Prevalence Collaborators, Lancet, 2016). Global estimates suggest that at least 7 million people suffer complications following surgery each year, including at least 1 million deaths. Delayed acute wound healing increases the post-surgical risk of morbidity and mortality. A good example are surgical site infections, which are the second leading cause of hospital-acquired infections. Major complications in acute wounds are linked to age-related failure to heal and hormone deficiency. Here, the 65+ population (currently 15-28% of total) is increasing globally.

While currently numerous wound care strategies exist (both mechanical and pharmaceutical), there remains an unmet need for effective wound care strategies and pharmaceutical compositions that aid in said wound care. Such compositions would ideally aid the wound healing of subjects with impaired wound healing, such as elderly subjects and subjects affected by chronic wounds caused by for example a lack of motility and/or underlying pathologies.

SUMMARY

As evidenced in detail by the examples enclosed herewith, the present inventors have surprisingly found that estetrol is particularly suited for use in wound healing, including wound healing in subjects characterised by impaired wound healing. By extensive experimentation, it was found that estetrol components can be safely included in pharmaceutical compositions aiming to assist in wound healing. Said compositions have no or limited effect on the increase in uterine weight that can occur with topical use of estrogens in female subjects through inadvertent systemic exposure. More particularly, the inventors have found that inclusion of particular amounts of an estetrol component in pharmaceutical compositions aiming to assist in wound healing provides an unprecedented compromise between efficacy and adverse effects such as an increase in uterus weight. The absence of uterus weight increase indicates that systemic effects of the pharmaceutical compositions comprising an estetrol component are limited and arguably even absent at certain dosages, even upon inclusion of a permeation enhancer.

From the *in vitro* and *in vivo* wound-healing experiments follows that estetrol exerts at least similar effects as estradiol on e.g. wound closure, re-epithelialisation, and anti-inflammation. Estradiol and estetrol treatment increases fibroblast ER expression, while estetrol also promotes fibronectin expression and inhibits MMP activity. Estetrol also seems to promote dermal fibroblast migration in scratch assays and promote epidermal keratinocyte migration to a higher extent than estradiol, Further, estetrol is show to modulate wound-relevant epidermal gene expression with a slightly higher magnitude of effect than estradiol and to promote wound closure more efficiently than estradiol. These improvements on wound-healing combined with reduced systemic effects (e.g. on uterine weight gain) make estetrol compositions an attractive alternative for estradiol and other estrogen-based compositions used for wound-healing.

Finally, in some examples, the compositions are additionally characterised by a gradual release profile which is a further advantage in the context of wound healing. The present disclosure thus contributes significantly to new and innovative wound care strategies.

Accordingly, the disclosure is directed to a pharmaceutical composition comprising of from 0.02% to 1.5% (w/w) of an estetrol component, preferably comprising of from 0.05% to 1.2% (w/w) of an estetrol component, of from about 0.02% to about 1% (w/w) of an estetrol component of from about 0.03% to about 1% (w/w) of an estetrol component, preferably of from about 0.04% to about 1% (w/w) of an estetrol component,

more preferably of from about 0.05% to about 1% (w/w) of an estetrol component, most preferably from about 0.06% to about 0.5% (w/w) of an estetrol component, more preferably of from about 0.09% to about 1.1 % (w/w), even more from 0.1% to 1% (w/w) of an estetrol component, most preferably of from 0.3% to 0.7% (w/w) of an estetrol component.

In one aspect, the disclosure is directed to a composition for topical application, comprising of from about 0.01% to about 5%, preferably of from 0.02% to 1.5% (w/w) of an estetrol component, or of from about 0.02% to about 1% (w/w) of an estetrol component, or of from about 0.05% to about 1.2% (w/w) of an estetrol component, more preferably of from about 0.09% to about 1.1 % (w/w), even more preferably from 0.1% to 1% (w/w) of an estetrol component, most preferably of from 0.3% to 0.7% (w/w) of an estetrol component.

Preferably, said composition is for topical use, or for topical application, such as for topical application to the skin.

Preferably, said composition does not result in a significant systemic effect in the subject upon or after topical application.

In particular examples, the pharmaceutical composition comprises of from about 0.03% to about 0.12% (w/w) of an estetrol component, preferably of from about 0.04% to about 0.08% (w/w) of an estetrol component, more preferably of from about 0.05% to about 0.07% w/w of an estetrol component, most preferably about 0.06% (w/w) of an estetrol component.

In particular examples, the pharmaceutical composition further comprises a permeation enhancer that enables permeation through the stratum corneum and/or permeation through the wound eschar.

In particular examples, the pharmaceutical composition is a composition for use in topical wound healing.

In another example, the disclosure is directed to a (pharmaceutical) composition comprising an estetrol component for use in topical wound healing, wherein the composition optionally further comprises a permeation enhancer enabling permeation through the stratum corneum.

In particular examples, the (pharmaceutical) composition comprises of from about 0.01% to about 5% (w/w) of an estetrol component, preferably of from about 0.02% to about 1% (w/w) of an estetrol component, more preferably of from about 0.03% to about 0.75% (w/w) of an estetrol component, yet more preferably of from about 0.04% to about 0.5% (w/w) of an estetrol component, most preferably about 0.06% (w/w) of an estetrol component.

The disclosure is also directed to a hydrogel formulation comprising of from about 0.02% to about 1.5 % (w/w) of an estetrol component, more particularly of about 0.05 to 1.2% (w/w), even more particularly of from about 0.09% to about 1.1 % (w/w), or from about 0.1% to about 1 % (w/w). In another aspect, the disclosure is directed to a hydrogel formulation comprising the composition as defined herein.

In particular examples, the hydrogel comprises from about 0.05 to about 1.3 % (w/w), more particularly from about 0.08 to about 1.2% (w/w), even more particularly of from about 0.09% to about 1.1 % (w/w), or from about 0.1% to about 1 % (w/w) of an estetrol component. In alternative examples, the hydrogel comprises from about 0.03% to about 0.75% (w/w) of an estetrol component, preferably of from

about 0.04% to about 0.5% (w/w) of an estetrol component, more preferably of from about 0.05% to about 0.25% (w/w) of an estetrol component, most preferably about 0.06% (w/w) of an estetrol component.

As can be derived from the examples section, a 0.06% (w/w) estetrol component was shown to have no effect on uterus weight increase in the tested mice, which is in strong contrast to the effect on uterus weight increase by applying the commercially available Estrogel® comprising 0.06% estradiol.

In addition, also higher concentrations of 0.22 and 0.5 % (w/w) estetrol still had a significantly lower effect on uterus weight increase in mice as compared to Estrogel®. This shows that topical application of a composition comprising estetrol is less prone to result in systemic effect in the subject, which is particularly important in female

subjects. In particular examples, the hydrogel further comprises a permeation enhancer that enables permeation through the stratum corneum.

In particular examples, the hydrogel is for use in topical wound healing.

Optionally, the (pharmaceutical) composition as described herein is in the form of a formulation selected from the group consisting of: emulsions, suspensions, ointments, pastes, lotions, gels (including hydrogels), foams, mousses, and creams.

In examples wherein the (pharmaceutical) composition is a hydrogel, said hydrogel is characterised by a favourable release profile, e.g. more favourable when compared to other formulations such as but not limited to creams.

In a preferred example, the hydrogel described herein is characterised by a mean cumulative amount of estetrol component released of at least about 2.5 μg/cm^2, at least about 5 μg/cm^2, at least about 7 μg/cm^2, at least about 10 μg/cm^2, at least about 15 μg/cm^2, at least about 20 μg/cm^2, at least about 25 μg/cm^2, preferably at least about 50 μg/cm^2, more preferably at least 100 μg/cm^2, more preferably at least about 150 μg/cm^2, more preferably at least about 200 μg/cm^2 within the square root of 1 hour across an isopore membrane in a receptor solution of 40:30:30 v/v/v ethanol:PEG400:water. Depending on the surface of the wound, the concentration of the estetrol component may need to be reduced in order not to result in a cumulative administration of estetrol in too high amounts. This can be easily calculated by a physician or pharmacist.

In preferred examples, the hydrogel described herein is characterised by a mean cumulative amount of estetrol component released of at least about 50 μg/cm^2, at least about 100 μg/cm^2, at least about 150 μg/cm^2, at least about 200 μg/cm^2, at least about 250 μg/cm^2 at least about 300 μg/cm^2, at least about 350 μg/cm^2, at least about 400 μg/cm^2, at least about 450 μg/cm^2 within 8 hours across an isopore membrane in a receptor solution of 40:30:30 v/v/v ethanol:PEG400:water. More preferably, the hydrogel described herein is characterised by a mean cumulative amount of estetrol component released of at least about 80 μg/cm^2.

Preferably, the hydrogel described herein is characterised by a mean % applied dose of the estetrol component into a receptor solution of 40:30:30 v/v/v ethanol:PEG400:water of at least about 15%, preferably at least about 20% after 1 hour and/or a mean % applied dose of the estetrol component into a receptor solution of 40:30:30 v/v/v ethanol:PEG400:water of at least about 40%, preferably at least about 50%, more preferably at least 80% after 8 hours and most preferably at least 90% after 8 hours.

In any of the above, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise a permeation enhancer in an amount of from about 0.5% to about 60% (w/w), or preferably in an amount of from about 0.05% to about 5% (w/w). Preferably, the permeation enhancer comprises a substance or molecule that enables permeation through the stratum corneum (i.e. a permeation enhancing molecule), and a solvent. Preferably, the permeation enhancing molecule is selected from the group consisting of: ethanol, ether such as diethylene glycol monoethyl ether (Transcutol®), benzyl alcohol, fatty acids and esters thereof, or any combination thereof. Preferably, the permeation enhancer comprises a solvent comprising one or more polyethylene glycols (PEG), propylene glycol (PG), or combinations thereof. Preferably, the PEG is a PEG having a molecular weight of between about 200 g/mol and about 600 g/mol such as a PEG selected from the group consisting of: PEG200, PEG300, PEG400, PEG500, PEG600, or any combination thereof. More preferably, the

permeation enhancer comprises a solvent comprising a PEG having a molecular weight of about 400g/mol such as PEG400. In some examples, the permeation enhancer comprises up to 50% PEG400 (w/w) and/or from about 15% to 45% PEG400 (w/w), and/or from about 20% to 40% PEG400 (w/w), and/or from about 30% to 35% PEG400 (w/w). Most preferably, the permeation enhancer comprises of from about 14% to about 21% PEG400 (w/w) and/or from about 10% to about 25% PEG (w/w). In alternative preferred examples, the permeation enhancer comprises from about 0.5% to about 10% of permeation enhancer such as for example PEG400. In further alternative preferred examples, the permeation enhancer comprises from about 0.5% to about 5% of permeation enhancer such as for example PEG400.

In certain examples, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel comprises benzyl alcohol, preferably in an amount of from about 1% to about 3%.

In any of the above, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise a thickener. In particular examples, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel comprises a thickener in an amount of from about 0.3% to about 20% (w/w), or preferably in an amount of from about 0.3% to about 3% (w/w), or more preferably in an amount of from 0.5% to 3% (w/w). Preferably, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel comprises a thickener selected from the group consisting of a hydroxyethyl cellulose (HEC), a carboxymethyl cellulose (CMC), a high molecular weight cross-linked acrylic based polymer, a non-ionic triblock copolymer, or any combination thereof. Preferably, the high molecular weight cross-linked acrylic based polymer is Carbopol®.

Preferably, the HEC is HEC250 HHX. Preferably, the non-ionic triblock copolymer has an approximate molecular mass of between about 1800 and about 4000 and a polyoxyethylene content of from about 70 to about 80%. Preferably, the non-ionic triblock copolymer is selected from a poloxamer, such as poloxamer 188, poloxamer 407, or a combination thereof.

In any of the above, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise a preservative. In particular examples, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise a preservative in an amount of from about 1% to about 10% (w/w), preferably of from about 1% to about 3% (w/w). Preferably, the preservative is selected from the group consisting of: lysozyme, nisin, quaternary ammonium preservatives, parabens, phenoxyethanol, benzyl alcohol, chlorobutanol, phenol, sorbic acid, thimerosal, natural preservatives, and any combination thereof.

In any of the above, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise an emollient. In particular examples, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise an emollient in an amount of from about 2.5% to about 30% (w/w), preferably of from about 8% to about 12% (w/w), most preferably in an amount of about 10% (w/w). Preferably, the emollient is selected from the group consisting of: glycerol, acetyl alcohol, stearyl alcohol, stearic acid, isopropyl palmitate, squalene, lanolin, glycerin, petrolatum, petroleum, and any combination thereof.

Therefore, as described herein, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise in addition to the estetrol component a permeation enhancer, a thickener, and as optional ingredient a preservative and/or an emollient, which are each preferably selected from the groups described herein. As described herein,

the (pharmaceutical) composition may be complemented to 100% (w/w) by means of an aqueous solution such as water.

In particular examples, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise in addition to the estetrol component (w/w):

- from about 0.1% to about 60% (w/w) of a permeation enhancer, preferably wherein said permeation enhancer comprises a permeation enhancer molecule and a solvent or solvent system;
- from about 0.3% to about 20% (w/w) of a thickener;
- optionally a preservative and/or an emollient;
- water up to 100% (w/w).

In further examples, the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise from 0.05% to 0.6% (w/w) estetrol and in addition:

- from about 0.1% to about 5% (w/w) of a permeation enhancer, preferably wherein said permeation enhancer comprises a permeation enhancer molecule and a solvent or solvent system;
- from about 0.3% to about 3% (w/w) of a thickener;
- optionally a preservative and/or an emollient;
- water up to 100% (w/w).

In further particular examples the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise in addition to the estetrol component (w/w):

- from about 16% to about 20% (w/w) PEG400;
- from about 18% to about 22% (w/w) PG;
- from about 8% to about 12% (w/w) glycerol;
- from about 1% to about 2 % (w/w) HEC; and
- from about 1.5% to about 2.5 % (w/w) benzyl alcohol.

In alternative examples the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise in addition to the estetrol component:

- from about 18% to about 22% (w/w) PEG400;
- from about 0.1% to about 1% (w/w) Carbopol®; and
- from about 4% to about 6% (w/w) Transcutol®.

In yet alternative examples the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise in addition to the estetrol component:

- from about 25% to about 55% (w/w) PEG400, preferably from about 35% to about 45% (w/w) PEG400;
- from about 0.1% to about 1% (w/w) Carbopol®, preferably from about 0.25% to about 0.75% (w/w) Carbopol®; and
- from about 0.1% to about 5% (w/w) Transcutol®, preferably from about 0.75% to about 3% Transcutol®.

In yet alternative examples the (pharmaceutical) composition, (pharmaceutical) composition for use, or hydrogel may comprise in addition to the estetrol component:

- from about 38% to about 45% (w/w) PEG400;
- from about 0.1% to about 1% (w/w) Carbopol®; and
- from about 0.8% to about 3% (w/w) Transcutol®.

The disclosure also encompasses each of the (pharmaceutical) compositions, hydrogels, and alternatives described herein as a medicament, i.e. in a therapeutic and/or prophylactic context. In another aspect, the disclosure is directed to the composition as defined herein or the hydrogen as defined herein for use as a medicament. In particular examples, the (pharmaceutical) compositions and hydrogels of the above are for use in wound healing. In further examples, the use in wound healing corresponds to their use as topical formulations in the treatment of wounds. Similarly, the disclosure relate to the use of a pharmaceutical composition or hydrogel described herein for the manufacture of a medicament for the topical treatment of wounds. In another aspect, the disclosure is directed to use of the composition as defined herein, or hydrogel as defined herein, in the manufacture of a medicament for topical wound healing or topical treatment of wounds. Related to the preceding, the disclosure equally encompass methods of topical wound treatment comprising administration of any one of the pharmaceutical compositions or hydrogels described herein to a wound or wound site of a subject.

In particular examples, the (pharmaceutical) compositions and hydrogels of the above are for use in treatment of acute wounds. Optionally, the acute wound is a surgical wound or a wound caused by acute injury. The wound can also be a partial thickness wound (e.g., at a skin graft donor site). In alternative examples, the pharmaceutical compositions and hydrogels of the above are for use in treatment of chronic wounds. Optionally, the chronic wound is a wound caused and/or maintained by a diabetic disease. Other major causative factors of chronic wounds are ischemia, radiation, foreign bodies and prolonged external pressure. Generally chronic wounds are divided into infected or ischemic wound.

In particular examples, the medical use or treatment as described herein results in improved histological healing parameters versus non-treated wounds. Preferably, the medical use or treatment results in improved incidence of complete wound closure, accelerated wound closure, and/or facilitation of surgical wound closure. In preferred examples, the medical use or treatment improves the quality of healing also referred to as cosmesis. Particularly for surgical wounds less scaring is observed.

In particular examples, the pharmaceutical compositions and hydrogels as described herein show a beneficial effect on inflamed wounds. With the use, the inflammation itself and/or the inflammatory progression is prevented. Wounds can also be prevented from recurring.

In particular examples, the (pharmaceutical) compositions and hydrogels of the above are for use in treatment of wounds of subjects having impaired wound healing including an impaired delayed cutaneous wound healing or bacterially delayed wound healing. In particular examples, the impaired wound healing is characterized by reduced wound edge migration. In other examples, the impaired wound healing is characterized by increased wound edge proliferation.

In particular examples, the (pharmaceutical) compositions and hydrogels of the above are for use in treatment of infected wound sites, combat wounds, burns, and chronic leg ulcers. In some examples, said infected wounds can be associated with reduced re-epithelialisation, increased proliferation, a heightened inflammatory response and perturbed wound matrix deposition. One particularly studied pathogen in this respect

is Klebsiella pneumoniae and the estetrol component containing compositions disclosed herein are shown to reduce inflammation in a model of Klebsiella pneumoniae infected wounds.

In particular examples, the (pharmaceutical) compositions and hydrogels of the above are for use in improving re-epithelialization of a wound site, increased proliferation of cells at a wound site, reducing an inflammatory response at/in a wound site, improving matrix deposition like matrix remodeling, and improving angiogenesis at wound sites.

In particular examples, the medical use or treatment as described herein results in improved quality of healing, also referred to as cosmesis. This is forming an interesting aspect, particularly in the context of surgical wound healing.

In particular examples, the medical use or treatment as described herein results in an improved inflammatory profile of the wound site versus non-treated wounds. Preferably, the medical use or treatment results in an improved macrophage and neutrophil profile indicative for a reduced local wound inflammation versus non-treated wounds.

Optionally, the subject is a subject of elderly age, such as a subject of $\geq$ 50 years, or preferably $\geq$ 60 years. Optionally, the (pharmaceutical) composition or hydrogel as described herein is applied to the wound site on at least two distinct instances as part of the treatment or medical use. Optionally, the treatment may span a period of at least 1 week, or even 1 month or longer, e.g. 12 weeks. Alternatively, the (pharmaceutical) composition or hydrogel as described herein is applied to the wound site continuously over a prolonged period of time. Preferably, the prolonged period of time corresponds to at least 1 day, at least 1 week, or at least 1 month. In particular examples, the (pharmaceutical) composition or hydrogel as described herein is comprised in a wound dressing, bandage, patch, or plaster. Each type of scaffold or matrix could be used. Treatment might also be needed for prolonged durations, e.g. 12 weeks and the forms as described herein are particularly suited to facilitate extended administration periods.

The disclosure is also directed to packaging units comprising the pharmaceutical composition of hydrogel described in any example herein. A packaging unit contains preferably one or more dosage units of the (pharmaceutical) composition (or optionally hydrogel) described herein. Suitable packaging units include any container that is capable of enclosing and preserving liquids. Optionally, the packaging unit is a box, a display unit, an ampoule, a bottle, a vial, a tube, a syringe, a cartridge, a bag, a sachet, a pouch, a film, a laminate, a foil, a can, a cylinder, or a pressurized container. In another aspect, the disclosure is directed to a packaging comprising one or more dosage units of the composition as defined herein or the hydrogel as defined herein, preferably wherein said packaging unit is a box, a display unit, an ampoule, a bottle, a vial, a tube, a syringe, a cartridge, a bag, a sachet, a pouch, a film, a laminate, a foil, a can, a cylinder, or a pressurized container.

The above and further aspects, embodiments and examples of the disclosure are described in the following sections and in the appended claims. The subject matter of the appended claims is hereby specifically incorporated in this specification.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1. Mean cumulative amount of estetrol monohydrate released per unit area (µg/cm^2) between the 1 and 8 h experimental period (presented as a square root of time) from 10 formulations across an isopore membrane in receptor solution 40:30:30 v/v/v ethanol: PEG400: water. Error bars represent the standard deviation of the mean (n=6).

CLAIMS

1. A composition for topical application, comprising of from about 0.01% to about 5%, preferably of from 0.02% to 1.5% (w/w) of an estetrol component, or of from about 0.02% to about 1% (w/w) of an estetrol component, or of from about 0.05% to about 1.2% (w/w) of an estetrol component, more preferably of from about 0.09% to about 1.1 % (w/w), even more preferably from 0.1% to 1% (w/w) of an estetrol component, most preferably of from 0.3% to 0.7% (w/w) of an estetrol component.

2. The composition according to claim 1, further comprising a permeation enhancer that enables permeation through the stratum corneum of the skin of a subject.

3. A hydrogel formulation comprising the composition according to claim 1 or 2.

4. Use of the composition according to claim 1 or 2, or hydrogel according to claim 3, in the manufacture of a medicament for topical wound healing or topical treatment of wounds.

5. The composition according to claim 1 or 2, hydrogel according to claim 3, or use according to claim 4, which is a formulation selected from the group consisting of: emulsions, suspensions, ointments, pastes, lotions, gels, foams, mousses, and creams.

6. The composition according to claim 1, 2 or 5, hydrogel according to claim 3 or 5, or use according to claim 4 or 5, comprising a permeation enhancer in an amount of from 0.05% to 60% (w/w), preferably in an amount of from 0.1% to 5% (w/w).

7. The composition, hydrogel, or use according to claim 6, wherein said permeation enhancer comprises a substance or molecule that enables permeation through the stratum corneum and a solvent, preferably wherein said permeation enhancing molecule is selected from the group consisting of: ethanol, ether such as diethylene glycol monoethyl ether (Transcutol®), benzyl alcohol, fatty acids and esters thereof, or any combination thereof; or

wherein said permeation enhancer comprises a solvent comprising one or more polyethylene glycols (PEG), propylene glycol (PG), or combinations thereof.

8. The composition, hydrogel, or use according to claim 7, wherein said PEG is a PEG having a molecular weight of between about 200 g/mol and about 600 g/mol such as a PEG selected from the group consisting of: PEG200, PEG300, PEG400, PEG500, PEG600, or any combination thereof.

9. The composition according to any one of claims 1, 2 or 5 to 8, hydrogel according to any one of claims 3 or 5 to 8, or use according to any one of claims 4 to 8, further comprising benzyl alcohol, preferably in an amount of from 1% to 3% and/or further comprising a thickener in an amount of from 0.3% to 20% (w/w), preferably comprising a thickener in an amount of from 0.5% to 3% (w/w).

10. The composition according to any one of claims 1, 2 or 5 to 9, hydrogel according to any one of claims 3 or 5 to 9, or use according to any one of claims 4 to 9, wherein said thickener is selected from the group consisting of a hydroxyethyl cellulose (HEC), a carboxymethyl cellulose (CMC), a high molecular weight cross-linked

acrylic based polymer, a non-ionic triblock copolymer, or any combination thereof, preferably wherein said high molecular weight cross-linked acrylic based polymer is Carbopol®, or wherein said HEC is HEC250 HHX, or wherein said non-ionic triblock copolymer has an approximate molecular mass of between about 1800 and about 4000 and a polyoxyethylene content of from about 70 to about 80%.

11. The composition according to any one of claims 1, 2 or 5 to 10, hydrogel according to any one of claims 3 or 5 to 10, or use according to any one of claims 4 to 10, further comprising a preservative in an amount of from 1% to 10% (w/w), preferably of from 1% to 3% (w/w), preferably wherein said preservative is selected from the group consisting of: lysozyme, nisin, quaternary ammonium preservatives, parabens, phenoxyethanol, benzyl alcohol, chlorobutanol, phenol, sorbic acid, thimerosal, natural preservatives, and any combination thereof.

12. The composition according to any one of claims 1, 2 or 5 to 11, hydrogel according to any one of claims 3 or 5 to 11, or use according to any one of claims 4 to 11, further comprising an emollient in an amount of from 2.5% to 30% (w/w), preferably of from 8% to 12% (w/w), preferably wherein said emollient is selected from the group consisting of: glycerol, acetyl alcohol, stearyl alcohol, stearic acid, isopropyl palmitate, squalene, lanolin, glycerin, petrolatum, petroleum, and any combination thereof.

13. The composition according to any one of claims 1, 2 or 5 to 12, hydrogel according to any one of claims 3 or 5 to 12, or use according to any one of claims 4 to 12, wherein said composition or formulation is complemented to 100% (w/w) by means of an aqueous solution such as water.

14. The composition according to claim 1 or 2, hydrogel according to claim 3, or use according to claim 4, comprising:

- from about 0.1% to about 5% (w/w) of a permeation enhancer, preferably from about 1% to about 2.5% (w/w/) of a permeation enhancer, more preferably wherein said permeation enhancer comprises a permeation enhancer molecule and a solvent or solvent system;
- from about 0.3% to about 3% (w/w) of a thickener;
- optionally a preservative and/or an emollient;
- water up to 100% (w/w); or

or comprising:

- from about 38% to about 45% (w/w) PEG400;
- from about 0.1% to about 1% (w/w) Carbopol®; and
- from about 0.8% to about 3% (w/w) Transcutol®.

15. The composition according to any one of claims 1, 2 or 5 to 14, hydrogel according to any one of claims 3 or 5 to 14, or use according to any one of claims 4 to 14, for use in treatment of acute wounds, surgical wounds, wounds caused by acute injury, chronic wounds, wounds caused and/or maintained by a diabetic disease, wounds of subjects having impaired wound healing including an impaired delayed cutaneous wound healing or bacterially delayed wound healing, wound healing characterized by reduced wound edge migration, infected wound sites, combat wounds, burns, and chronic leg ulcers.

16. The composition according to any one of claims 1, 2 or 5 to 14, hydrogel according to any one of claims 3 or 5 to 14, or use according to any one of claims 4 to 14, comprised in a wound dressing, bandage, band-aid, patch, or plaster.

17. A packaging comprising one or more dosage units of the composition according to any one of claims 1, 2 or 5 to 14 or the hydrogel according to any one of claims 3 or 5 to 14, preferably wherein said packaging unit is a box, a display unit, an ampoule, a bottle, a vial, a tube, a syringe, a cartridge, a bag, a sachet, a pouch, a film, a laminate, a foil, a can, a cylinder, or a pressurized container.

18. The composition according to any one of claims 1, 2 or 5 to 14 or the hydrogel according to any one of claims 3 or 5 to 14 for use as a medicament.