of diseases and an effect of eliminating said diseases.

In another preferred embodiment, it is possible to treat water containing emulsion, such as for example butter, margarine, mayonnaise, gels or paint and by doing so obtain an increased shelf-life and durability. In a particularly preferred embodiment, it is possible to obtain a reduction or elimination of microbial growth in said emulsion. In another particularly preferred embodiment, the self-life of milk can be improved by treating the milk with the composition according to the invention.

A preferred and not-limiting embodiment of the invention will be described herein below in the example. the person skilled in the art will be capable of understanding and evaluating the example and not interpret this in a limiting way.

**Description of the drawing**

Figure 1 illustrates a current passing through two plane electrodes.
Figure 2 illustrates a current passing through two cylindrical electrodes.

Figure 3 illustrates an experimental design for treating a composition with atmospheric ions, optionally in combination with a ion generator which preferably is connected to a neutral electrode. Ions generated by the ion generator will be brought into contact with the surface of the liquid and result in an electrical current in the liquid. This electrical current is measurable by means of an electrometer.

Figure 4 shows an experimental design for treating a composition with an electrical current. A copper electrode (7.25 cm in diameter) is brought in contact with the surface of the solution. The electrode is connected to one terminal of a generator providing a constant current and the second terminal is neutral. The electrometer monitors the electrical current in the composition.

Figure 5 shows the result of sending a current through the cell liquid in two different ways and, subsequently, transferring mast cells to the treated cell liquid. The cell liquid must first be treated with an electrical current of about 1.5 μA in 1 hour, corresponding to the transfer of a total charge of about 5.4 mC respectively, and the effect of an electrical current of essentially the same value generated by the current generator and having the same direction. Measurements are made without adding compound 48/88 and by adding compound 48/80 in three different concentrations. The figures show the known effect of compound 48/80 on histamine secretion. It is, furthermore, evident that the secretion of histamine is reduced even quite significantly in the case where the liquid has been electrically treated. The effect of negative ions and a direct electrical current from metal electrodes is perceived according to one presently hypothesis to be the same.

Figure 6 shows a comparison of the effect on positive and negative ions. By regulating the distance of the ionisator from the surface of the liquid, the electrical current of both positive and negative ions is kept as close to 1.5 μA as possible. The time of exposure is also in this case 1 hour. Again, a marked reduction in the histamine secretion is observed.

Figure 7 shows the intracellular pH value as function of time determined during the experiments described herein above. At the time T = 300 s, compound 48/80 is
added and it can be seen that the cells present in the liquid, that is treated either with ions (black curve) or directly with electrical current (green curve), is inhibited in their pH response when stimulated with compound 48/89. A control (red curve) shows the untreated cells. It can be seen that treatment with an electrical current reduces the observed increase in the intracellular pH value. The effect is the same for the treatment with the ion generator and with treatment directly with an electrical current.

Example 1

Analysis of histamine secretion from peritoneal mast cells under the influence of an electrically treated composition.

The following analyses of mast cells makes it possible to gain an insight into the signal mechanisms, which via exocytose leads to secretion of mediators. Histamine secretion is typically a result of an attack of asthma or allergy and gives rise to discomfort and unpleasant side-effects. The peritoneal mast cells of the rat are the cells that contain histamine. These cells can be isolated and purified to a degree of purity of more than 95% and have for many years with success been used in histological, biochemical and pharmacological examinations of the cellular changes which takes place under the secretory process. Even though some heterogeneity exists among mast cells in different species and in different parts of the body of single species, certain similarities exist between the steps that lead to secretion via exocytose. Therefore, the mast cell is a good model for analysing secretion by means of exocytos (Diamant, 1990).

Technical terms and explanations

The below mentioned explanations and technical terms aims to introduce words and technical terms used in the description of the achieved results.

Spontaneous histamine: Indicates if the cells which have been removed from the rat and are now present in a cell liquid have been damaged during the purification process, or if the histamine secretion is generated by the cell liquid, wherein the cells are present. If spontaneous histamine is below 5%, the cells have not been
damaged. If, however, the spontaneous histamine is above 5%, the cells are in a form of stress. Spontaneous histamine is a control indicating whether the cells, which are used in the experiments, initially appears to behave as normal, healthy cells.

**Histamine secretion:** Histamine secretions is a term indicating that the cell is secreting its granular contents to the surrounding media.

**Exocytosis:** The process whereby the mast cell is capable of secreting histamine.

**Cell suspension:** Cells and cell liquid.

**Zero electrode:** A neutral electrode present in an ion generator. Is necessary in order for the current to pass through the cell liquid.

**Compound 48/80:** During an attack of allergy or asthma, the mast cells are provoked to secrete histamine. In the laboratory, it is possible via a chemically produced, secretory active compound, termed compound 48/80, to simulate the secretory process taking place in the body, when a mast cell is secreting histamine. Histamine secretion in the body during an asthma or allergy response is thought not to be above 20%. By adding different concentrations of 48/80, it is possible to make the cell secrete different amounts of its content of histamine. On that basis, it is possible to examine the extent to which a treatment may suppress the unwanted secretion of histamine from mast cells.

**Materials and methods**

**Composition of a cell liquid.** A preferred cell liquid, buffer B, according to the invention contains, 140 mM NaCl, 1 mM CaCl₂, 1.2 mM MgSO₄, 4.0 mM KCl, 2.46 mM Na₂HPO₄, 0.615 mM KH₂PO₄, 10 mM HEPES, 5.6 mM glucose, and 0.1% BSA (Bovint Serum Albimun). The cell liquid is preferably comprised so that it corresponds to the composition of the physiological plasma of the rat.
Isolation of peritoneal rat mast cells. The rats are anaesthetised with CO₂ gas, whereafter they are decapitated in a guillotine. 10 ml cell liquid (ambient temperature) are containing 50 μg/ml heparin, to avoid coagulation of any present blood from damaged blood vessels, are injected in the abdominal cavity of the rat to a small hole which has previously been cut. The hole is closed with a peang, whereafter the abdomen is massaged in about 1 min. In this way, the mast cells are released from the surface of the tissue of the abdominal cavity, whereafter a mixed population of peritoneal mast cells is obtained. The extraction of the cells is achieved by carefully cutting the wall of the abdominal cavity and removing the internal organs. The latter is importing since they can easily be perforated when the mast cells are extracted. If this happens, various compounds are released to abdominal cavity, which may cause problems during the further isolation procedure. Abdominal liquid is carefully removed from the abdominal cavity with a syringes and is placed in a 45 ml centrifuge tube, which is already placed on ice (about 4°C). The rest of the isolation procedure takes place at about 2-4°C.

The cells are centrifuges (230 g in 10 min at 4°C). The supernatant is removed and the cells are resuspended in 0.5 ml cell liquid. The cell suspension is hereafter transferred to an ostonic Percoll (density: 1.017 g/ml), which is centrifuged at 10,000 g in 20 min at 4°C.

This generates a density gradient in which the mast cells are located in the bottom third of gradient and the peritonealeleukocytes and macrophages and any optionally erythrocytes are located in the top two thirds. The top two thirds of the Percoll gradient is removed and the mast cells are transferred to a 45 ml centrifuge tube in which the cells are washed twice with 40 ml cell liquid each followed by a centrifugation (230 g in 10 min at 4°C). This isolation procedure provides 96-99% mast cells. After the last wash, the supernatant is removed and the cells are resuspended in a know volume so that the cell density is known. The cell suspension is transferred to a incubation tubes (10 ml test tubes). 2 x 20 μl is removed for cell counting and 2 x 40 μl is removed for histamine determination.

Stimulation of mast cells and determination of histamine. In the experiments where the mast cell is stimulated for secretion, the chemically synthesised polypep-
tide compound 48/80 is used. Histamine release is examined by transferring 40 μl cell suspension to a 10 ml test tube. The samples are diluted with buffer to a volume of 500 μl. The samples are now incubated with the selected gas mixture in various periods of time. Incubation is terminated by adding 1.5 ml cold buffer (2°C). The samples are centrifuged (230 g in 10 min at 4°C), whereafter the supernatant is removed to a new test tube and frozen. These samples will show the spontaneous histamine secretion which may have taken place during the incubation. The pelleted cells are lysed by boiling for 3 min. in 250 μl physiological selin (0.9% NaCl). After boiling, the samples are diluted with a 1.75 ml cold buffer (2°C), whereafter they are centrifuged (0 min at 500 g). The supernatant is removed to a new test tube and frozen down. These samples will be indicative of the cellular histamine content. Freeze is optionally, however, preferred since it is easier to freeze the samples and test only a few days during the month instead of testing 4 samples during each day.

The determination of the histamine content in the samples is carried out as described by Shore et al. (1959). This method involves condensation of o-phthaldehyde (OPT) with histamine at a high pH. In a spectro-fluorometer, the condensed substance will fluoresce at a low pH at 360 nm. This light can be measured at 450 nm. In order to determine the exact content of histamine in the samples, at standard histamine curve is made indicating the quantity of light as a function of various known histamine concentrations. The concentration of histamine (μg/ml) in these standards are 0.250; 0.200; 0.125; 0.050; 0.025 respectively in a total volume of 1 ml (the standards are mixed in buffer). In order to correct the samples for background fotofluorecens, a histamine free sample of 1 ml buffer is also made. The samples are thawed. A suitable amount of the test volume are transferred to a new test tube and diluted with buffer to a final volume of 1 ml. Thereafter, all the samples are treated the same, irrespective of whether they are samples or standards. 1 ml HCl (0.1 N) is added to denature proteins that may contain histidine since histidine can disturb the measurement histamine. In order to achieve a high pH prior to addition of OPT, 0.4 ml NaOH (1N) was added to the samples. 0.1 ml 1% OPT solution (74 mM) was added to the histamine at T=0 min., and 0.2 ml H₃PO₄ (2M) was added at T=4 min., and this caused a significant reduction in the pH value which counter acted further OPT labelling of the histamine and ensures a low pH as required by the measurement procedure. All the samples are centrifuges in 10 min. at 1000 g, whereafter the supernatant was decanted to 1 ml quarts cuvettes. The samples
were measured in a spectro-fluorometer at an excitation of 360 nm and an emission of 450 nm. The standard curve makes it possible to determine the content of histamine in the samples. Histamine secretion is calculated as percent of the total histamine content in the cells.

Method of treating a cell liquid. Plastic bowls with a diameter of 7.25 cm and a height of 3.75 cm are applied. The bottom plate of the bowls is made of copper. The bottom plate is connected via a wire to a measurement means which all the time measures how much current passes through the cell liquid and reaches the bottom plate. When cell liquid (32 ml) is treated with a electrical current, a copper plate is placed on top of the cell liquid and in contact with cell liquid. The copper plate is also connected to a power source.

Measurement of pH. After the last wash of the isolated peritoneal rat mast cells (see above), the mast cells are resuspended in the cell liquid. The mast cells are loaded with the fluorescent indicator BCECF-AM (final concentration: 5 μM) for 30 min at 37°C in the dark (final volume 400 μl). BCECF-AM quickly enters the cells across the cell membrane in esterified, uncharged form. In the cell, BCECF-AM is hydrolysed by the esterases present in the cell. Hydrolysis results in the BCECF being charged and, thus, maintained in the cytoplasm of the cell. BCECF is an indicator that can be used to measure pH and indicate variations of pH in the cell.

After loading, the cells are washed and centrifuged (230 g for 10 min at room temperature) and resuspended in 1.9 ml of the respective assay buffer (37°C), which results in any released dye being removed prior to the experimental observations. 1.8 ml of the cell suspension is transferred to a cuvette which subsequently is placed in a thermo-static cuvette house (37°C) with a stirrer in a spectro-fluorometer.

The handling of the spectro-fluorometer and the data collection was carried out online by a computer. The BCECF fluorescent was registered in "ratio mode" by changing the wave length of the excitation from 490 nm and 435 nm in intervals of 0.5 seconds. The emission was measured at 530 nm. The BCECF fluorescent is independent of pH at an excitation wave length of 435 nm (Rink, 1988).
calculated ratio of the two emission signals at 490 and 435 nm excitation respectively, gives an indication of the intracellular pH, which is independent of differences in the intracellular BCECF concentration, the number of mast cells, and optionally artefacts related to experimental changes (for example changes in the reflection of light occurring due to changes of the cell volume) (Rink 1998).

Calibration of the fluorescent-signal was carried out with nigericin/K⁺ method (Thomas et al. 1979) and the 490/440 ratio was linear between pH 6.4-7.6 results.

**Results**

Figure 5 shows the result of sending a current through the cell liquid in two different ways and, thereafter, adding mast cells to the treated liquid. The current provided by the electrodes was about 1.5 μA and it was passed through the liquid for 1 hour (white bar indicated by "II"). Atmospheric negative ions were provided with current corresponding to about 1.5 μA for 1 hour (dark grey bar indicated by "III"). The cells were, thereafter, treated with 0.1; 0.2 and 0.3 μg/ml compound 48/80, respectively. The light gray bar indicated by "I" is a control of how much histamine the cells secrete when they are merely added untreated cell liquid.

It turns out that a current through the cell liquid of about 1.5 μA provided by the added electrons is capable of inhibiting the cells in secreting up to 37% histamine which is sufficient to inhibit a physiological response during an asthmatic attack, where the histamine secretion typically is a maximum of about 20%.

Figure 6 shows an experiment whereby the current is provide by atmospheric negative ions and a current is provided by the atmospheric negative ions to the cell liquid, which are thereafter added to the cells. A current of about 1.5 μA provided by atmospheric positive ions for 1 hour (white bar indicated by "II") and a current of about 1.5 μA provided by atmospheric negative ions for 1 hour (dark grey bar indicated by "III") was used respectively. The cells were, thereafter, treated with 0.1; 0.2 and 0.3 μg/ml compound 48/80, respectively. The light gray bar indicated by "I" is again a control of how much histamine the cells secrete when they are merely added untreated cell liquid.
The results again document that when a current of about 1.5 μA provided by the added charged particles is being passed through to the cell liquid, the cells are prevented from secreting up to 37% histamine, which is enough to inhibit the physiological response during an asthma attack, where histamine secretion is a maximum of about 20%.

Figure 7 shows that the intracellular pH changes during the secretion of histamine (trace indicated by "B"). The observed pH increase is primarily due to an activation of protein kinase C and Na⁺/H⁺ exchange, wherein the Na⁺ is transported in and the H⁺ is transported out of the mast cell in a reaction driven by the electro-chemical gradient for natrium into the cell.

Figure 7 shows that the intracellular pH increase during histamine secretion is also reduced, when the cells are added a cell liquid treated with a current provided by electrodes having an electrical potential (about 1.5 μA for 1 hour) (trace indicated by "C") or provided by atmospheric negative ions (about 1.5 μA for 1 hour) (trace indicated by "A").

Example 2

A suspension of Staphylococcus aureus 502A was adjusted to an optical density 0.2 at 546 nm equivalent of approximately 1×10⁸ bacteria / ml was prepared. This suspension was diluted to 1:10 in saline. The bacterial suspensions were then treated for one hour with either ionized air or direct current.

20 ml of the suspension was transferred to a 50 ml steril tube and then incubated for 24 hrs at 37 oC. Following incubation 0.1 ml of this suspension and two 0.1 ml aliquotes of subsequent 1:10 dilutions were plated on blood agar plates.

Colony forming units (CFU) were counted after overnight incubation at 37oC. The experiment was performed in triplicates. The data are shown as the mean number of CFU / plate.
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<thead>
<tr>
<th>Inoculum</th>
<th>Ionized air</th>
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<th>No treatment</th>
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<td></td>
<td>$1 \times 10^4$</td>
<td>&gt; 100 (a)</td>
<td>&gt; 100 (b)</td>
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a: small colonies.
b: large colonies.

**Example 3**

A suspension of *Staphylococcus aureus* 502A was adjusted to an optical density 0.2 at 546 nm equivalent of approximately $1 \times 10^8$ bacteria / ml was prepared. This suspension was diluted to 1:10 in saline. The bacterial suspensions were then treated for one hour with either ionized air or direct current. 20 ml of the suspension was transferred to a 50 ml sterile tube and then incubated for 24 hrs at 37°C. On day 2 the bacterial suspension was treated again for one hour with either ionized air or direct current. Following incubation 0.1 ml of this suspension and two 0.1 ml aliquotes of subsequent 1:10 dilutions were plated on blood agar plates. Colony forming units (CFU) were counted after overnight incubation at 37°C. The experiment was performed in triplicates. The data are shown as the mean number of CFU / plate.

<table>
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<td>&gt; 100 (a)</td>
<td>&gt; 100 (b)</td>
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</table>
a: small colonies; b: large colonies.

References


Palti Y, De Nour E, Abrahamov A. The effect of atmospheric ions on the respiratory system of infants. Pediatrics 1966;38: 405-11.


Patent claims

1. Method of providing a composition with a predetermined property, said property being obtainable by contacting said composition with a charged particle, preferably an ion.

2. Method of claim 1, wherein said predetermined property is essentially sustainable over time.

3. Method of claim 1, wherein said composition is transiently contacted by said charged particle.

4. Method of claim 1, wherein said predetermined property is essentially sustainable over time, and wherein said composition is transiently contacted by said charged particle.

5. Method of claim 1, wherein said predetermined property remains associated with said composition for a period of time which is at least essentially the same as the period of time in which said composition is contacted by said charged particle.

6. Method of claim 1, wherein said predetermined property is essentially sustainable over time irrespective of the period of time in which said composition is contacted by said charged particle.

7. Method of claim 1, wherein said predetermined property is sustainable for at least one week, such as one month, for example six months, for example one year, such as two years, for example five years, such as ten years.

8. Method of claim 1, wherein said contacting of said charged particle results in the passage of a current through said composition.

9. Method of claim 2, wherein said current corresponds to at least about 0.01 μA and preferably less than about 1.5 A.
10. Method of claim 3, wherein said current results in a charge being provided to said composition, said charge being at least about 0.01 mC and preferably less than 10000 mC.

11. Method of claim 1 wherein said composition comprising said predetermined property is a medicament.

12. Composition obtainable by the method of any of claims 1 to 11.

13. Composition according to claim 12 for use as a medicament.


15. Composition according to claim 12 for use in a method for treatment of the human body by therapy.

16. Composition according to claim 12 for use in a diagnostic method practised on the human or animal body.

17. Composition according to claim 12 for use in a method of prophylactically treating an allergic condition in an individual.

18. Composition according to claim 12 for use in a method of therapeutically treating an allergic condition in an individual.

19. Composition according to claim 12 for use in a diagnostic method capable of diagnosing an allergic condition in an individual.

20. Composition according to any of claims 17 to 19, wherein said allergic condition is occurring in the airways of said individual.

21. Composition wherein said allergic condition is selected from the group consisting of asthma, rhinitis, urticaria, and allergic conjunctivitis.
22. Composition according to claim 12 for use in a method of prophylactically treating an infection in an individual.

23. Composition according to claim 12 for use in a method of therapeutically treating an infection in an individual.

24. Composition according to claim 12 for use in a diagnostic method capable of diagnosing an infection in an individual.

25. Composition according to any of claims 22 to 24, wherein said infection is occurring in the airways of said individual.

26. Composition according to claim 25 wherein said infection is an obstructive disease of the airways.

27. Composition according to claim 25, wherein said condition is sporadically, periodically or chronically occurring.

28. Composition according to claim 25, wherein said infection results in an increased mucoid production.

29. Composition according to claim 25, wherein said infection is bronchitis.

30. Composition according to claim 12 for use in a method of treatment of a human being or an animal, said method being capable of reducing or eliminating the secretion of histamin from mast cells.

31. Composition according to claim 12 for use in a method of treatment of a human being or an animal, said method being capable of controlling the intracellular pH value of a human or animal cell.

32. Composition according to claim 12 for use in a method of treatment of a human being or an animal, said method being capable of reducing the increase in the intracellular pH-value in a human or animal cell during an allergic attack.
33. Composition according to claim 12 for use in a method of prophylactically treating in a human or an animal body a cell at risk of developing cancer, or for therapeutically treating a cancer cell.

34. Composition according to claim 12 for use in a method of prophylactically or therapeutically treating a cardiovascular disease in an individual.

35. Composition according to claim 12 for use in a method of diagnosing an immune deficient condition in an individual.

36. Composition according to claim 12 for use in a method of prophylactically or therapeutically treating a rheumatic condition in an individual.

37. Composition according to claim 12 for use in a method of prophylactically or therapeutically treating a lesion to the skin including burns in an individual.

38. Composition according to claim 12 for use in a method of prophylactically or therapeutically treating a disease to the skin in an individual.

39. Composition according to claim 12 for use in a method of prophylactically or therapeutically treating eczema, a fungus infection, a bacterial infection, exanthema, or psoriasis in an individual.

40. Composition according to claim 12 for use in a method of boosting the immune response of a human or animal cell.

41. Use of the composition according to claim 12 in the manufacture of a medicament for the treatment of a condition in a human or animal in need of said treatment.

42. Use of claim 41, wherein said medicament is capable of prophylactically treating an allergic condition in an individual.

43. Use of claim 41, wherein said medicament is capable of therapeutically treating an allergic condition in an individual.
44. Use of claim 41, wherein said medicament is capable of diagnosing an allergic condition in an individual.

45. Use of claim 41, wherein said medicament is capable of prophylactically treating an infection in an individual.

46. Use of claim 41, wherein said medicament is capable of therapeutically treating an infection in an individual.

47. Use of claim 41, wherein said medicament is capable of diagnosing an infection in an individual.

48. Use of claim 41, wherein said medicament is capable of prophylactically or therapeutically treating a cardiovascular disease in an individual.

49. Use of claim 41, wherein said medicament is capable of diagnosing an immunodeficient condition in an individual.

50. Use of claim 41, wherein said medicament is capable of prophylactically or therapeutically treating a rheumatic condition in an individual.

51. Use of claim 41, wherein said medicament is capable of prophylactically or therapeutically treating a lesion to the skin including burns in an individual.

52. Use of claim 41, wherein said medicament is capable of prophylactically or therapeutically treating a disease to the skin in an individual.

53. Use of claim 41, wherein said medicament is capable of prophylactically or therapeutically treating eczema, a fungus infection, a bacterial infection, exanthema, or psoriasis in an individual.

54. Use of claim 41, wherein said medicament is capable of boosting the immune response of a human or animal cell.
Fig. 1  Plane electrodes
Fig. 2  Cylindrical electrodes
Fig. 3
Fig. 6
Fig. 7
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IP: C 7 AG1K41/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
IP: C 7 AG1K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>GB 2 335 485 A (BRODSKY STANISLAV ; BRODSKY) ANN (GB) 22 September 1999 (1999-09-22) page 1, paragraph 1: claims page 2, paragraph 1</td>
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</table>

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents:
  
  "A" document defining the general state of the art which is not considered to be of particular relevance
  
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Date of the actual completion of the international search 19 January 2000

Date of mailing of the international search report 02/02/2000

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3018

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Berte, M

Form PCT/ISA/210 (second sheet) (July 1992)
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### INTERNATIONAL SEARCH REPORT

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
   - because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.:
   - because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
     - See FURTHER INFORMATION SHEET PCT/ISA/210

3. ☐ Claims Nos.:
   - because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)
Continuation of Box I.2

Present claims 1-54 relate to an extremely large number of possible compositions or methods. In fact, the claims contain so many options that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely the examples 2 or 3 where suspensions of Staphylococcus aureus are treated with either ionized air or direct current.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.
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