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(54) Title: A DRESSING PRODUCT AND A COSMETIC OR MEDICAL COMPOSITION WITH *KIGELIA AFRICANA*

(57) Abstract: The present invention relates to a dressing product comprising a backing layer and an active ingredient layer comprising an extract of Kigelia africana, which active ingredient layer is coated or adhered to the backing layer and to a method of producing the dressing product. The invention further relates to a cosmetic or medical composition for topical application on the skin of a subject, which composition comprises: brine 40 - 80 %w/w an extract of Kigelia africana 2 - 15 %w/w one or more excipients 5 - 50 %w/w water balance which excipients are selected from emulsifiers, suspending agents, gelling agents, binders, fillers, surfactants, anti-oxidants, preservatives, emollients, humectants, moisturisers, natural oils, UV-absorbers, sunscreens, and thickeners. The dressing product and the composition are suitable for use in the treatment of skin damages, diseases and conditions.

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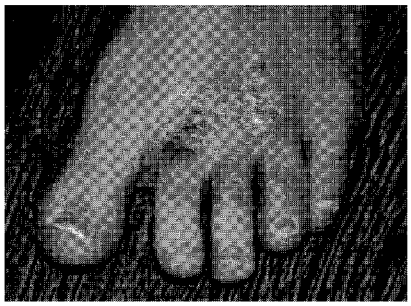

Fig. 1a

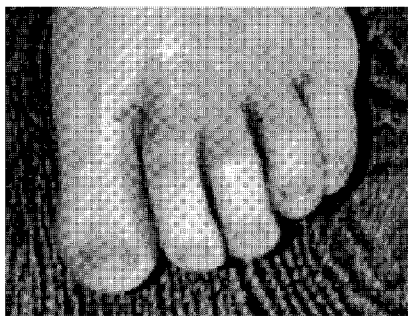

Fig. 1b

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A dressing product and a cosmetic or medical composition with *Kigelia africana*

Field of the invention

The present invention relates to a dressing product comprising an extract of *Kigelia africana*, and to a method of producing the dressing product. The invention also relates to a cosmetic or medical composition for topical application on the skin of a subject, which composition comprises an extract of *K. africana*. The dressing product and the composition are suitable for use in the treatment of skin damages, diseases and conditions. The dressing product and the composition provide a longer lasting effect of the activities of *K. africana*.

Background

In general the use of extracts and other products from the plant *Kigelia africana* for the treatment of skin diseases and conditions is well known. For example, WO 2006/002443 describes pharmaceutical and cosmetic preparations based on *K. africana*. The preparations of WO 2006/002443 may be in the form of a cream, ointment or gel, and it is intended as a general pain reliever, an anti-septic, an anti-inflammatory or an anti-pruritic. Specific applications are for the treatment of cuts, bruises, insect bites, stings, sun exposure of the skin, psoriasis, eczema, solar keratosis, and cancerous sores.

FR 2 759 910 also describes cosmetic compositions for skin care and body care containing extracts of *K. africana*. The may be used for firming of the bust, limiting hair loss, and limiting hair growth. Further skin creams of *K. africana* are provided by ZW 10292.

The constituents of *K. africana*, their extraction and known medical effects are described in *Kigelia africana* (Lam.) Benth - An overview, S. Saini, H. Kaur, B. Vherma, Ripudaman, S. K. Singh, 2009, *Nature Product Radiance*, 8: 190-197, and Comprehensive scientific demystification of *Kigelia africana*: A review, Olatunji A. Gabriel and Atolani Olubunmi, 2009, *African Journal of Pure and Applied Chemistry*, 3: 158-164. Saini *et al.*, 2009, describe how an ethanol extract was tested for pharmacological activity in animal studies in mice and in cell lines. It was concluded from the tests that ethanolic extracts

of *K. Africana* have a significant positive effect on use against skin irritation / oedema and a significant antibacterial/ antimicrobial inhibitory effect on both Gram-positive and Gram-negative bacteria

There is however still a need for further and improved products relying on the medical and cosmetic activities of *K. africana*. In particular, there is a need for products providing a longer lasting effect of the activities of *K. africana*. It is the aim of the present invention to provide improved medical and cosmetic compositions and dressings for delivery of *K. africana* extracts and methods for their production.

Summary of the invention

A first aspect the present invention relates to a dressing product comprising a backing layer and an active ingredient layer comprising an extract of *Kigelia africana*, which active ingredient layer is coated or adhered to the backing layer. The extract, e.g. an ethanolic extract, from *K. Africana*, e.g. the fruit, shows a significant effect on treatment skin diseases and conditions, such as psoriasis, eczemas, dermatitis and acne. The dressing product of the invention is suitable for application to the skin of a subject, e.g. a human subject, in order to provide the effect of the *K. africana* extract to the skin of the subject. The active ingredient layer may comprise an adhesive, preferably a hydrocolloid adhesive, allowing the dressing product to adhere to the skin of the subject. Hydrocolloid adhesives provide excellent adhesive properties to the skin of subject, so that the dressing sticks efficiently. Furthermore, the hydrocolloid adhesive will serve as a carrier for the *K. africana* extract and allowing the active compounds of *K. africana* to diffuse to the skin of the subject. In particular, the hydrocolloid adhesive absorbs moisture from damaged skin forming a liquid gel over the damaged skin resulting in delivery of the *K. africana* extract to the damaged skin. The active ingredient layer, especially in the form of a hydrocolloid adhesive, provides that the *K. africana* extract is kept in place on the skin. Thus, the combined effects of the stickiness of the hydrocolloid adhesive, and the aqueous nature, i.e. the "gel effect", allow a long-term diffusion of the active compounds of *K. africana* to the skin of the subject where the dressing product is applied. Such a long-term effect cannot readily be obtained when the *K. africana* extract is applied directly to the skin

or via a dressing not comprising a hydrocolloid adhesive. Any hydrocolloid adhesive may be employed for the dressing of the invention.

The backing layer may be any suitable material, such as a polymer film or film of non-woven polymer fibres. The polymer film may be permeable to gasses, e.g. to allow diffusion of water molecules from the skin or the dressing product, or to allow diffusion of oxygen from the surroundings to the skin. The polymer film may also be non-permeable. A preferred polymer material is polyurethane.

The active ingredient layer is coated on or adhered to the backing layer to form the dressing product. The hydrocolloid adhesive layer is generally applied to the backing layer as a hot-melt solution, which is applied in its liquid form and allowed to solidify on the backing layer. Due to the sticky and viscous properties of liquid hydrocolloid adhesives it is problematic to mix an active ingredient into the molten hydrocolloid adhesive. This is particularly relevant in industrial scale preparation of dressing products where the viscosity of the hot-melt solution may result in an uneven distribution of the active ingredient in the dressing products, even to the point where certain specimens of the dressing product contain no active ingredient. The present inventors have now found that the active ingredient, e.g. in the form of an extract, solution, suspension or the like, may be sprayed onto the dressing product during its manufacture.

Thus, in another aspect the invention relates to a method of preparing the dressing product of the invention. The method comprises the steps of:

a) providing a backing layer;

b) applying a hot-melt hydrocolloid adhesive in a liquid form to the backing layer;

c) allowing the liquid hydrocolloid adhesive to solidify;

d) providing a *Kigelia africana* extract; and

e) spraying the *K. africana* extract onto the backing layer and/or to the solidified hydrocolloid adhesive.

Thus, the *K. africana* extract may be sprayed onto the backing layer, the solidified hydrocolloid adhesive or both. It is also possible in the method of the invention to prepare a dressing product comprising several layers of the hydrocolloid adhesive where the steps b) to e) are repeated. For example, after application and formation of a layer of the hydrocolloid adhesive

and application of the *K. africana* extract, another layer of the hydrocolloid adhesive is applied followed by spraying the *K. africana* extract onto the second layer of hydrocolloid extract. The multi-layered method allows formation of a hydrocolloid adhesive on the backing layer where the amount of *K. africana* extract is controlled over the total thickness of the hydrocolloid adhesive layer.

It is also contemplated that the method is generally applicable to other active ingredients. Thus, in another aspect the invention relates to a method of preparing a dressing product for the delivery, e.g. transdermal delivery, of an active ingredient. The method comprises the steps of:

a) providing a backing layer;

b) applying a hot-melt hydrocolloid adhesive in a liquid form to the backing layer;

c) allowing the liquid hydrocolloid adhesive to solidify;

d) providing a solution or suspension of an active ingredient; and

e) spraying the solution or suspension of the active ingredient onto the backing layer and/or to the solidified hydrocolloid adhesive.

In general all features of the method of preparing the dressing product of the invention, i.e. the dressing product suitable for delivery of a *K. africana* extract, may be used in the method of preparing a dressing product for the delivery of other active ingredients, so that any embodiment described for the preparation of a dressing product with the *K. africana* extract is relevant also for other active ingredients, and vice versa.

In the methods of the invention any technology for spraying a liquid onto a surface may be applied. For example, the liquid with the active ingredient may be sprayed onto the surface using a spray nozzle. It is preferred that the liquid with the active ingredient is sprayed onto the backing layer and/or to the solidified hydrocolloid adhesive using ink-jet technology, e.g. piezoelectric ink-jet technology. Piezoelectric inkjet technology is advantageous in the present invention since this technology allows controlled deposition of active ingredient to the surface of interest. Thus, the active ingredient may be applied precisely and accurately to the dressing product. Furthermore, it is possible to control the location of application of the active ingredient on the dressing product allowing production of a dressing product containing multiple, e.g. different, active ingredients distributed in discrete and

separate areas on the dressing product. When the dressing product contains multiple layers of the hydrocolloid adhesive it is possible to apply the active ingredient in different amounts in different layers providing control of the concentration of the active ingredient over the thickness of the dressing product. Moreover application of active ingredient by spraying is contact-free making the production of a dressing easier thus providing a cheaper manufacturing process. Neither of these advantages is readily obtainable when the active ingredient is mixed with a molten hydrocolloid adhesive.

The liquid to be sprayed onto the backing layer and/or to the solidified hydrocolloid adhesive, e.g. the solution or suspension of the active ingredient or the *K. africana* extract, may contain any component, e.g. auxiliary components, appropriate for the spraying technology employed. In an embodiment of the invention the liquid comprises a volatile solvent, e.g. ethanol, and the methods may further comprise the step of allowing the volatile solvent to evaporate. In a specific embodiment the liquid comprises 30% ethanol in water, and in another embodiment the liquid comprises 70% ethanol in water; an ethanol concentration of 70% can improve evaporation of both water and ethanol due to the azeotropic effect. In another embodiment the method further comprises the step of allowing the active ingredient to diffuse into the hydrocolloid adhesive. In this embodiment the liquid is preferably generally aqueous although it may also contain a volatile solvent. Diffusion of the active ingredient into the hydrocolloid adhesive and also evaporation of the volatile solvent may be furthered by increasing the temperature over ambient temperature. Thus for example, in certain embodiments of the method of the invention the steps of allowing the volatile solvent to evaporate and/or allowing the active ingredient to diffuse into the hydrocolloid adhesive may be performed at an increased temperature, e.g. in the range of 50 to 150°C. The increased temperature will, however, generally be below the melting point of the hydrocolloid adhesive.

The dressing product of the invention, e.g. the dressing product obtainable in the method of the invention, may be comprised in a carrier system. The carrier system may comprise a foil member supporting the dressing product and a cover member covering the surface of hydrocolloid adhesive.

The foil member may be a sheet or layer of a material onto which the backing layer may be adhered. The foil member may have the same size as

the backing layer, or the foil member may be larger than the backing layer so that the backing layer is surrounded by an edge or rim of the material of the foil member. Any appropriate material may be used for the foil member, e.g. paper or a polymer film. The dressing product may be adhered to the foil member using any appropriate adhesive. For example, the hydrocolloid adhesive material may be applied to adhere the dressing product to the foil member. In a specific embodiment, the superficial area of the hydrocolloid adhesive is larger than the superficial area of the backing layer so that the hydrocolloid adhesive is allowed to contact the foil member and adhere both the hydrocolloid adhesive and the backing layer, i.e. the dressing product, to the foil member.

The carrier system further comprises a cover member. The cover member may be a sheet or layer of the same material as the foil member, e.g. paper or polymer film, or of another material. The cover member covers the hydrocolloid face of the dressing product to prevent premature contact with the hydrocolloid adhesive carrying the active ingredient. The cover member preferably allows easy removal of the cover member from the dressing product before application of the dressing product to the skin of a subject. For example, the cover member may be siliconised, in particular on the area covering the surface of the hydrocolloid adhesive. The siliconised area allows the cover member to stick to the hydrocolloid surface while being easy to remove before application of the dressing product to the skin. When the foil member is larger than the hydrocolloid adhesive, e.g. has a larger superficial area, it is possible to prevent that the hydrocolloid surface is touched directly by the fingers of the applicant. Thus, the applicant can remove the cover member without touching the hydrocolloid adhesive surface and apply the dressing product to the skin. Further, when the foil member is larger than the hydrocolloid adhesive, e.g. has a larger superficial area the rim of the foil area surrounding the hydrocolloid adhesive may comprise a glue for adhering the foil member to the skin of the subject.

In another aspect the invention relates to a cosmetic or medical composition for topical application on the skin of a subject, which composition comprises:

brine	40 - 80 %w/w
an extract of *Kigelia africana*	2 - 15 %w/w

one or more excipients	5 - 50 %w/w
water	balance

which excipients are selected from emulsifiers, suspending agents, gelling agents, binders, fillers, surfactants, anti-oxidants, preservatives, emollients, humectants, moisturisers, natural oils, UV-absorbers, sunscreens, and thickeners. The present inventors have now surprisingly found that the composition of the invention is advantageous for the delivery of the active ingredient. Thus, the effects of an extract of *K. Africana*, e.g. an ethanolic extract, on skin diseases and conditions, such as psoriasis, eczemas, dermatitis and acne, are advantageously longer lasting when applied in combination with the salts and minerals from the brine. By applying the composition, e.g. as a gel or cream, to the skin of a subject suffering from psoriasis, the psoriasis significantly turns into more relaxed skin after 2-3 applications in 3 days, and after 5-6 days of treatment the skin stops itching. Moreover, it has surprisingly been found that the extract of *K. Africana* and the brine act synergistically so that the effect can be said to be stronger than when either of the brine or the extract of *K. Africana* are applied individually. The cosmetic or medical composition may be a cream, gel, ointment, lotion or paste. It is also contemplated that the extract of *K. africana* may be replaced with any other active ingredient and that the advantages of obtaining a longer lasting effect may also be realised for other active ingredients so that the composition of the invention is suitable for transdermal delivery of any active ingredient.

Any extract of *K. africana* may be used in all aspects of the present invention. It is preferred that the extract is an ethanolic extract from the fruits of the plant. Both the dressing product and the cosmetic or medical composition of the invention provide a longer lasting effect of the active compounds of *K. africana*, than is obtainable when a *K. africana* extract is applied in a formulation without brine or directly onto the skin. Furthermore, the dressing product and the cosmetic or medical composition also provide a stronger effect of the extract of *K. africana*.

Brine, e.g. in the form of thermal water, is known from its positive effects to damaged skin, and to drive other active ingredients into the skin's layers and pores. In particular, when the brine is a thermal water salts and minerals, e.g. other than NaCl, are advantageous to the skin. This effect will also be observed when the brine is derived from e.g. sea water which has

been evaporated to saturation of NaCl. In combination with the known positive effects from *K. africana* the resulting mixture produces the unique properties to the transportation of the active compounds from the surface of the skin and into the pores of the skin. Without being bound by theory it is believed that the effect, e.g. the moisturising action, from the composition is longer lasting because of the effects of the salts of the brine as a hydrating agent. Appropriate thermal waters are those emerging from a depth of 800 meters from Central Europe, where the geothermal temperatures constantly is 20°C (22.1°C per km of depth or 1°F per 70 feet of depth). The saturated brine generally contains about 26% sodium chloride (NaCl) and a range of different minerals.

The cosmetic or medical composition of the invention may be formulated as a cream or as a gel. When formulated as a cream the composition comprises from 2 to 8 %w/w extract of *K. africana*, from 40 to 60 %w/w brine and from 30 to 40 %w/w excipients. When formulated as a gel the composition comprises from 5 to 15 %w/w extract of *K. africana*, from 60 to 80 %w/w brine and from 5 to 15 %w/w excipients, which comprise a gelling agent, e.g. xanthan gum. The excipients may be any excipients, in particular excipients known to the skilled person for formulating the composition as a cream or gel, respectively. In a specific embodiment the composition is a cream comprising:

brine	50 %w/w
an extract of *K. africana*	5 %w/w
octyldodecyl stearate	10 %w/w
cetyl alcohol	8 %w/w
glycerine	4.2 %w/w
dicaprylyl carbonate	2.5 %w/w
lauryl polyglucose	2 %w/w
cera alba	2 %w/w
PEG-50 Shea butter	1.25 %w/w
glycerol stearate	1 %w/w
PEG-75 Stearate	1 %w/w
ceteth-20	1 %w/w
steareth-20	1 %w/w
polyglyceryl-2 dipolyhydroxystearate	0.5 %w/w

tocopherol	0.15 %w/w
allantoin	0.13 %w/w
water	balance.

In a specific embodiment the composition is a gel comprising:

brine	70 %w/w
an extract of *K. africana*	10 %w/w
glycerin	5 %w/w
propylene glycol	2 %w/w
xanthan gum	1 %w/w
water	balance, where the gelling agent is xanthan gum.

The dressing product and the cosmetic or medical composition of the invention are suitable for use in the treatment of skin damages, diseases and conditions, such as psoriasis, eczemas, dermatitis or acne. Thus, in an embodiment of the invention the dressing product or the composition is for use in medicine, e.g. in the treatment of skin damages, diseases and conditions. Specific examples of the diseases and conditions are psoriasis, eczemas, dermatitis or acne. In another embodiment of the invention the dressing product or the composition is for cosmetic use.

Brief description of the figures

The invention will be readily understood from the following detailed description in conjunction with the accompanying figure, in which

Figure 1 shows photographs of the skin of a subject suffering from psoriasis before and after treatment with a composition of the invention.

Detailed description of the invention

In order to more fully explain the invention it is disclosed in more detail below, and definitions of the terms used throughout the document are given. The present invention relates to a dressing product comprising a backing layer and an active ingredient layer comprising an extract of *Kigelia africana*, which active ingredient layer is coated or adhered to the backing layer, and to a cosmetic or medical composition for topical application on the skin of a subject, which composition comprises:

brine	40 - 80 %w/w
an extract of *Kigelia africana*	2 - 15 %w/w
one or more excipients	5 - 50 %w/w
water	balance

which excipients are selected from emulsifiers, suspending agents, gelling agents, binders, fillers, surfactants, anti-oxidants, preservatives, emollients, humectants, moisturisers, natural oils, UV-absorbers, sunscreens, and thickeners.

The term "extract" should be understood broadly and the extract may be prepared using any solvent or supercritical solvent. The "extract" is not limited to a liquid form but also comprises the residue provided from a liquid extract after removal of the solvent. In general, an extract is prepared by providing a part of a *K. africana* plant, e.g. fruits, leaves, bark, stem bark, root bark etc., and contacting the plant part with a solvent or supercritical solvent. Prior to extraction, the plant part may be cut into smaller pieces and/or be disrupted to increase the extraction efficiency. The extraction may also comprise any other processing step. For example, the plant part may be dried before extraction. In a specific embodiment the fruit of the *K. Africana* tree is cut into smaller pieces, which are dried in a ventilated oven at 75°C for approximately 48 hours before pulverising the smaller pieces. One part pulverised fruit is then mixed with 10 parts 30% ethanol in water solution, stirred overnight and filtered. The brown water/ethanol phase is spray-dried using maltodextrin as a matrix. The spray dried extract can be used directly in the products of the invention or it can be reconstituted in a solvent for use in the method of the invention. In general, the extractant may be selected from its polarity in order to selectively extract components of the plant part; appropriate solvents and corresponding components are provided by Saini *et al.*, 2009 and Gabriel *et al.*, 2009 which are hereby incorporated by reference. An ethanolic extract of the fruits is preferred. In certain embodiments, the solvent is removed from the extract so that the extract is employed in a dry form. For the cosmetic or medical product of the invention it is preferred that the extract is in a dry form. In the method of the invention the extract is in a liquid form. The liquid form may be the extract obtained from the *K. africana* plant part, e.g. 30% ethanol in water, without spray drying or the liquid form may be reconstituted from a spray dried extract. It is also possible to

modify an extract obtained from the *K. africana* plant part, e.g. when the extract is prepared using 30% ethanol in water the ethanol concentration may be increased, e.g. to 70%, prior to spraying the *K. africana* extract onto the backing layer and/or to the solidified hydrocolloid adhesive. In general, the content of *K. africana* extract is expressed in percent by weight (%w/w). This percentage is thus the dry matter content of the *K. africana* extract, e.g. as measured after spray drying a liquid extract, relative to the total mass of the composition. The extract need not be spray dried in order to estimate the dry matter content, and other methods of estimating the dry matter content are known to the skilled person.

The dressing product of the invention and the method of preparing the dressing product require an "active ingredient". Any active ingredient may be used, preferably the active ingredient is an extract of *K. africana*. The extract of *K. africana* is not limited to bulk extract but may also be a purified single active compound from *K. africana*. The terms "active ingredient" and "*K. africana* extract" may be used interchangeably. The active ingredient may also be any other pharmaceutically or pharmacologically active agent or a natural remedy or a plant extract.

The dressing product of the invention is or forms part of a dressing, e.g. when contained in a carrier system. In terms of the invention a "dressing" is an adjunct used by a person for application to the skin, so that the dressing is in contact with the skin. In particular, the hydrocolloid adhesive is in contact with the skin in order to adhere to the skin for the dressing to stay in place. The presence of the active ingredient, e.g. compounds from *K. africana*, in the hydrocolloid adhesive provides that the active ingredient is delivered to the skin. The dressing may be suitable for application on any part of the subject's skin. The dressing product may be used in the treatment of skin damages, diseases and conditions, e.g. psoriasis, eczemas, dermatitis or acne.

In an embodiment of the invention, the dressing product is prepared by applying a molten hot-melt hydrocolloid to the backing layer. Any hydrocolloid that may be applied in a molten form is considered a "hot-melt hydrocolloid" in the context of the invention. Exemplary hot-melt hydrocolloids are carboxymethyl-cellulose or other cellulose derivatives, agar, carrageenan, gelatin, pectin, xanthan gum, gum arabic, guar gum, locust bean gum, and

alginate. The hydrocolloid adhesive may also be any mixture of these components, and the hydrocolloid may also comprise other components, e.g. polymers, excipients or the like. In a specific embodiment the hydrocolloid adhesive comprises carboxymethyl-cellulose, polyisobutylene, pectin and optionally one or more further components. For example, the hydrocolloid adhesive may contain about 40% by weight of low molecular weight polyisobutylene, about 20% by weight of sodium carboxymethylcellulose, about 20% by weight of pectin, and about 20% by weight of gelatin. The hydrocolloid may generally serve two functions in the dressing product, and both rely on the ability of the hydrocolloid material to absorb aqueous liquids. This ability allows the hydrocolloid material to absorb an active ingredient and deliver it to the skin of a subject. Furthermore, liquids, such as wound exudates, may be absorbed to make the hydrocolloid material swell, forming a gel which is held within the structure of the hydrocolloid matrix. As this process happens the extract of *K. Africana* is kept in place by the hydrocolloid matrix and is therefore in prolonged contact with the skin (as opposed to when used in a topical ointment). This in turn provides an enhancement of the properties of *K. Africana* due to the prolonged active exposure of the extract to the skin. No dressing products of the prior art provide this effect.

The hydrocolloid adhesive may be applied to a large surface of the backing material, e.g. a polyurethane film, in particular a permeable polyurethane film, before being allowed to solidify. The thickness of the layer of the hydrocolloid adhesive may be from about 100 µm to about 5 mm, e.g. about 1 mm. After solidification of the hydrocolloid adhesive, the extract of *K. africana* or the solution of the active ingredient is sprayed onto the hydrocolloid adhesive, e.g. the surface of the hydrocolloid adhesive, for example using piezoelectric ink-jet technology. The "piezoelectric ink-jet technology" allows precise deposition of droplets of even picoliter volumes of the extract of *K. africana* or the solution of the active ingredient. Thus for example, the liquid may be spotted in volumes from about 1 pL to about 1 µL or more, e.g. about 10 pL, about 100 pL, about 1 nL, about 10 nL or about 100 nL. This may create spot diameters of extract or solution of about 1 µm to about 1 mm. This control of application of active compounds by mixing the active compound in a molten hot-melt hydrocolloid adhesive is not possible. Exemplary ink-jet deposition equipment comprises Dimatix Materials Printers, e.g. DMP-2800,

DMP-3000, DMP-5000, DMP-5005, supplied by Fujifilm Dimatix, although the invention is not limited to these printers. In general, the extract may be adjusted to be suitable for the specific ink-jet equipment. For example, the viscosity of the extract may be raised or lowered, e.g. by addition of glycol or ethanol, respectively, to the extract, to bring the viscosity within the range of from about 1 to 50 mPas, e.g. about 10 mPas. The viscosity may also be outside these ranges. The extract may also be filtered, e.g. through a 0.45 µm or 0.2 µm filter, prior to loading in the ink-jet equipment. Following application by spraying, the extract may now be allowed to diffuse into the hydrocolloid adhesive, or a volatile solvent may be allowed to evaporate from the hydrocolloid adhesive. The extract may for example be prepared as outlined above. In a specific embodiment the spray dried extract is dissolved or suspended in a liquid appropriate for the piezoelectric ink-jet technology. For example, the liquid may comprise ethanol as a solvent, with the extract being present in an amount of from 0.1 %w/w to 20 %w/w or more, e.g. from 1 %w/w to 10 %w/w, expressed as the dry weight content of the extract, e.g. the weight of the spray dried extract to the total weight of the solution. In another embodiment the extract is not spray dried but may be the filtered extract prepared as outlined above, optionally modified to bring the dry matter content and/or the solvent composition within the desired ranges, e.g. by addition of liquid, such as ethanol, or the removal of liquid.

Following application of the *K. africana* extract or another active ingredient to the hydrocolloid adhesive, smaller pieces may be punched out of the dressing product, e.g. in sizes of 2 by 2 cm or larger or smaller as desired. The smaller pieces of the dressing product may then be applied to a foil member, e.g. a sheet of paper. For example, each piece of dressing product may be applied to a larger sheet of paper, so that the piece of dressing product can be adhered to the piece of paper, e.g. by applying the same hydrocolloid material as used in the preparation of the dressing product in a molten state around the perimeter of the piece of the dressing product. The piece of paper now provides the foil member for the piece of dressing product. The surface of the hydrocolloid adhesive may now be covered with a cover member, e.g. of the same size and shape as the foil member. The cover member is preferably siliconised on the surface contacting the hydrocolloid adhesive in order to allow easy removal and application of the dressing product to the

skin of a subject. The carrier system comprising the dressing product can then be packaged as desired.

In another aspect the invention relates to a cosmetic or medical composition comprising the extract of *K. africana* and a brine, in particular a brine derived from a thermal water. In the context of the present invention the term "brine" refers to a saturated aqueous salt solution. The salt is preferably mineral salt or sea salt, and the major cationic component of the brine is thus sodium ions, and the major anionic component is chloride ions. Other ionic components may be sulphate, magnesium, calcium, potassium, bicarbonate, bromide, borate, and strontium. In certain embodiments the brine is provided by concentrating seawater or saline groundwater. For example seawater or saline groundwater may be heated to evaporate water and to precipitate salts; separation of the precipitated salts will provide the brine. In a specific embodiment the relative contents of sodium and chloride in solution are lowered compared to the starting material, e.g. sea water, so that the brine will be enriched in other ions, while being saturated in the major components, e.g. sodium and chloride ions. In another embodiment, the brine is a "thermal water" derived from geothermal heated groundwater, in particular from groundwater with a high mineral and/or salts content. In general, the brine, e.g. as a saturated solution, comprises about 26% NaCl.

In the context of the invention an "excipient" is any generally pharmacologically inactive substance used as an aid in the formulation of the cosmetic or medical composition, or which provides another non-pharmacologically related function to the composition. Any excipient providing a desired functionality may be employed in the composition of the invention. The cosmetic or medical composition may comprise one or more excipients selected from emulsifiers, suspending agents, gelling agents, binders, fillers, surfactants, anti-oxidants, preservatives, emollients, humectants, moisturisers, natural oils, UV-absorbers, sunscreens, and thickeners. Excipients are well-known to the skilled person, e.g. from the European Pharmacopoeia.

The cosmetic or medical composition is preferably formulated as a cream or a gel. A "cream" is a topical preparation for application to the skin generally consisting of an emulsion of an oil phase and a water phase with an appropriate emulsifier. When the composition is formulated as a cream it can

be considered to be an oil-in-water emulsion. A "gel" is an aqueous composition comprising a gelling agent, which may be a hydrophilic polymer, allowing formation of a viscous solution or suspension. Thus, a cream can be described as "greasy" and the gel can be described as "dry". A greasy cream is especially advantageous when applied to the skin of a subject suffering from dermatitis or psoriasis since the cream will strengthen and restore the lipids in the epidermis which will strengthen the barrier characteristics of the skin. A dry gel is especially advantageous when applied to the skin of a subject suffering from acne since the gel will form a thin layer on the skin and provide the effects of the brine and the extract of *K. africana*. The advantages of the dry gel are also relevant for a subject suffering from psoriasis. The composition of the invention may be applied to any part of the skin of a subject, e.g. to skin near or at the subject's joints.

The invention is now described in the following non-limiting examples.

Examples

Example 1

A composition of the invention in the form of a gel was prepared. The gel comprised:

brine	70 %w/w
an extract of *K. africana*	10 %w/w
glycerin	5 %w/w
propylene glycol	2 %w/w
xanthan gum	1 %w/w
water	balance.

The gel was tested on a subject suffering from psoriasis. A typical way of treatment of psoriasis damaged skin: 2-3 times of daily application of the gel containing *K. africana* and brine. The gel provides a thin protecting layer with a significant improving result discovered through a number of tests on psoriasis patients. The brine is known to give the protecting layer effect on skin, and in combination with the described positive effects from *K. africana* achieves a better treatment than could be obtained with either brine or *K. africana* alone, where the active compounds obtain a longer and more effective contact to skin. The pictures in Figure 1 show the results before and after

3 weeks of treatment (3 x applications per day in 21 days) of a psoriasis damaged skin on a left foot. The picture in Figure 1a shows the untreated skin, and the picture in Figure 1b shows the result after 21 days of treatment. The patient concluded that the level of irritation and itching was significantly bettered using the gel containing *K. africana* and brine compared to his experience with products only containing brine. This patient describes positive effects after the first 3 times of application. This example is representative for all the conducted tests in this group of patients.

Example 2

A composition of the invention in the form of a cream was prepared. The cream comprised:

brine	50 %w/w
an extract of *K. africana*	5 %w/w
octyldodecyl stearate	10 %w/w
cetyl alcohol	8 %w/w
glycerine	4.2 %w/w
dicaprylyl carbonate	2.5 %w/w
lauryl polyglucose	2 %w/w
cera alba	2 %w/w
PEG-50 Shea butter	1.25 %w/w
glycerol stearate	1 %w/w
PEG-75 Stearate	1 %w/w
ceteth-20	1 %w/w
steareth-20	1 %w/w
polyglyceryl-2 dipolyhydroxystearate	0.5 %w/w
tocopherol	0.15 %w/w
allantoin	0.13 %w/w
water	balance.

A typical way of using the cream containing *K. africana* and brine: The product was applied on the irritated skin 2-3 times per day or as needed. Compared to products only containing brine the test on patients conclude, that the combination of *K. africana* and brine gives a significant healing effect. The itching stops after 1-2 applications and this effect continued as long as the product was applied.

PATENT CLAIMS

1. A dressing product comprising a backing layer and an active ingredient layer comprising an extract of *Kigelia africana*, which active ingredient layer is coated or adhered to the backing layer.

2. The dressing product according to claim 1, wherein the active ingredient layer comprises a hydrocolloid adhesive.

3. The dressing product according to claim 1 or 2, wherein the backing layer is a polymer film.

4. A method of producing a dressing product according to any one of claims 1 to 3, the method comprising the steps of:

a) providing a backing layer;

b) applying a hot-melt hydrocolloid adhesive in a liquid form to the backing layer;

c) allowing the liquid hydrocolloid adhesive to solidify;

d) providing a *Kigelia africana* extract; and

e) spraying the *K. africana* extract onto the backing layer and/or to the solidified hydrocolloid adhesive.

5. The method according to claim 4, wherein piezoelectric ink-jet technology is employed in step e).

6. The method according to claim 4 or 5, wherein steps b) to e) are repeated.

7. The method according to any one of claims 4 to 6, wherein the extract comprises a volatile solvent, and the method further comprises the step of allowing the volatile solvent to evaporate.

8. The method according to any one of claims 4 to 7 further comprising the step of allowing the active ingredient to diffuse into the hydrocolloid adhesive.

9. A dressing product obtainable in a method according to any one of claims 4 to 8.

10. The dressing product according to any one of claims 1 to 3 or 9 contained in a carrier system comprising a foil member supporting the dressing product and a cover member covering the surface of hydrocolloid adhesive.

11. The dressing product according to claim 10, wherein the foil member and/or the cover member is paper or a polymer film.

12. The dressing product according to claim 10 or 11, wherein the cover member is siliconised.

13. A cosmetic or medical composition for topical application on the skin of a subject, which composition comprises:

brine	40 - 80 %w/w
an extract of *Kigelia africana*	2 - 15 %w/w
one or more excipients	5 - 50 %w/w
water	balance

which excipients are selected from emulsifiers, suspending agents, gelling agents, binders, fillers, surfactants, anti-oxidants, preservatives, emollients, humectants, moisturisers, natural oils, UV-absorbers, sunscreens, and thickeners.

14. The cosmetic or medical composition according to claim 13, wherein the cosmetic or medical composition is a cream, gel, ointment, lotion or paste.

15. The cosmetic or medical composition according to claim 13 or 14, wherein the cosmetic or medical composition is a cream comprising:

brine	40 - 60 %w/w
an extract of *K. africana*	2 - 8 %w/w
one or more excipients	30 - 40 %w/w
water	balance.

16. The cosmetic or medical composition according to claim 15, wherein the cosmetic or medical composition is a cream comprising:

brine	50 %w/w
an extract of *K. africana*	5 %w/w
octyldodecyl stearate	10 %w/w
cetyl alcohol	8 %w/w
glycerine	4.2 %w/w
dicaprylyl carbonate	2.5 %w/w
lauryl polyglucose	2 %w/w
cera alba	2 %w/w
PEG-50 Shea butter	1.25 %w/w
glycerol stearate	1 %w/w
PEG-75 Stearate	1 %w/w
ceteth-20	1 %w/w

steareth-20	1 %w/w
polyglyceryl-2 dipolyhydroxystearate	0.5 %w/w
tocopherol	0.15 %w/w
allantoin	0.13 %w/w
water	balance.

17. The cosmetic or medical composition according to claim 13 or 14, wherein the cosmetic or medical composition is a gel comprising:

brine	60 - 80 %w/w
an extract of *K. africana*	5 - 15 %w/w
one or more excipients	5 - 15 %w/w
water	balance,

wherein the excipients comprise a gelling agent.

18. The cosmetic or medical composition according to claim 17, wherein the cosmetic or medical composition is a gel comprising:

brine	70 %w/w
an extract of *K. africana*	10 %w/w
glycerin	5 %w/w
propylene glycol	2 %w/w
xanthan gum	1 %w/w
water	balance.

19. The dressing product according to any one of claims 1 to 3 or 9 to 12, or the composition according to any one of claims 13 to 18 for use in the treatment of skin damages, diseases and conditions.

20. The dressing product according to claim 19, or the composition according to claim 19, wherein the disease or condition is psoriasis, eczemas, dermatitis or acne.

21. The dressing product according to any one of claims 1 to 3 or 9 to 12, or the composition according to any one of claims 13 to 18 for cosmetic use.

Fig. 1a

Fig. 1b

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2012/050280

A. CLASSIFICATION OF SUBJECT MATTER
IPC & ECLA: A61K 36/00 (2006.01), A61P 17/00 (2006.01), A61P 17/06 (2006.01), A61P 17/10 (2006.01)
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)

A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
DK, NO, SE, FI: Classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPODOC, WPI, Full Text (English, German, French), Medline, PubChem, XPESP, XPESP2

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US2002176874 A1 (DAMPEIROU CHRISTIAN [FR]; SERIN FREDERIC [FR]) 28/11/2002. See whole document and especially [0011], [0013]-[0014] and [0016]-[0017]	1-12, 19-21
X	WO2006002443 A1 (SCHLEIPFER RUDOLF KARL [ZA]) 05/01/2006. See claims 1, 4, 6, 10-13, 17-18 and page 6 lines 36-37.	1-12, 19-21
A	O'Mahony, J., "Transdermal Technology", Pharmaceutical Manufacturing and Packing Sourcer May '09 issue.	

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13/02/2013	14/02/2013
Name and mailing address of the ISA Nordic Patent Institute Helgeshøj Allé 81 DK - 2630 Taastrup, Denmark. Facsimile No. + 45 43 50 80 08	Authorized officer Rikke L. Vinther Telephone No. +45 43 50 82 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2012/050280

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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:

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 No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows: 2 inventions (see below)

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 additional fees, this Authority did not invite payment of additional fees.

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.: 1-12 (complete) and 19-21 (in part)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

The international application does not comply with the requirement of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

Invention I (claims 1-12 (complete) and 19-21 (in part): Relates to a dressing product comprising a backing layer and an active ingredient layer comprising Kigelia Africana extract.

Invention II (claims 13-18 (complete) and 19-21 (in part): Relates to a cosmetic or medical composition for topical application comprising a combination of brine and Kigelia Africana extract as active ingredients.

The only technical feature which is common to the two inventions is the Kigelia Africana extract. Such extracts are however known in the art (see the description of the present application). Accordingly, the two inventions do not share a common patentable technical feature. Therefore, the two inventions lack unity.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/DK2012/050280

Patent document cited in search report / Publication date	Patent family member(s) / Publication date
US2002176874 A1 20021128	WO0002531 A1 20000120 FR2780885 A1 20000114 FR2780885 B1 20011012
WO2006002443 A1 20060105	WO2006002443 A1 20060105