(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
05 March 2020 (05.03.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/043665 A1

(51) International Patent Classification:
A61L 15/42 (2006.01) *A61L 24/10* (2006.01)
A61L 15/44 (2006.01) *A61L 31/10* (2006.01)
A61L 15/46 (2006.01) *A61L 31/14* (2006.01)
A61L 15/60 (2006.01) *A61L 31/16* (2006.01)
A61L 24/00 (2006.01) *A61F 13/00* (2006.01)
A61L 24/04 (2006.01)

(21) International Application Number:
PCT/EP2019/072717

(22) International Filing Date:
26 August 2019 (26.08.2019)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
A 50731/2018 27 August 2018 (27.08.2018) AT

(72) Inventors; and
(71) Applicants: **EDER, Claudia** [AT/AT]; Zimmermanngasse 24/4, 1090 Vienna (AT). **LANDOWSKI, Peter** [AT/AT]; Franz-Asenbauer-Gasse 53/11, 1230 Vienna (AT).

(74) Agent: **LOIDL, Manuela** et al.; REDL Life Science Patent Attorneys, Donau-City-Straße 11, 1220 Vienna (AT).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) Title: ANTISEPTIC GEL

(57) Abstract: An antiseptic plaster comprising an adhesive medical dressing, wherein the dressing is partially coated with a composition comprising an antiseptic compound, which is 8-hydroxyquinoline or octenidine, and a biocompatible gelling agent, and optionally comprises an indicator, which indicates a pre-defined application time.

WO 2020/043665 A1

ANTISEPTIC GEL

FIELD OF THE INVENTION

The invention relates to compositions and devices useful in skin disinfection and wound care. In particular, the invention relates to antiseptic compositions that can be used to partially or fully cover medical dressings, textile wound care material or wound foam or implants or intracorporal medical devices.

BACKGROUND OF THE INVENTION

Surgical site infections are one of the most common complications of surgical procedures. The most important preventive measure is skin disinfection. Preoperative skin disinfection currently is performed by applying a liquid antiseptic solution via cotton swabs for several times onto the patient´s skin. This procedure does not allow for control of the applied dosage and does not guarantee compliance with the incubation time required. Due to increasing patient sues for malpractice liability; a proof of compliance with the standard disinfection protocol is of increasing importance. Using the current, unstandardized procedure, aseptic conditions in the operation area can only be achieved in 78% of the patients. In 22%, pathogenic bacteria are still detectable after skin disinfection[1] and increase the risk of wound healing disorders and postoperative infection.

There are several studies indicating that antiseptic agents applied in a liquid form can have significant side effects on wound healing: PVP-iodine, quaternary ammonium and Bispyridin inhibit fibroblast- and keratinocyte proliferation and decrease cell viability[2,3,4,5,6]. Additionally, significant tissue toxicity even in clinically applied dosages[7] has been observed, making the application of antiseptics an independent risk factor for wound healing disorders. The antiseptic effect of 8-Hydroxyquinoline and its derivatives has been known for a long time and was used to treat diarrhea in former times. Due to severe adverse effects after long-term parenteral application, 8-Hydroxyquinoline is not used for this indication any longer[8]. However, the substance is still applied as a topical antiseptic solution (e.g. Solution Hydroxychinolini[9]) and as preservative agent. Like other liquid antiseptic solutions, 8-Hydroxyquinoline demonstrates a significant cytotoxic effect, which is currently investigated for the treatment of malignant diseases[10,11]. An inhibition of fibroblast functions has also been reported[12].

CN 103356738 A describes a disinfection gel for hand- and skin disinfection, which is used in the liquid phase without any adhesive material.

WO9528964 A1 describes a collagen preparation for controlled release of active substances, characterized by a mixture of acid-soluble collagens with different molecular weights. Among other supplements, disinfectants are mentioned as a potential additive.

DE 19860759 A1 describes an antiseptic plaster to be used with injections, containing a liquid antiseptic in a reservoir, which is released to the injection site by pressure.

CN 204072492 contains a multi-layered plaster to cover venous punction sites.

CN103655042 A describes an electronic timer to evaluate the using time of an adhesive bandage.

DE102009049506A1 discloses a wound cover comprising transparent film, covered with a transparent hydrogel comprising octenidinedihydrochloride.

EP0401893B1 discloses a sterilizing dressing for use with needle injections comprising a resealable patch containing throughout its volume a sterilizing pre-incorporated therein.

US2009/0187130A1 discloses an adhesive hydrogel island dressing and delivery system that facilitates removal of a release liner from the adhesive hydrogel dressing during application. The adhesive hydrogel dressing comprises a patch partially covered with hydrogel, which may comprise an antimicrobial agent.

DE102006001954A1 discloses compositions useful for wound covers or wound dressing comprising at least an alginate and a compound comprising antiseptic properties.

Currently, effectiveness of skin disinfection varies due to different application procedures and varying incubation times of liquid antiseptics resulting in a significant number of patients with detectable pathogens remaining at the disinfected area. Accordingly, there is an urgent need for disinfection methods that guarantee uniform and effective disinfection of surgical sites or wounds to be treated.

SUMMARY OF THE INVENTION

It is the objective of the present invention to provide methods of skin disinfection, preferably pre-surgical skin disinfection, with improved efficacy and increased biocompatibility.

The problem is solved by the present invention.

The inventors have developed an antiseptic gel with significantly improved biocompatibility features, specifically allowing standardization of the dosage and, if desired, incubation time of an antiseptic. Specifically, such standardization facilitates compliance with quality management regulations and increases the efficacy of the skin disinfection procedure.

According to the invention there is provided an antiseptic plaster comprising an adhesive medical dressing partially coated with a composition comprising an antiseptic compound and a biocompatible gelling agent.

Specifically, there is provided an antiseptic plaster comprising an adhesive medical dressing, wherein a first surface of the dressing is partially coated with a composition comprising an antiseptic compound, specifically 8-hydroxyquinoline or octenidine, and a biocompatible gelling agent, and a second surface of the dressing optionally comprises an indicator, which indicates a pre-defined application time.

Specifically, the antiseptic compound can be any of a virucide, a fungicide and/or a bactericide. Therefore, the antiseptic plaster provided herein can have virucidal, fungicidal and/or bactericidal activity.

Specifically, the antiseptic compound is selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof, octenidine, povidone iodine, alcohol, chlorhexidine, guanidine, phenol-and phenol derivatives, quaternary ammonium derivatives, iodine and iodine derivatives, alkyl amine and alkyl amine derivatives, pyrimidine and pyridine, pyrimidine and pyridine derivatives, halogenated compounds, quinoline and quinoline derivatives, benzoquinone and benzoquinone derivatives, silver containing compounds, and hexetidine. Preferably, the pharmaceutically acceptable salt of hydroxyquinoline is hydroxyquinoline-sulfate.

Specifically, the antiseptic compound is 8-hydroxyquinoline.

According to a specific embodiment, the antiseptic plaster described herein comprises an adhesive medical dressing which is partially coated with a composition comprising 8-hydroxyquinoline and a biocompatible gelling agent

According to a specific embodiment, the antiseptic compound is present at a concentration of 0.001 to 10%, preferably 0.1 to 5% by weight of the composition. Specifically, the antiseptic compound is present in the composition partially coating the adhesive medical dressing of the antiseptic plaster provided herein at a concentration of

at least 0.001, 0.01, 0.05, 0.1, 0.25, 0.5, 0.75, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5 or 5.0% by weight of the composition.

According to a specific embodiment, the antiseptic plaster provided herein further comprises an indicator, which indicates a pre-defined application time. Preferably, such time indicator can indicate the passing of 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 or 60 minutes or more.

According to a specific embodiment, the antiseptic plaster described herein comprises an adhesive medical dressing, wherein a first surface of the dressing is partially coated with a composition comprising an antiseptic compound and a biocompatible gelling agent, and a second surface of the dressing optionally comprises an indicator, which indicates a pre-defined application time.

According to a specific embodiment, the biocompatible gelling agent is selected from the group consisting of agarose, fibronectin, collagen, carrageenan, gelatin, agar agar, methylcellulose, hydroxypropyl methylcellulose, hyaluronan, elastin-like polypeptides, polyvinyl alcohol, sodium polyacrylate, acrylate polymers, polysorbate 20 and polyethylene glycol.

According to a specific embodiment, the biocompatible gelling agent is present at a concentration of 0.01 to 10%, preferably 0.25% to 5% and even more preferably 0.5 to 1% by weight of the composition. Specifically, the biocompatible gelling agent is present in the composition partially coating the adhesive medical dressing of the antiseptic plaster provided herein at a concentration of 0.25, 0.3, 0.35, 0.4, 0.45, 0.50, 0.55, 0.60, 0.65, 0.70, 0.75, 0.80, 0.85, 0.90, 0.95, 1.0, 1.25, 1.50, 1.75, 2.00, 2.5, 3.0, 3.5, 4.5 or 5% by weight of the composition.

According to a preferred embodiment of the invention, the antiseptic compound is selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof and octenidine and the biocompatible gelling agent is selected from the group consisting of agarose, collagen and fibronectin.

According to a specific embodiment of the invention, the plaster comprises the features shown in Figure 1:

(1) A composition comprising an antiseptic compound and a biocompatible gelling agent, partially coating an

(2) adhesive medical dressing, and optionally

(3) an outer area of the composition comprising the antiseptic compound and the biocompatible gelling agent which is stained with a biocompatible dye,

(4) a small stripe of the composition comprising the antiseptic compound and the biocompatible gelling agent which is stained with a biocompatible dye in a different colour to mark the area for sterile draping,

(5) a central area of the composition comprising the antiseptic compound and the biocompatible gelling agent which is not stained with a dye to allow visibility of the area underneath,

(6) a time indicator, and

(7) a button activating the time indicator.

If desired, further supplements can be added to the gel prior to solidification. For example, addition of wound healing agents is desirable when the antiseptic plaster provided herein is used for post-operative protection of an operation site or when it is used to cover wounds, specifically large wounds or chronic wounds.

According to a specific embodiment of the antiseptic plaster provided herein, the composition further comprises wound healing agents selected from the group consisting of albumin, β-carotin, zinc, ascorbic acid, TGFβ and FGF.

According to a specific embodiment of the antiseptic plaster provided herein, the composition further comprises a local anesthetic.

According to a further specific embodiment of the antiseptic plaster provided herein, the composition further comprises at least one biocompatible dye.

According to a preferred embodiment of the antiseptic plaster provided herein, the adhesive medical dressing is an adhesive film dressing, preferably transparent and semi-permeable or porous.

Specifically, the adhesive medical dressing described herein is a skin-compatible dressing with adhesive properties which is selected from the group consisting of polyurethane, zinc oxide, rubber, latex, lanoline, acetate, cellulose, polyethylene, cotton, polyacrylate, polyvinylchloride, polyester and silicone.

Further described herein, is use of the antiseptic plaster described herein for skin disinfection, preferably pre-operative skin disinfection and/or for post-operative protection of the operation site. Specifically, the antiseptic plaster described herein can be used to protect the surgical site from infection after wound closure by applying the antiseptic plaster described herein on top of the wound.

According to a further specific embodiment, the antiseptic plaster described herein is used as an antiseptic cover of acute or chronic wounds.

Further provided herein is a method of producing the antiseptic plaster described herein, wherein a liquid solution comprising the at least one antiseptic compound is added to the biocompatible gelling agent to generate the composition partially coating the adhesive patch, and wherein the liquid solution optionally further comprises at least one wound healing agent and/or at least one biocompatible dye and/or a local anesthetic.

Further provided herein is a textile wound care material or wound foam coated with a composition comprising an antiseptic compound selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof, including but not limited to 8-hydroxyquinolinesulfate, and octenidine, and a biocompatible gelling agent selected from the group consisting of fibronectin, methylcellulose, collagen, hyaluronan, carrageenan and agarose.

Specifically, the composition coating the textile wound care material or wound foam described herein comprises an antiseptic compound which is 8-hydroxyquinolinesulfate and a biocompatible gelling agent which is fibronectin.

Further provided herein is an implant or intracorporal medical device coated with a composition comprising an antiseptic compound which is 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof, and a biocompatible gelling agent selected from the group consisting of collagen, agarose, carrageenan, fibronectin and methylcellulose.

Specifically, the composition coating the implant or intracorporal medical device described herein comprises an antiseptic compound which is 8-hydroxyquinolinsulfate and a biocompatible gelling agent which is fibronectin.

According to a further specific embodiment, the antiseptic plaster described herein is used in combination with a composition comprising an antiseptic compound and a biocompatible gelling agent, for skin or wound disinfection, preferably for pre-operative skin disinfection.

According to a preferred embodiment, the composition to be used in combination with the antiseptic plaster comprises an antiseptic compound selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof and

octenidine and a biocompatible gelling agent selected from the group consisting of agarose, fibronectin, collagen, carrageenan, methylcellulose and hyaluronan.

FIGURES

Fig. 1: Schematic drawing of an exemplary antiseptic plaster for pre-operative skin disinfection. (1) composition comprising antiseptic compound and biocompatible gelling agent, (2) adhesive medical dressing, (3) outer area of the composition comprising antiseptic compound and biocompatible gelling agent stained with a biocompatible dye, (4) small stripe of the composition comprising antiseptic compound and biocompatible gelling agent stained with a biocompatible dye in a different colour to mark area for sterile draping, (5) central area of the composition comprising antiseptic compound and biocompatible gelling agent without dye to allow visibility of skin, (6) time indicator, (7) activation button of time indicator.

Fig. 2: Mitochondrial activity of NIH-3T3 fibroblasts after disinfection with the antiseptic gel is comparable to control while disinfection with the liquid disinfectant solutions Braunol™ and Octenisept™ leads to a significant inhibition of mitochondrial activity.

Fig. 3: Embedding the antiseptic compound into a gel led to a significant improvement of biocompatibility: A wound gap in a monolayer cell culture disinfected with an 8-Hydroxyquinolin-Sulfate or Octenisept™ containing gel was completely closed after 72 hours comparably to untreated control wounds. In contrast, cell layers disinfected with 8-Hydroxyquinolin-Sulfate or Octenisept™ in a liquid aggregation state did not show any signs of healing within the first 72 hours after disinfection.

Fig. 4: No significant difference regarding cell proliferation and viability was observed between untreated control cell cultures and cultures disinfected with an antiseptic gel with or without the addition of Toluidine Blue for identification of the disinfected area. Viable cells could not be retrieved for counting and viability evaluation after disinfection with the liquid antiseptic solutions Braunol™, Kodan™ or Octenisept™.

Fig. 5: The efficacy of an antiseptic gel against MRSA, Staph. aureus and Staph. epidermidis/P. aeruginosa is higher than the effect of a liquid antiseptic solution.

Fig. 6: Average OD 600 after 3 days was 1,168 for controls but only 0.030 in HQS-treated patches ($p<0.0001$).

Fig. 7: OD 600 of MRSA-contaminated Lysogeny Broth medium containing HQS-treated screws was 0,47 vs 1,47 of untreated screws after 7 days of incubation ($p<0.013$).

Fig. 8: The HQS-Fibronectin-gel coated wound dressing demonstrates a significantly higher efficacy against MRSA than the commercially available antiseptic dressing (Kerlix™) and the untreated control dressing.

Fig. 9: Average collagen synthesis was 101 pg in untreated cells, 100 µg in cells treated with an HQS gel for 24 hours and 112 pg ($p<0.006$) when human serum albumin was added to the antiseptic gel.

Fig. 10: Addition of ZNSO4 or FGF to the antiseptic gel significantly increased collagen synthesis.

Fig. 11: The antiseptic gel was significantly more effective in reducing bacterial proliferation than an equivalent concentration of 8-Hydroxyquinolinesulfate (HQS) in a. dest.

Fig. 12: Applying 8-Hydroxyquinolinsulfate as an antiseptic gel did not significantly impair mitochondrial activity. In contrast, when applying HQS dissolved in ultra low agarose and omission of the gelling step or dissolved in distilled water, mitochondrial activity was significantly reduced.

Fig. 13: Disinfection with Octeniderm™ resulted in an average number of 12.7 (+/- 5.4) CFUs per visual field while disinfection with the antiseptic gel demonstrated a significantly higher suppression of bacterial proliferation with an average of 0.5 (+/-1) CFU per visual field ($p<0.0001$).

Fig. 14: Diffusion kinetics of an antiseptic gel and an equivalent dosage of liquid 8-Hydroxyquinoline.

DETAILED DESCRIPTION

Infections, such as surgical site infections, are one of the most common complications of acute or chronic wounds and surgical procedures. Using current disinfection methods, aseptic conditions in the operation area can only be achieved in about 78% of the patients. In about 22%, pathogens, such as bacteria, are still detectable after skin disinfection and increase the risk of wound healing disorders and infection, following for example surgical procedures[13]. Accordingly, there is an urgent need for

disinfection methods with increased efficacy and improved biocompatibility that preferably allow standardization of the disinfection procedure.

Accordingly, the present invention provides methods and devices for effective disinfection of skin areas or wound dressings or coating implants or intracorporal medical devices prior to surgical or medical treatment or for wound care of acute or chronic wounds. Specifically, herein provided, is an antiseptic plaster comprising an adhesive medical dressing partially coated with a composition comprising an antiseptic compound and a biocompatible gelling agent, with significantly reduced cytotoxicity and increased antiseptic efficacy.

As used herein, the term "about" encompasses the explicitly recited values as well as small deviations therefrom. Accordingly, a deviation from a recited value for 10%, preferably 5%, preferably 1% is encompassed by the term "about".

As used herein, the term "subject" or "individual" or "patient" shall preferably refer to a warm-blooded mammal, particularly a human being.

The term "patient" includes human and other mammalian subjects that are subjected to surgery or receive wound care treatment.

Classification herein of an ingredient as an active or carrier ingredient is made for clarity and convenience, and no inference should be drawn that a particular ingredient necessarily functions in the composition in accordance with its classification herein. Furthermore, a particular ingredient can serve a plurality of functions, thus disclosure of an ingredient herein as exemplifying one functional class does not exclude the possibility that it can also exemplify another functional class.

As used herein, the term "biocompatible" refers to a material's compatibility with living tissue or a living system by not being toxic, injurious, or physiologically reactive and not causing immunological rejection. Compounds referred to as biocompatible herein, perform their desired function without eliciting any undesirable local or systemic effects in the patient.

The antiseptic plaster provided herein, comprises a flexible adhesive medical dressing which is a carrier partially coated with a soft but solid gel composition comprising an antiseptic compound and a biocompatible gelling agent.

The term "adhesive medical dressing" as used herein refers to a flexible material which allows the antiseptic plaster to be placed on the desired surface, such as skin, organ, tissue, in a manner that allows the antiseptic plaster to conform to the topology

of the surface. Preferably, the medical dressing is transparent to allow visibility of the surface underneath. The medical dressing further can include a pressure sensitive adhesive on at least one face, to assist in placement of the antiseptic plaster on the desired surface and hold it in place. It may be porous, elastic or biodegradable and it may have some memory effect. The adhesive medical dressing is non-toxic as it is intended to be used on biological tissues such as skin and on open wounds and is biocompatible with the desired surface. Preferably, it is a material that is governmentally approved or generally regarded as safe for the desired purpose.

Suitable adhesive medical dressing can be formed of synthetic or natural materials or fabrics, such as for example any suitable polymeric film, woven or non-woven fabric or mixtures thereof. Examples of suitable flexible, biocompatible materials include but are not limited to nylon, polyethylene, polypropylene, ethylene propylene copolymers, ethylene butylene copolymers, polyurethane, polystyrene, plasticized polyvinylchloride, polyester, polyamide, cotton, polytetrafluoroethylene (PTFE), zinc oxide, rubber, latex, lanoline, acetate, cellulose, cotton, polyacrylate, silicone and biovascular material.

The size and shape of the antiseptic plaster can be tailored to the specific intended use by shaping the gel composition according to the desired surface (e.g. rectangular, triangular, round or any other shape). Preferably, the size of the adhesive medical dressing is bigger than that of the gel composition to allow adhesive overhangs to keep the gel composition in place on the desired surface. Preferably, the antiseptic plaster comprises adhesive overhangs on all sides, however, depending on the shape of the desired surface less or no overhangs are possible.

For example, a rectangular or square antiseptic plaster can range in width from about 1cm to about 50cm or more, preferably 10cm to 30cm and can range in length from about 1cm to about 100cm or more, preferably 5cm to 30cm. However, also smaller dimensions are possible. Preferably, the antiseptic plaster comprises an overhang of adhesive medical dressing over the gel composition of at least 0.5cm, preferably at least 1cm or more.

Still, other configurations of the antiseptic plaster described herein will be apparent to those skilled in the art. For example, although described above as being in rectangular or square configurations, the antiseptic plaster can take any number of other shapes, which can be designed for particular applications. For example, circular or round

(disc-shaped) flexible materials can be used, such as to cover round wounds or blister bases, sores, or the like; arc-shaped (curved rectangular shaped) flexible materials can be used, such as to cover curved lacerations or incisions; and the like. Other shapes, such as oval, triangular, polygonal, semi-circular, and the like, can also be used.

As used herein, the term "antiseptic" refers to means of preventing or reducing growth of disease-causing microorganisms or to killing or deactivating disease-causing microorganisms, specifically it refers to exhibiting any of virucidal, fungicidal and/or bactericidal activity. Accordingly, the antiseptic plaster provided herein can have virucidal, fungicidal and/or bactericidal or sporicidal activity. Specifically, the antiseptic plaster provided herein comprises an antiseptic compound which has virucidal, fungicidal, sporicidal and/or bactericidal activity or the antiseptic plaster provided herein comprises three different antiseptic compounds, a virucide, a fungicide and a bactericide.

Specifically, a virucide is any natural or artificial organic or inorganic compound that deactivates or destroys viruses. Preferably, the antiseptic compound which is a virucide is selected from the group consisting of quinolinoles and their derivates, octenidine, PVP-Iodine, alcohol, hexetidine and guanidine.

Specifically, a fungicide is any natural or artificial organic or inorganic compound that deactivates or destroys parasitic fungi or their spores. Preferably, the antiseptic compound which is a fungicide is selected from the group consisting of allylamines, squaleneperoxidase-inhibitors, naftifine, tolnaftate, morpholines, amorolfine, pyrroles, pyrrolnitrin, imidazole, azoles, polyene-antimycotics (e.g. amphotericin B, nystatin, natamycin), griseofulvin, caspofungin 5-fluorcytosine, ciclopirox.

Specifically, a bactericide is any natural or artificial organic or inorganic compound that kills bacteria or limits their growth. Preferably, the antiseptic compound which is a bactericide is selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof, octenidine, povidone iodine, alcohol, chlorhexidine, guanidine, phenol- and phenol derivatives, quaternary ammonium derivatives, iodine and iodine derivatives, alkyl amine and alkyl amine derivatives, pyrimidine and pyridine, pyrimidine and pyridine derivatives, halogenated compounds, quinoline and quinoline derivatives, benzoquinone and benzoquinone derivatives, silver containing compounds, and hexetidine.

The gel composition partially coating the adhesive medical dressing can be generated using various antiseptic compounds. Preferably, the antiseptic compound is selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof, octenidine, povidone iodine, alcohol, chlorhexidine, guanidine, phenol-derivatives, quaternary ammonium derivatives, iodine derivatives, alkyl amine derivatives, pyrimidine and pyridine derivatives, halogenated compounds, quinoline derivatives, benzoquinone derivatives, silver containing compounds, and hexetidine.

According to a preferred embodiment of the invention, the antiseptic compound used is 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof. 8-hydroxyquinoline is an organic compound with the formula C_9H_7NO. It is a metal chelator with antimicrobial and antifungal activity and mild anthelmintic and amebicidal action. The substance exists as a free lipophilic base or in form of water-soluble salts, such as for example 8-hydroxyquinoline sulfate. Its bacteriostatic and fungistatic action is believed to be due to the chelation of essential trace minerals on the surface of bacteria and fungi.

Specifically, where the antiseptic compound comprised in the composition partially coating the adhesive medical dressing is 8-hydroxyquinolinsulfate it is present in the composition at a concentration of 0.001 to 5%, preferably about 0.25% and even more preferably about 0.5% - 1% by volume of the composition.

According to a preferred embodiment of the invention, the antiseptic compound used is octenidine. Octenidine dihydrochloride, synonymously used with octenidine, is a cationic surfactant, with a gemini-surfactant structure, derived from pyridine. Octenidine is active against Gram-positive and Gram-negative bacteria and it has been used primarily in Europe as an antiseptic prior to medical procedures, including neonates. According to a preferred embodiment, the ready-to-use solutions of octenidine, octenisept and octeniderm, are used as antiseptic compound comprised in the composition partially coating the adhesive medical dressing. Octenisept™ from Schülke is a ready-to-use antiseptic solution comprising octenidine. 100g Octenisept solution contains: Octenidine dihydrochloride 0.1g, 2-Phenoxyethanol (Ph.Eur.) 2.0g. cocamidopropyl betaine, sodium D gluconate, glycerol 85%, sodium chloride, sodium hydroxide and purified water are listed as further ingredients of Octenisept. Octeniderm™ from Schülke is a ready-to-use antiseptic solution comprising octenidine.

100 g solution contains: octenidine dihydrochloride 0.1 g, 1-propanol (Ph.Eur.) 30.0 g, 2-propanol (Ph.Eur.) 45.0 g. Other ingredients: purified water.

Specifically, where the antiseptic compound comprised in the composition partially coating the adhesive medical dressing is octenidine it is present in the composition at a concentration of 0.001 to 5%, preferably about 0,05 – 0,1% and even more preferably about 0,07 % per weight of the composition.

Most liquid antiseptic solutions, such as 8-hydroxyquinoline sulfate or octenisept, demonstrate a significant cytotoxic effect, which is in the case of 8-hydroxyquinoline even investigated for the treatment of malignant diseases. Specifically, the cytotoxic effect of octenisept or 8-hydroxyquinoline sulfate can be significantly reduced by embedding the antiseptic compound into a gel allowing constant release over a prolonged period of time. Specifically, embedding octenidine or 8-hydroxyquinoline sulfate into a gel significantly improves tissue compatibility features and strongly reduces the side effects observed on fibroblast and keratinocyte proliferation and viability.

According to further preferred embodiments, antiseptic compounds such as triclosan (5-chlorine-2-(2,4-dichlorphenoxy)-phenol), PVP–iodine (poly(vinylpyrrolidone)–iodine complex), polyhexanide (polyhexamethylene biguanide) and chlorhexidine di-gluconate (chlorhexidine) which are widely used for the prevention and therapy of infections, and are governmentally approved or generally found to be safe are used in the antiseptic plaster described herein.

Specifically, commercially available antiseptic solutions such as Octenisept™, Braunol™, Kodan™ or Isozid™ can be used to generate the antiseptic gel of the antiseptic plaster provided herein.

Braunol™ of Ratiopharm is a liquid antiseptic comprising 7.5 g of povidone-iodine (average molecular weight 40,000, containing 10% available iodine) in 100 g of solution, corresponding to 0.75 g of iodine in 100 g of solution and the excipients sodium dihydrogen phosphate dihydrate, sodium iodate, macrogol lauryl ether 9, sodium hydroxide and purified water.

Kodan™ of Schülke and Mayr is a liquid antiseptic comprising the active ingredients 1-propanol, 2-propanol and 2-phenylphenolum. 1mL of Kodan™ solution typically comprises 403mg of 2-propanol, 90 mg of 1-propanol and 1.8mg of 2-phenylphenolum.

Isozid™ of Gebro Pharma is a liquid antiseptic solution with bactericidal, fungicidal and virucidal activity. It contains the active ingredients 1-propanol, 2-propanol and hexetidine.

Specifically, the composition partially coating the adhesive medical dressing of the antiseptic plaster provided herein is prepared by adding Octenisept™, Braunol™, Kodan™ or Isozid™ antiseptic solution 2:1 or 1:2 (v/v) to an agarose gel of a final concentration between 0,2% and 0.6%.

According to the invention, the cytotoxic effect of an antiseptic compound can be significantly reduced by embedding the antiseptic compound into a gel allowing a constant release of the antiseptic compound over a prolonged period of time.

As used herein, the term "biocompatible gelling agent" refers to any substance which increases the viscosity and provides a composition with the texture of a gel. The biocompatible gelling agent is selected from the group consisting of agarose, fibronectin, collagen, carrageenan, gelatine, agar agar, hyaluronan, elastin-like polypeptides, polyvinyl alcohol, sodium polyacrylate, acrylate polymers, polysorbate 20, polyethylene glycol, polyvinyl alcohol, polyvinylpyrrolidone, or a cellulosic gelling agent such as methyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, carboxymethylcellulose, hydroxy propyl cellulose, or the like, and a combination thereof.

In a preferred embodiment, the gelling agent is present at a concentration sufficient to produce a solid gel. Advantageously, such solid gel is still flexible and soft enough to adjust to irregularities of the desired surface such as for example various parts of the human body including even surfaces such as the stomach or back and uneven surfaces such as legs or arms.

Specifically, where the biocompatible gelling agent comprised in the composition partially coating the adhesive medical dressing is agarose it is preferably present in the composition at a concentration of 0.5 to 1%, preferably about 0.6% by weight of the composition.

According to a preferred embodiment of the invention, the antiseptic compound is selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof and octenidine and the biocompatible gelling agent is selected from the group consisting of agarose, collagen and fibronectin.

According to a further preferred embodiment, the antiseptic compound is 8-hydroxyquinolinsulfate and the biocompatible gelling agent is agarose. Specifically, the

composition partially coating the adhesive medical dressing of the antiseptic plaster provided herein is prepared by adding at least 0.25% 8-hydroxyquinolinsulfate to a gel that is still in the liquid phase comprising 0.5% to 1% agarose, preferably about 0.6% agarose.

According to yet a further preferred embodiment, the antiseptic compound is octenidine and the biocompatible gelling agent is agarose. Specifically, the composition partially coating the adhesive medical dressing of the antiseptic plaster provided herein is prepared by adding at least 0.05% octenidine to a gel that is still in the liquid phase comprising 0.5% to 1% agarose, preferably about 0.6% agarose.

As used herein, the term "indicator" refers to a time indicator, which indicates a pre-defined application time. Specifically, such time indicator allows for standardization of the incubation time by indicating that the desired incubation time has been reached. Preferably, said indicator is a small, tamper-proof label that is irreversibly activated by applying pressure, for example, with a finger. Preferably, said indicator is flexible. An exemplary time indicator comprises a clear window, which window is increasingly filled with colour upon the passing of time, once the pre-defined application time has been reached the window is entirely filled. Another exemplary time indicator comprises a certain colour, which colour changes once a pre-defined amount of time has passed. Specifically, such time indicator can indicate the passing of 1, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 or 60 minutes or more.

According to a specific embodiment, the indicator is an elapsed time indicator device comprising a switch, a power source and a power-driven elapsed time display for indicating the elapse of a limited predetermined segment of time upon activation of said switch and irrespective of the actual time of activation thereof. Specifically, said components are functionally interconnected and are printed on at least one substrate. Preferably, said time indicator device further comprises a controlling electronic circuit for controlling said display. The display displays progressive time increments and at the elapse of the predetermined time period, there is clear indication that this time period has elapsed.

In a specific example, the predetermined time elapse indicator consists of a power source connected to a switching device and the switching mechanism is of the type On/stay-on such that upon activation the elapse of the time is commenced. Activation of the mechanism causes the current from the power source to flow to the controlling unit.

The controlling unit determines the flow of current from the power source to the display in such a manner as to ensure that the predetermined time of the predetermined time elapse indicator device is proportioned uniformly to the display.

Such time indicators are readily available to a person skilled in the art. Exemplary time indicators are described in WO 2007/034473 A2.

According to a further specific embodiment, the indicator is an indicator system comprising a sensor mounted on the first surface of the dressing partially coated with a composition comprising an antiseptic compound as described herein, wherein the sensor is arranged in a way that it is able to determine a parameter of the dressing or of the individual's skin. The indicator further comprises a linking element, operatively coupled to the sensor such that during operation of the indicator system the linking element receives a signal from the sensor and transmits the signal from the sensor to a display. Specifically, the sensor is able to measure a moisture level and/or temperature. The measurement of the moisture level can be used to indicate, when it is time to replace the wound dressing.

The time indicator can be combined with an RFID (radio-frequency identification) transponder allowing digital documentation of the application time. Specifically, the time indicator can be an RFID tag.

RFID "radio-frequency identification" refers to a technology whereby digital data encoded in RFID tags or smart labels are captured by a reader via radio waves. RFID is similar to barcoding in that data from a tag or label are captured by a device that stores the data in a database. RFID tag data can be read outside the line-of-sight.

Specifically, the RFID tag consists of an integrated circuit and an antenna. The tag is also composed of a protective material that holds the pieces together and shields them from various environmental conditions. RFID tags are typically made from durable plastic, and the tag is embedded between the layers of plastic. RFID tags come in a variety of shapes and sizes and are either passive or active.

Typically, for an antiseptic to work properly and exert its full antiseptic activity, it has to be applied to skin for a certain amount of time. Infections contracted in hospitals could be significantly reduced if the full application time of antiseptics is complied with, however, it is often not possible to accurately determine the time an antiseptic has been in contact with a patient's skin. Using a time indicator on the antiseptic plaster described

herein has the profound advantage that the exposure time to the antiseptic can be accurately determined and therefore the application time can be complied with.

This advantage is not only true in surgical settings, but also in wound care, where a time indicator can be used to determine the application time and prevent application of a single wound dressing for too long. If a wound dressing is worn too long, it can cause damage to the skin, for example through a build-up of moisture under the dressing. Using a time indicator, or an indicator system as described herein able to measure moisture, excessive long-term application which is potentially harmful to an individual's skin can be prevented.

According to a preferred embodiment, the antiseptic plaster has the features as shown in Figure 1. Specifically, the antiseptic plaster can be of any size or shape to the desired application area. The plaster is either created by gelling the components of the antiseptic gel in a template to obtain a solid gel of the desired shape and size or by soaking a suitable absorbent material in the antiseptic gel prior to solidification. The gel composition (1) is then attached to the adhesive medical dressing (2) designed to remain on the patient's skin. A mesh or any other removal device can be integrated into the gel to facilitate aseptic removal of the gel from the patient´s skin. The exterior area of the gel (3) contains a dye that will stain the patient's skin to visualize the disinfected area. A small stripe (4) stained in a different colour will create a landmark for sterile draping. The interior area (5) remains uncoloured to allow for visualization of skin perfusion. The adhesive medical dressing can have slight fluid absorbing properties in order to absorb water from the surroundings while protecting the gel from dehydration. An indicator sticker (6) is applied on top of the adhesive fabric facing away from the gel. The sticker is activated at the application time of the antiseptic plaster by pressing the activation button (7). Reaching the pre-set application time can be indicated by a colour change of the control field (8), but any other ways of indication (including an RFID transponder) are applicable as well. The described procedure of combining an antiseptic plaster with a time indicator allows for standardization of the antiseptic dosage (µg/cm^2 skin area) and incubation time and therefore increases efficacy of surgical site antisepsis.

According to a specific embodiment, the antiseptic plaster described herein further comprises one or more wound healing agents. As used herein, the term "wound healing agents" refers to any synthetic or natural, biological or chemical agent, which

promotes the healing of acute or chronic wounds and/or prevents or lessens the formation of scar tissue.

Addition of wound healing agents to the antiseptic plaster described herein can significantly reduce the time required for a wound to heal and it can reduce the formation of scar tissue.

Wound healing is divided into four stages: (1) haemostasis, (2) inflammation, (3) proliferation, and (4) maturation. Each of these phases is controlled and regulated by biologically active substances called growth factors. Growth factors are polypeptides that control the growth, differentiation, and metabolism of cells. These growth factors are hormone-like molecules that interact with specific cell surface receptors to control the process of tissue repair and exert a powerful influence on wound healing and repair.

Preferably, the one or more wound healing agents comprised in the antiseptic plaster described herein are albumin, β-carotin, zinc, ascorbic acid, and growth factors such as transforming growth factor β (TGFβ), transforming growth factor α (TGFα), epidermal growth factor (EGF), hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF) and fibroblast growth factor (FGF).

Preferably, ascorbic acid is present at a concentration of about 0.01-0.05 mg/ml, β-carotene is present at a concentration of about 1-5 µg/ml, zinc is present at a concentration of about 0.015-0.025 mg/ml and FGF is present at a concentration of about 5-10 ng/ml. Preferably, human serum albumin is present in the gel composition at a concentration of at least 20 mg/mL, preferably at least 40 mg/ml.

According to a further preferred embodiment, the composition partially coating the adhesive medical dressing of the antiseptic plaster described herein comprises further suitable bioactive materials. Specifically, such suitable bioactive materials include, but are not limited to, medicaments such as antibiotics, antimicrobials, bacteriocins, bacteriostats, steroids, anti-inflammatory agents, anti-tumor agents, antioxidants, or mixtures thereof.

According to a specific embodiment, a biocompatible dye can be included in the gel composition. One or more biocompatible dyes can be present. Biocompatible colorants herein include pigments, dyes, lakes and agents imparting a particular luster or reflectivity such as pearling agents. A colorant can serve a number of functions, including for example to act as an indicator of locations on the skin that have been

effectively contacted by the composition, to create landmarks for the area of surgical incision or for sterile drapings to be applied during the preparation for surgery and/or to modify appearance, in particular color and/or opacity, of the gel composition to enhance attractiveness to the consumer. Any biocompatible colorant can be used, including without limitation toluidine blue, talc, mica, magnesium carbonate, calcium carbonate, magnesium silicate, magnesium aluminum silicate, silica, alumina, hydroxyapatite, titanium dioxide, zinc oxide, red, yellow, brown and black iron oxides, ferric ammonium ferrocyanide, manganese violet, ultramarine titaniated mica, bismuth oxychloride and the like. If included, one or more colorants can be present in a total amount of about 0.001% to about 20%, for example about 0.01% to about 10% or about 0.1% to about 5% by weight of the composition.

Specifically, for pre-operative disinfection, a biocompatible dye such as for example toluidine blue can be added to the composition partially coating the adhesive medical dressing of the antiseptic plaster provided herein to ensure proper identification of the disinfected area. During the incubation time, the dye can diffuse from the gel onto the skin and stain the area in contact with the antiseptic plaster. Specifically, the dye can be applied to selected areas of the antiseptic plaster only, to create landmarks for the placement of aseptic cover clothes on the patient during the preparation for surgery. Preferably, a central area of the antiseptic plaster is not stained with biocompatible dye to create a clear window through which the skin underneath the antiseptic plaster remains visible.

According to a specific embodiment of the antiseptic plaster provided herein, the composition further comprises a local anesthetic. Specifically, local anesthetic is any natural or artificial organic or inorganic compound that causes reversible absence of pain sensation. Specifically, clinical local anesthetics belong to one of two classes, aminoamide and aminoester local anesthetics. Exemplary compounds used as local anesthetics include, but are not limited to, lidocaine, mepivacaine, prilocaine, articaine, bupivacaine, ropivacaine, etidocaine, dyclonine procaine, benzocaine, 2-chlorprocaine, oxybuprocaine, tetracaine or formocaine.

Preferably, the local anesthetic is present at a concentration ranging from 0.5 to 10 % by weight of the composition. Local anesthetics vary in their potency, which is largely the result of differences in lipid solubility, which enhances diffusion through nerve sheaths and neural membranes. This property is determined by the aromatic ring and

its substitutions, along with those added to the tertiary amine. For example, bupivacaine is more lipid soluble and potent than articaine, allowing it to be formulated as a 0.5% concentration (5 mg/mL) rather than a 4% concentration (40 mg/mL).

According to a specific embodiment, the antiseptic plaster provided herein is used for skin disinfection, preferably pre-operative skin disinfection. Currently, pre-operative skin disinfection is performed by applying a liquid antiseptic solution with cotton swabs onto a patient's skin on and around the surgical incision site. Such a method does not allow control of the actual dosage of antiseptic solution applied and it does not guarantee compliance with the required incubation times of antiseptic solutions. In contrast, using the antiseptic plaster described herein, the dosage of antiseptic compound that is contacted with the patient's skin can be determined precisely and uniform application of the antiseptic compound is guaranteed as the antiseptic plaster covers the surgical site and optionally surrounding areas completely. Specifically, the incubation time can be monitored with the help of the time indicator as described herein.

According to a specific embodiment, the antiseptic plaster described herein is applied to a patient's skin at the site of a planned surgical procedure or on top of the surgical wound closure after surgery. Specifically, the antiseptic plaster comprising a biocompatible dye as described herein is applied to the patient´s skin prior to the transfer to the operating room and advantageously allows surgical site identification and antiseptic skin preparation to be performed in one step. Specifically, the antiseptic plaster is removed in the operating room only after the indicator sticker indicates that the required incubation time has been reached. Specifically, after removal of the antiseptic plaster, the disinfected area is clearly identifiable as a clear area surrounded by a coloured area, wherein both areas are disinfected and the clear area is the area of surgical incision.

According to a specific embodiment, the antiseptic plaster provided herein is used for prevention or treatment of wound infection in acute or chronic wounds.

As used herein the term "wound" refers to minor lacerations, abrasions, avulsions, cuts, scrapes, scratches, bums, sunburns, ulcers, external vascular sites, internal vascular sites, deep wound trauma and surgical incisions. Specifically, the antiseptic plaster described herein can be used to protect such wound sites from further environmental insult. Specifically, the antiseptic plaster described herein can be used for post-operative protection of the operation site.

Specifically, the composition partially coating the adhesive medical dressing of the antiseptic plaster provided herein further comprises an analgesic compound to reduce the pain of chronic or acute wounds, preferably it comprises an analgesic medication compounded for topical use. Specifically, an analgesic compound is any natural or artificial organic or inorganic compound that provides relief from pain. Preferably, compounded topical medications use a mixture of 3 or more single medications to achieve multiple complementary effects at lower doses of each individual medication. Exemplary analgesic compounds include but are not limited to non-stereoidal anti-inflammatory substances, lidocaine, opioids, acetaminophen, metamizole. Preferably, the antiseptic plaster used as described herein on top of acute or chronic wounds comprises a wound healing agent and an analgesic agent and/or a local anesthetic.

The term “gel composition” as used herein refers to a composition comprising an antiseptic compound and a biocompatible gelling agent as described herein. The gel composition may be used to partially coat an adhesive medical dressing to generate the antiseptic plaster described herein. It may further be used to fully coat textile wound care material or wound foam or to fully coat implant material or intracorporal medical devices.

Specifically, the gel composition can be used in combination with the antiseptic plaster described herein, wherein the gel composition is applied as a gel, semi-gel, liquid, spray or dried powder.

Further provided herein is a method of producing the antiseptic plaster described herein. Specifically, the gel composition described herein, is produced by dissolving an antiseptic compound in a gel during the liquid phase. Any natural or synthetic gel or hydrogel as described herein can be used to generate the gel composition. Optionally at least one wound healing agent and/or at least one biocompatible dye and/or a local anesthetic are additionally dissolved in the gel. Specifically, further compounds may be added to the gel before polymerization. Such further compounds exemplary are analgesics, antibiotics or anti-inflammatory agents.

According to a specific embodiment of the method provided herein, the gelling agent is added to a liquid solution comprising the at least one antiseptic compound to generate the gel composition. The liquid solution optionally further comprises at least one wound healing agent and/or at least one biocompatible dye and/or a local anesthetic.

According to a specific embodiment of the invention, textile wound care material or wound foam is coated with a gel composition as described herein. Specifically, the textile wound care material or wound foam is coated with the gel composition under vacuum and subsequently dried under lamina flow prior to use.

Specifically, said gel composition comprises an antiseptic compound selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof and octenidine, and a biocompatible gelling agent selected from the group consisting of fibronectin, methylcellulose, collagen, hyaluronan, carrageenan and agarose. Specifically, the textile wound care material or wound foam can be any generally used wound care material such as woven or non-woven synthetic or natural materials or fabrics or wound foam such as for example polyurethane sponges or carotid patches.

According to a preferred embodiment, the textile wound care material or wound foam is coated with a gel composition comprising at least 0.25% 8-hydroxyquinoline sulfate and 5% fibronectin, v/v.

According to a further preferred embodiment, textile wound care material or wound foam is coated with a gel composition comprising at least 1% 8-hydroxyquinoline sulfate and at least 0,4% (w/v) collagen.

Further provided herein are implants or medical devices coated with the gel composition described herein. For example, antiseptic coatings can be used to combat the possibility of infection, which can arise from contaminated medical devices the hands of medical personnel who implant these devices, and autoinfection from the patient's own microflora. These infections are not easily treated. Proliferating bacteria on the surface of the implant can secrete a bio film or slime, which is difficult, if not impossible, for antibiotics to penetrate. Moreover, the presence of bacteria can change the pH around the implant. This can result in the release of ions and the production of corrosion products.

Coating implants or medical devices for intracorporal use with the gel composition described herein, permits sustained release of the active ingredients comprised in the gel composition. Specifically, implants or medical devices are coated with a composition comprising an antiseptic compound which is 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof, and a biocompatible gelling agent selected from the group consisting of collagen, agarose, carrageenan, fibronectin and methylcellulose.

Preferably, the gel composition further comprises at least one wound healing agent and optionally an antibiotic. Such antiseptic coating on the one hand prevents infections with increased efficacy and on the other hand should an infection appear it permits sustained release of the antibiotic at the site of the infection and thus decreases the amount of bacteria surrounding the coated surface.

Although there are many different techniques for depositing a material on the surface of an implant, all have in common that some extra material is being added to the implant, or in other words that there is a positive material transport to the implant. For example, in one very common technique a fine powder is applied to the surface of the object to be coated and the powder is compacted by heat treatment.

According to a further specific embodiment, the antiseptic plaster described herein is used in combination with a gel composition, as described herein, comprising an antiseptic compound and a biocompatible gelling agent, for skin or wound disinfection, preferably for pre-operative skin disinfection. Specifically, if the anatomical situs of the patient or the operation area is not suitable to ensure complete and full contact skin coverage with the antiseptic plaster, the application site is additionally disinfected with a more gelatinous composition comprising an antiseptic compound, a biocompatible gelling agent, and optionally a wound healing agent and a biocompatible dye. Preferably, the antiseptic plaster is then applied to the planned area of skin incision only. Specifically, the more gelatinous composition can either be applied using sterile swabs or sprayed onto the skin as an aerosol.

According to a preferred embodiment, the more gelatinous composition to be used in combination with the antiseptic plaster comprises an antiseptic compound selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof and octenidine and a biocompatible gelling agent selected from the group consisting of agarose, fibronectin, collagen, carrageenan, methylcellulose and hyaluronan.

Preferably, the more gelatinous composition comprises an antiseptic compound which is 8-hydroxyquinolinsulfate a biocompatible gelling agent which is ultra-low gelling agarose. Specifically, the more gelatinous composition is prepared by dissolving at least 0.25% 8-hydroxyquinolinsulfate in at least 0.6% ultra-low gelling agarose.

The examples described herein are illustrative of the present invention and are not intended to be limitations thereon. Different embodiments of the present invention have been described according to the present invention. Many modifications and variations may be made to the techniques described and illustrated herein without departing from the spirit and scope of the invention. Accordingly, it should be understood that the examples are illustrative only and are not limiting upon the scope of the invention.

EXAMPLES

Example 1: Antiseptic plaster for pre-operative skin disinfection

An exemplary antiseptic plaster is shown in Figure 1. It can be of any size or shape to fit the desired application area. The plaster is either created by gelling the components of the antiseptic gel in a template to obtain a solid gel of the desired shape and size or by soaking a suitable absorbent material in the antiseptic gel prior to solidification. The gel/absorbent material (1) is then attached to an adhesive fabric (2) designed to remain on the wearer´s skin. A mesh or any other removal device can be integrated into the gel to facilitate aseptic removal of the gel from the patient´s skin. The exterior area of the gel (3) contains a dye that will stain the recipient's skin to visualize the disinfected area. A small stripe (4) stained in a different colour will create a landmark for sterile draping. The interior area (5) remains uncoloured to allow for visualization of skin perfusion. The adhesive fabric can have slight fluid absorbing properties in order to absorb water from the antiseptic plaster while protecting the gel from dehydration. An indicator sticker (6) is applied on top of the adhesive fabric facing away from the gel. The sticker is activated by the health care professional at the application time of the antiseptic plaster by pressing the activation button (7). Reaching the pre-set application time can be indicated by a colour change of the control field (8), but any other ways of indication (including an RFID transponder) are applicable as well. The described procedure of combining an antiseptic solution in a gel with a time indicator allows for standardization of the antiseptic dosage (µg/cm^2 skin area) and incubation time and therefore increases efficacy of surgical site antisepsis.

The indicator sticker (6) used in this specific example was a time indicator by Time Strip UK Ltd, specifically Timestrip® 1 hour (TS-310). This indicator can be modified to display a shorter indication time. For sterilization monitoring, e.g. pre-surgical

sterilization, timestrips with a shorter indication time, of e.g. 2, 3, 4, 5, 10, 20 or 30 minutes, are preferably used.

The antiseptic plaster can be applied to the patient´s skin prior to the transfer to the operating room (OR) and allows surgical site identification and antiseptic skin preparation to be performed in one step. The antiseptic plaster can be removed in the OR as soon as the indicator sticker indicates that the required incubation time has been reached. After removal of the antiseptic plaster, the disinfected area is clearly visible and ready for skin incision.

The antiseptic plaster can also be used to protect the surgical site from infection after wound closure. For this purpose, the patch is applied on top of the wound immediately after wound closure and left there for 48 hours. Another application is the treatment of acute and chronic wounds if wound antisepsis is desired.

Example 2: Improved biocompatibility features of a solid antiseptic gel

An antiseptic gel was prepared by gelling 0.5% respectively 0.25% 8-Hydroxyquinolinesulfate (HQS) in a 0.6% agarose gel. After solidification, miniature gels to fit the size of the test plate were excised using sterile test tubes. NIH-3T3 P173 fibroblasts were plated into 24 well tissue culture plates at a density of $5x10^5$ cells / well in triplicates. After reaching confluency, the cells were disinfected either with the liquid disinfectants Braunol™ or Octenisept™ for 5 minutes or by applying the HQS-containing gels for 1 hour. Untreated cell cultures were used as controls. At the end of the incubation period, the culture medium was exchanged and cell proliferation was assessed via the reduction of tetrazolium salt towards formazan using the Ez4U cytotoxicity assay.

Mitochondrial activity of cell cultures treated with an antiseptic gel was comparable to control ($p<0.2$). Cells disinfected using liquid antiseptic solutions in contrast demonstrated a significant inhibition of mitochondrial activity (Fig. 2, $p<0.0001$ for Braunol™ resp. $p<0.0005$ for Octenisept™).

Potential side effects on wound healing were evaluated using the 2D scratch test. Antiseptic gels were prepared by gelling 0.5% 8-Hydroxyquinolinesulfate in a 0.6% agarose or by adding Octenisept™ antiseptic solution 1:2 (v/v) to a 0.6% agarose gel. NIH-3T3 fibroblasts were plated at a density of $5x10^5$ cells/well into 12 well plates. After

reaching confluence, the cell layer was aseptically scratched using a sterile pipet tip to create a wound gap. The cultures were then disinfected either with liquid 8-Hydroxyquinolinsulfate or Octenisept™ in an equivalent concentration for 5 minutes or treated by application of the solid antiseptic gels for 30 minutes. Cultures were inspected daily for signs of wound gap closure and documented as soon as the wound gap of the untreated control was closed.

While cell cultures treated with liquid antiseptic solutions did not show any sign of wound healing 72 hours after disinfection, the wound gap of the control group as well as the antiseptic gel groups were completely closed (Fig. 3).

Additionally, the influence of an antiseptic gel on cell proliferation and viability was evaluated. An antiseptic gel was prepared by gelling 0.25% 8-Hydroxyquinolinesulfate in a 0.6% agarose gel. Toluidine blue was added to a concentration of 0.0005% to allow for identification of the disinfected area. After solidification, miniature gels to fit the size of the test plate were excised using sterile test tubes. Human keratinocytes HaCaT P40 were plated into 24 well tissue culture plates at a density of $5x10^5$ cells / well in triplicates. After reaching confluency, the cells were disinfected either with the liquid disinfectants Braunol™, Kodan™ or Octenisept™ for 5 minutes or by applying the HQS-containing gels for 30 minutes. Cells were allowed to recover from antiseptic treatment for 48 hours prior to evaluation of cell count and viability.

Average cell counts after a 48 hours recovery period were $65.94x10^4$ for untreated control cell cultures, $79.83x10^4$ for cells treated with an uncoloured antiseptic gel and $72.5x10^4$ after the addition of Toluidine Blue to the antiseptic gel. No significant differences in cell proliferation were observed between the groups (Fig. 4A, $p<0.13$). Cells disinfected with the liquid antiseptic solutions Braunol™, Kodan™ or Octenisept™ did not show any signs of proliferation during the observation period. No viable cells could be retrieved for the evaluation of cell count and viability after disinfection with liquid disinfectants. A reason for this might be an impairment of cell attachment and subsequent loss of cells during the washing steps. This experiment was repeated 5 times by 3 different researchers to rule out a potential handling mistake. Average viability was 100% in the control group and 99.67 resp. 99.25 after treatment with an antiseptic gel with/without the addition of Toluidine Blue (Fig. 4B, $p<0.16$).

Cells treated with an antiseptic gel supplemented with Toluidine Blue were stained blue after antiseptic treatment and clearly visible macroscopically as well as in the phase contrast microscope.

Example 3: Visibility and efficacy *in vivo* against the resident flora of the skin

To assess staining capacity of an antiseptic gel supplemented with Toluidine Blue *in vivo*, the gel was applied onto a test person´s skin and incubated for 30 minutes. The disinfected area of the skin was clearly visible after removal of the gel. To evaluate antiseptic efficacy of the antiseptic gel *in vivo*, a wipe test was performed: The disinfected skin area as well as a non-disinfected area serving as control were covered with a sterile Lysogeny Broth agar film, which was then incubated at 37° and evaluated for bacterial and fungal growth.

While colony forming units as well as fungal hyphae were visible on the agar film contacted with the not disinfected area of the skin, the agar contacted with the disinfected skin area remained sterile after 4 days of incubation.

Example 4: *In vitro* efficacy against typical bacteria causing surgical site infection, including a multi resistant Staph. aureus (MRSA) strain

An Octenisept™ antiseptic gel was prepared as described in example 2. Bacterial cultures of MRSA, Staph. aureus and a mixed culture of Staph. epidermidis and Pseudomonas aeruginosa were isolated from patient derived wound swabs and cultured in Lysogeny Broth Medium at 37 °C. The bacterial suspension was applied onto 24 well cell culture plates ad allowed to attach for 24 hours. An antiseptic gel or the equivalent amount of liquid Octenisept™ were then added to the culture medium and bacterial proliferation was monitored for 72 hours. Untreated bacterial cultures served as control.

Bacterial proliferation was significantly inhibited in both disinfected groups (Fig. 5). The effect of the antiseptic gel was higher than the effect of the liquid antiseptic solution and biocompatibility - as demonstrated in example 2 – was significantly better.

Additionally, 200 µl of a Staph. aureus suspension culture were plated onto an agar plate and incubated for two hours at 37°C prior to disinfection with either an antiseptic gel or an equivalent dosage of liquid Octenisept™. The plates were the

incubated for further 24 hours prior to documentation. Untreated bacterial cultures served as control.

Proliferation of Staph. aureus was significantly inhibited after disinfection with liquid Octenisept™ or an Octenisept™ gel compared to control.

Example 5: Antimicrobial coating of a vascular patch

A polyester gelatine impregnated carotid patch (Flouropassiv™ / Vascutec) was submersed in an antiseptic gel containing 1% 8-Hydroxyquinolinsulfate dissolved in Rat Tail Collagen and incubated for 1 hour under constant agitation. Patches submersed in Phosphate Buffered Saline (PBS) were used as control. Samples were dried under a Laminar Air flow for 24 hours and stored at room temperature until experimentation. The patches were placed in Lysogeny Broth Medium containing a methicillin resistant Staphylococcus aureus strain and incubated at 37 °C and 40% humidity. Bacterial proliferation was monitored for 7 days after infection of the test samples.

The HQS-treated vascular patches demonstrated a significantly smaller bacterial load compared to control samples (Fig 6, $p<0.0001$). Average OD 600 after 7 days was 1,168 for controls but only 0.030 in HQS-treated patches.

Example 6: Antimicrobial coating of a screw (proof of concept for pedicle screw coating)

To generate a proof of concept for antimicrobial coating of implant materials, stainless steel screws obtained from a DIY-store were coated with HQS-collagen as described in example 4. The screws were placed in Lysogeny Broth Medium containing a Methicillin Resistant Staphylococcus aureus strain and incubated at 37 °C and 40% humidity. Bacterial proliferation was monitored for 7 days after infection of the test samples.

Significantly less turbidity of the culture medium was observed at a macroscopic level: While the control medium was turbid due to bacterial proliferation, the medium containing HQS coated screws was still clear.

After 7 days incubation in MRSA contamination culture medium, average OD 600 of the control screws was 1.47 versus 0.47 after screw impregnation with HQS-collagen ($p<0.013$, Fig. 7).

Example 7: Antiseptic coating of a wound dressing material against a multi resistant bacterial strain

An aqueous solution of 8-Hydroxyquinolinsulfate was dissolved 5% v/v in Fibronectin. A polyurethane sponge for continuous negative pressure wound therapy was cut into 5x5 mm squares and sterilized using ethylene oxide. The squares were then coated with the 8-Hydroxyquinolinsulfate-fibronectin-gel under vacuum and dried under laminar airflow.

A methicillin resistant Staphylococcus aureus (MRSA) strain was applied onto agar plates as well as 24 well plates in Lysogeny broth medium. A commercially available antiseptic dressing (Kerlix™) as well as uncoated polyurethane sponges served as control. The samples were applied in triplicates onto agar plates and inspected for bacterial proliferation after one week. Additionally, the test materials were placed in liquid MRSA cultures and incubated for 8 days followed by evaluation of OD 600.

After 8 days of incubation, OD 600 was 1.22 (+/- 0,1) for the untreated polyurethane sponge and 0,71 (+/-0.11) for the Kerlix™ dressing. HQS-Fibronectin coated sponges were significantly more effective resulting in an OD of 0.02 (+/-0.3; $p<0.02$) (Fig. 8).

Bacterial proliferation was visible underneath the uncoated CNP-sponge and to a lesser extent underneath the Kerlix™ dressing material after one week. The HQS-Fibronectin coated sponges in contrast did not show any bacterial proliferation underneath the sponge. An inhibition zone of 2-3 cm was present in the surrounding of the coated material.

Example 8: Effect of an antiseptic gel supplemented with additives promoting wound healing on collagen synthesis *in vitro*

An antiseptic gel was prepared by gelling 0.25% 8-Hydroxyquinolinesulfate in a 0.6% agarose gel. Human serum albumin was added to a concentration of 40 mg/ml to promote wound healing. After solidification, miniature gels to fit the size of the test plate were excised using sterile test tubes. HaCaT P36 human keratinocytes were plated into 24 well tissue culture plates at a density of 5x105 cells / well in triplicates. After reaching confluency, the cells were treated with the antiseptic gel for 24 hours. Untreated cells served as control. At the end of the incubation period, total collagen synthesis was quantified by Picro-Sirius red-staining and measuring absorption at 550 nm.

No significant differences in collagen synthesis were observed in control and HQS-gel treated cells. Average collagen synthesis was 101 pg in the control cell cultures and 100 pg in the HQS treated cells (n.s.). The addition of human serum albumin to the gel increased collagen synthesis to 112 pg ($p<0.006$) within 24 hours of incubation (Fig. 9).

Additionally, the effect of wound healing supplements was investigated in combination with a more gelatinous gel based on ultra-low agarose. An antiseptic gel was prepared by gelling 0.25% 8-Hydroxyquinolinesulfate in a 0.6% ultra-low agarose gel. Either 10 ng/ml FGF or 0,015 mg/ml $ZnSO_4$ were added to the gel. Human keratinocytes HaCaT P45 were plated at a density of $5x10^4$ cells into 24 well plates. After reaching confluency, cells were disinfected with the gelatinous antiseptic gel containing wound healing supplements for 5 minutes. Cells were allowed to recover from disinfection for 24 hours prior to evaluation of total collagen synthesis.

Total collagen synthesis was 36.55 pg in the untreated control group and increased to 63.98 pg resp. 77.26 pg after addition of either $ZnSO_4$ or FGF (Fig. 10).

Example 9: More gelatinous antiseptic gel for disinfection of an anatomical site difficult to cover completely with an antiseptic patch

A gelatinous antiseptic gel was prepared by dissolving 0.25% 8-Hydroxyquinolinesulfate in 0.6% ultra-low gelling agarose. This combination does not solidify at room temperature. Bacterial cultures of Streptococcus sp., Proteus mirabilis, MRSA, Enterococcus faecalis, Corynebacterium spp. and Staph epidermidis were isolated from patient derived wound swabs and cultured in Lysogeny Broth Medium at 37 °C. The bacterial suspension was applied onto 24 well cell culture plates ad allowed to attach for 24 hours prior to disinfection with the gelatinous antiseptic gel or an equivalent concentration of 8-Hydroxyquinolinsulfate in A. dest. Inhibition of bacterial proliferation was evaluated by measuring optical density at 600 nm 24 hours after disinfection.

The antiseptic gel was significantly more effective in reducing bacterial proliferation than an equivalent concentration of 8-Hydroxyquinolinesulfate (HQS) in A. dest. 24 hours after disinfection, OD 600 was 0.60 in the control group and 0.29 after

disinfection with HQS in A. dest. A combination of HQS with ultra-low gelling agarose (ULA) reduced bacterial proliferation to 0.04 after 24 hours ($p<0.0001$) (Fig. 11).

Example 10: Biocompatibility evaluation of different types of 8-Hydroxyquinolisulfate-gels

A gelatinous antiseptic gel was prepared by dissolving 0.25% 8-Hydroxyquinolinesulfate in 0.6% either ultra-low gelling agarose, standard agarose for gel electrophoresis, Carrageenan or Gelatin. After solidification, miniature gels to fit the size of the test plate were excised using sterile test tubes. Additionally, equivalent dosages of 8-Hydroxyquinolinsulfate in A. dest and ultra-low agarose (omitting the gelling procedure to be tested in a liquid aggregation state) were evaluated.

NIH-3T3 cells were plated into 24 well tissue culture plates at a density of $5x10^5$ cells/well in triplicates. After reaching confluency, the cells were disinfected either with 8-Hydroxyquinolinesulfate dissolved in A. dest or ultra-low agarose for 5 minutes or by placing miniature gels of 0.25% 8-Hydroxyquinolinesulfate in agarose, ultra-low agarose, gelatine or carrageenan in the test plates. The gels were incubated for 24 hours. Untreated cell cultures were used as controls. At the end of the incubation period, the culture medium was exchanged and cell proliferation was assessed via the reduction of tetrazolium salt towards formazan using the Ez4U cytotoxicity assay.

Mitochondrial activity after disinfection with the antiseptic gels was comparable to control. OD 450nm was 1.10 in untreated control cell cultures and after disinfection with a Carrageenan-based gel, 1.05 after disinfection with a gelatine-based gel and 0.97 after disinfection with a standard agarose-based gel. Using a gel based on ultra-low gelling temperature agarose resulted in an OD of 0.86. If the gelling step was omitted and the same combination applied in a liquid aggregation state, no mitochondrial activity could be detected. Applying 8-Hydroxyquinolinesulfate in A. dest. led to a significant suppression of mitochondrial activity to an OD of 0.40 (Fig. 12).

Example 11: Improved efficacy and prolonged antiseptic effect of an antiseptic gel

The numbers of postoperative infections caused by Propionibacterium acnes and Staph. epidermidis are increasing. As P. acnes and Staph. epidermidis are localized close to hair follicles and sebaceous glands in the deeper layers of the dermis, antisepsis

of the sebaceous areas of the skin represents a specific challenge. As the deeper layers of the skin also function as a bacterial reservoir allowing re-colonisation of the disinfected area over time, an antiseptic agent with a prolonged effect is highly desirable.

To evaluate the ability of two antiseptic agents to allow for penetration of the antiseptic compound into deeper layers, an agar diffusion assay was performed. 100 µl of a Staph. epidermidis and Pseudomonas aeruginosa suspension culture were plated onto an agar plate and covered with a 0.6% agarose gel. Another 30 µl of bacterial suspension were plated on top of the Gel. The top gel was then disinfected with either 30 µl of Octeniderm™ or 30 µl of a 1% aqueous 8-Hydroxyquinolinesulfate solution. The Plates were incubated for 24 hours at 37°C followed by documentation and evaluation of bacterial proliferation.

After disinfection with Octeniderm™, no bacterial proliferation was observed on top of the directly disinfected agarose gel. However, colony forming units were present on the underlying agar that had not directly been contacted with the antiseptic agent. Disinfection with 8-Hydroxyquinolinesulfate led to an inhibition of bacterial proliferation on top of the agarose-gel as well as on the underlying agar.

Disinfection with Octeniderm™ resulted in an average of 12.7 (+/- 5.4) Colony Forming Units (CFU) per visual field on the underlying agar plate, while disinfection with 8-Hydroxyquinolinsulfate demonstrated a significantly higher suppression of bacterial proliferation with an average of 0.5 (+/-1) CFU per visual field ($p<0.0001$) (Fig. 13).

Additionally, P. acnes was plated in suspension culture in 24 well plates in triplicates and incubated at 37°C under anaerobic conditions for 24 hours. After evaluation of OD 600, the test plates were disinfected with either Kodan™, Isozid™, Braunol™, Octenisept™ for 5 minutes or by application of a 0.25% 8-Hydroxyquinolinsulfate-agarose gel for 30 minutes. Bacterial proliferation was evaluated by measuring optical density at 600 nm after disinfection and after 30, 60 and 180 minutes to evaluate the long-term effect of disinfection.

While all antiseptic solutions were highly efficient immediately after disinfection, significant differences were observed during the follow up period: One hour after disinfection - at a timepoint where an average operation would still be ongoing - optical densities were 0.041 for Isozid™, 0.035 for Braunol™, 0.036 for Kodan™ and 0.02 for Octenisept. Disinfection with an 8-Hydroxyquinolinsulfate-agarose gel led to the lowest

bacterial proliferation with an OD of 0.01 after 1 hour which did not increase during the observation period.

Table 1: Optical density indicating bacterial proliferation at different time points after disinfection

	control	8-Hydroxyquinolinsulfate	Isozid	Braunol	Kodan	Octenisept
prior to disinfection	0.22975	0.22975	0.22975	0.22975	0.22975	0.22975
after disinfection	0.017	0.006	0.007	0.009	0.008	0.011
30 min	0.049	0.011	0.023	0.026	0.017	0.013
60 min	0.087	0.01	0.041	0.035	0.036	0.02
3 hours	0.102	0.009	0.065	0.047	0.044	0.019

Example 12: Evaluation of antiseptic diffusion kinetics from an antiseptic gel

Antiseptic gels were prepared by dissolving 0.06g agarose in 10 ml distilled water and boiling the gel for 2.5 minutes. After cooling, 200 µl of an aqueous 8-Hydroxyquinolinesulfate-solution at a concentration of 1 mg/µl were added to 2800µl of agarose solution, which was the allowed to gel at room temperature for 30 minutes. After gelling, miniature gels were excised with a sterile 1000 µl pipet tip. The gels were then placed in 48 well tissue culture plates and covered with 350 µl of distilled water. An equivalent concentration of liquid 8-Hydroxyquinolin was diluted in distilled water and tested as control: 100µl of distilled water were removed in triplicates from the gel containing wells resp. the control wells every 15 minutes and absorbance at 450 nm was determined.

While application of liquid 8-Hydroxyquinolinesulfate immediately reached a peak concentration, embedding 8-Hydroxyquinolinesulfate in an agarose gel resulted in a lower initial concentration with further slow, constant release of the antiseptic compound with an average pace of 10 µg per minute (Fig. 14).

REFERENCES

1. Eder C. et al. Antiseptikum ist nicht gleich Antiseptikum – Evaluierung der präoperativen Hautdesinfektion in der Wirbelsäulenchirurgie. 12. Jahrestagung der deutschen Wirbelsäulengesellschaft, Stuttgart 2017

2. Hagdorn M. et al. Local antisepsis and wound healing: in vitro and in vivo examination. Der Hautarzt 1995,46(5):319-324

3. Sanchez I et al. Veterinary Surgery 1988, 17(4):182-185

4. Sunil Kumar P. et al. PVP-iodine revisited. Indian Journal of dental advancements 2011, 3 (3):617-620

5. Damour et al. Cytotoxicity evaluation of antiseptics and antibiotics on cultured human fibroblasts. Burns 1992; 18(6):479-485

6. Hirsch T. et al. Vergleichende in vitro Studie zur Zytotoxizität klinisch eingesetzter Antiseptika. Der Hautarzt 2009, 60:984

7. Manquardt C. et al. Evaluation of the tissue toxicity of antiseptics by the hen´s egg test on the chorionallantoic membrane. European Journal of medical research 2010, 15:204

8. Konagaya M. SMON:Toxicity Evaluation of Some 8-Hydroxyquinoline Derivates. Journal of Pharmacy and Pharmacology 1999,51(5):543-548

9. https://medikamio.com/de-de/medikamente/solutio-hydroxychinolini-04/pil last accessed 06092017

10. Al-Yun Shen. Synthesis and Cytotoxicity Evaluation of some 8-Hydroxyquinoline Derivates. Journal of Pharmacy and Pharmacology 1999(51):

11. Veda Prachayasittikul. 8-Hydroxyquinolines: A review of their metal chelating properties and medicinal applications. Drug Des Devel Ther 2013;7:1157-1178

12. M. A. Epstein. International Review of Connective Tissue Research Vol. 1, 2016, Academic Press

13. Eder C. et al. Eur Spine J, 2017, 26:2978–3057

CLAIMS

1. An antiseptic plaster comprising an adhesive medical dressing, wherein the dressing is partially coated with a composition comprising an antiseptic compound, which is 8-hydroxyquinoline or octenidine, and a biocompatible gelling agent, and optionally comprises an indicator, which indicates a pre-defined application time.

2. The antiseptic plaster of claim 1, wherein the antiseptic compound is 8-hydroxyquinoline.

3. The antiseptic plaster of claim 1 or 2, wherein the composition further comprises an antiseptic compound selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof, octenidine, povidone iodine, alcohol, chlorhexidine, guanidine, phenol-derivatives, quaternary ammonium derivatives, iodine derivatives, alkyl amine derivatives, pyrimidine and pyridine derivatives, quinoline derivatives, benzoquinone derivatives, silver containing compounds, and hexetidine.

4. The antiseptic plaster of any one of claims 1 to 3, wherein the antiseptic compound is present at a concentration of 0.001 to 10% (w/w), preferably 0.1 to 5% (w/w).

5. The antiseptic plaster of any one of claims 1 to 4, wherein the biocompatible gelling agent is selected from the group consisting of agarose, fibronectin, collagen, carrageenan, gelatine, agar agar, methylcellulose, hyaluronan, polyvinyl alcohol, sodium polyacrylate, acrylate polymers, polysorbate 20, and polyethylene glycol.

6. The antiseptic plaster of any one of claims 1 to 5, wherein the biocompatible gelling agent is present at a concentration of 0.25 to 5% (w/w), preferably 0.5 to 1% (w/w).

7. The antiseptic plaster of any one of claims 1 to 6, wherein the antiseptic compound is selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof and octenidine and the biocompatible gelling agent is selected from the group consisting of agarose, collagen, and fibronectin.

8. The antiseptic plaster of any one of claims 1 to 7, wherein the composition further comprises wound healing agents selected from the group consisting of albumin, β-carotin, zinc, ascorbic acid, TGFβ, and FGF.

9. The antiseptic plaster of any one of claims 1 to 8, wherein the composition further comprises a local anesthetic.

10. The antiseptic plaster of any one of claims 1 to 9, wherein the composition further comprises at least one biocompatible dye.

11. The antiseptic plaster of any one of claims 1 to 10, wherein the medical dressing is a skin-compatible dressing with adhesive properties which is selected from the group consisting of polyurethane, zinc oxide, rubber, latex, lanoline, acetate, cellulose, polyethylene, cotton, polyacrylate, polyvinylchloride, polyester, and silicone.

12. The antiseptic plaster of any one of claims 1 to 11 for use in skin disinfection, preferably pre-operative skin disinfection and/or for post-operative protection of the operation site.

13. The antiseptic plaster of any one of claims 1 to 11 for use in prevention or treatment of wound infection in acute or chronic wounds.

14. A method of producing the antiseptic plaster of any one of claims 1 to 11, wherein a liquid solution comprising the at least one antiseptic compound is added to the biocompatible gelling agent to generate the composition partially coating the adhesive patch, and wherein the liquid solution optionally further comprises at least one wound healing agent and/or at least one biocompatible dye and/or a local anesthetic.

15. A textile wound care material or wound foam coated with a composition comprising an antiseptic compound selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof and octenidine, and a biocompatible gelling agent selected from the group consisting of fibronectin, methylcellulose, collagen, hyaluronan, carrageenan and agarose.

16. The textile wound care material or wound foam of claim 15, wherein the antiseptic compound is 8-hydroxyquinolinesulfate and the gelling agent is fibronectin.

17. An implant or intracorporal medical device coated with a composition comprising an antiseptic compound which is 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof, and a biocompatible gelling agent selected from the group consisting of collagen, agarose, carrageenan, fibronectin and methylcellulose.

18. The implant or medical device of claim 17, wherein the antiseptic compound is 8-hydroxyquinolinesulfate and the biocompatible gelling agent is fibronectin.

19. Use of the antiseptic plaster of any one of claims 1 to 11 in combination with a second composition comprising an antiseptic compound and a biocompatible gelling agent, for skin or wound disinfection, preferably for pre-operative skin disinfection.

20. Use of the antiseptic plaster according to claim 19, wherein the antiseptic compound of the second composition is selected from the group consisting of 8-hydroxyquinoline or a pharmaceutically acceptable salt thereof and octenidine and the biocompatible gelling agent is selected from the group consisting of agarose, fibronectin, collagen, carrageenan, methylcellulose and hyaluronan.

FIGURES

Figure 1

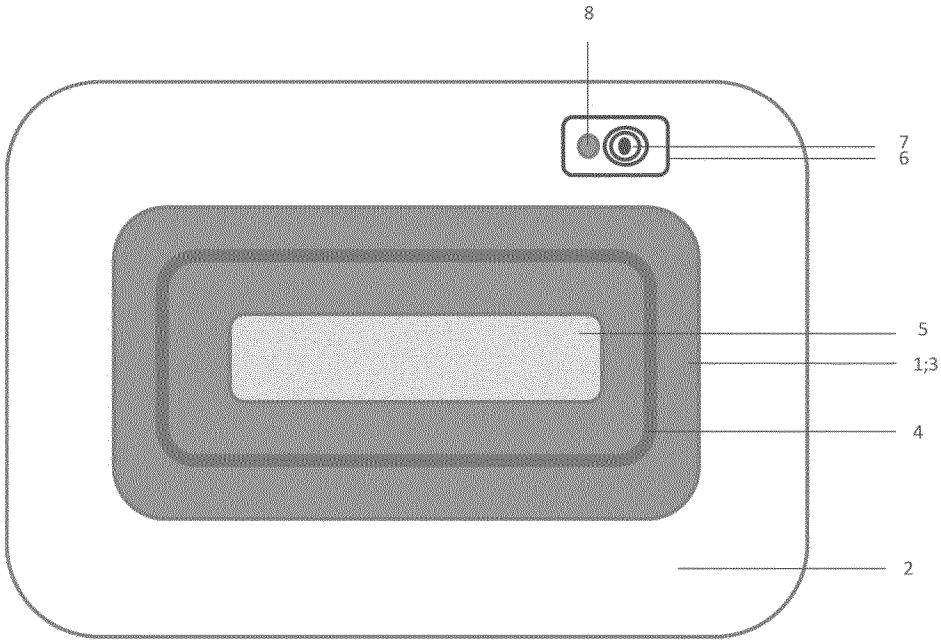


Figure 2

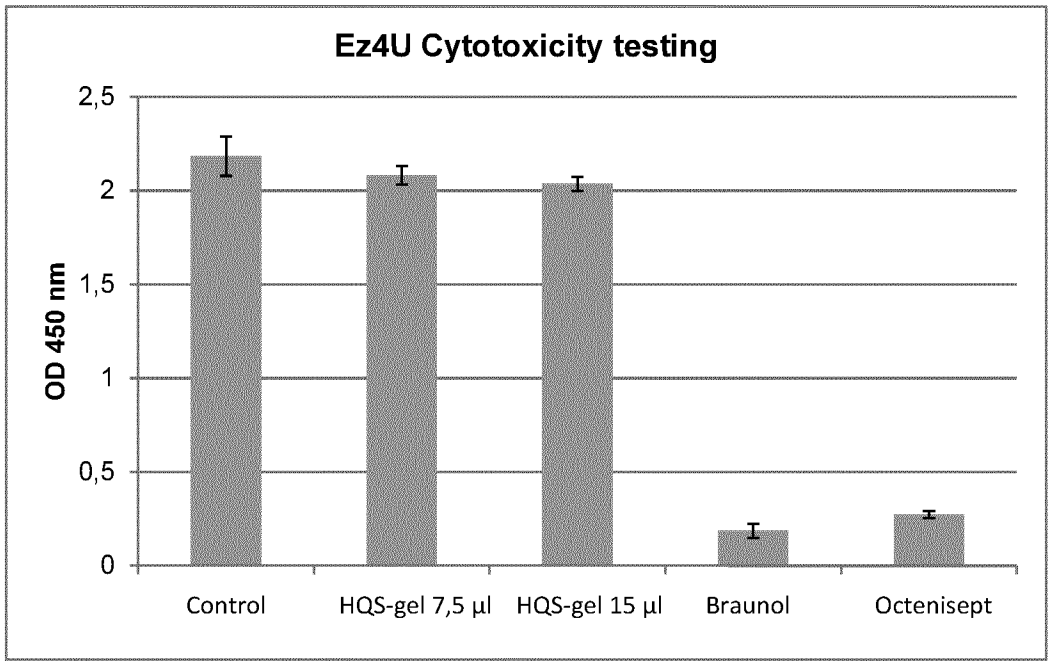


Figure 3

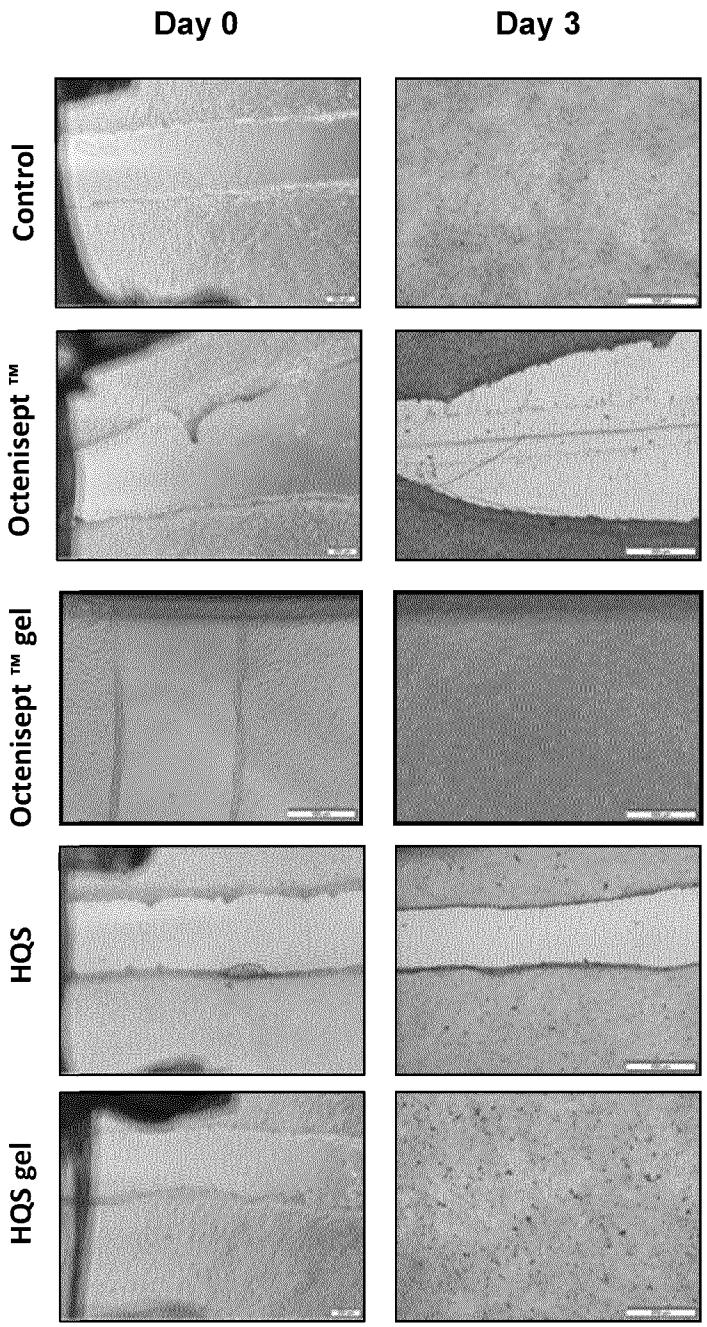


Figure 4

Figure 4A

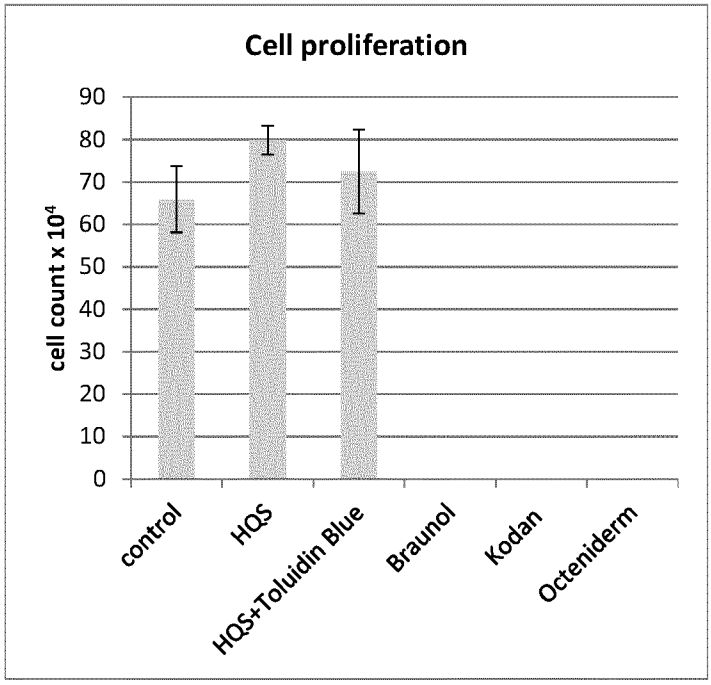


Figure 4B

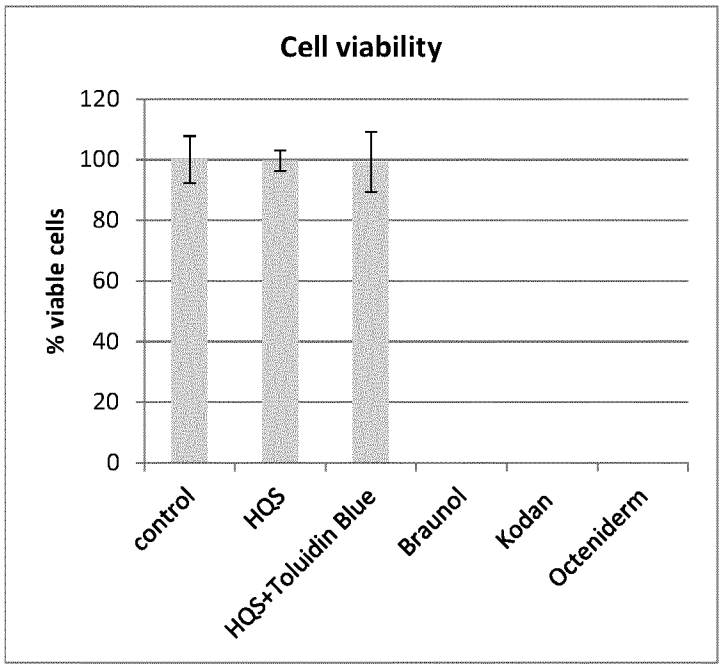


Figure 5

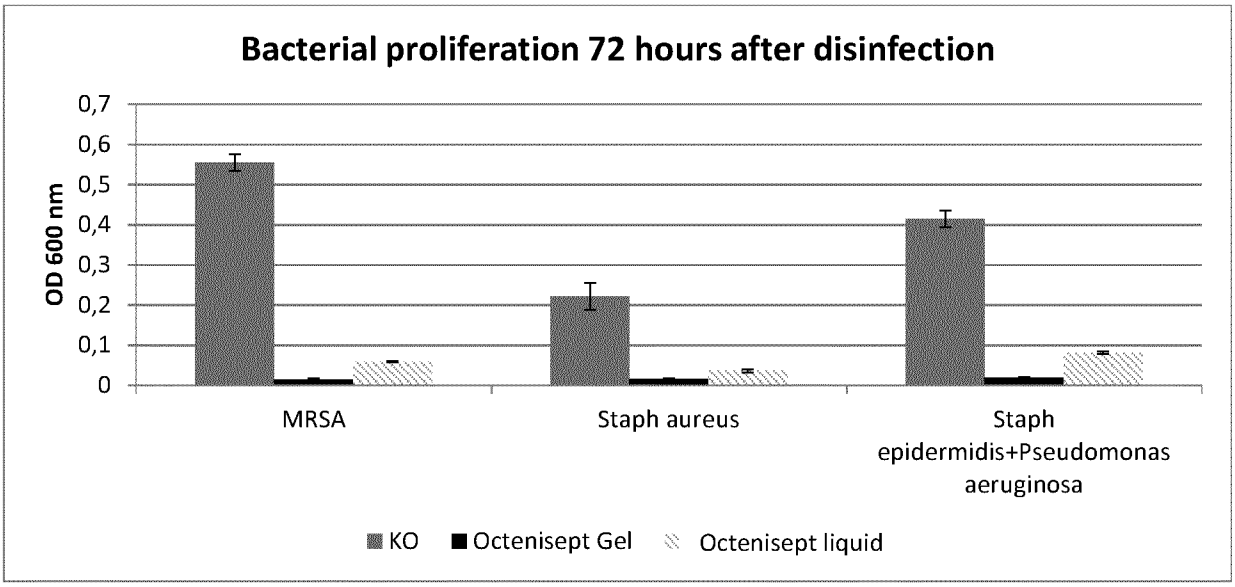


Figure 6

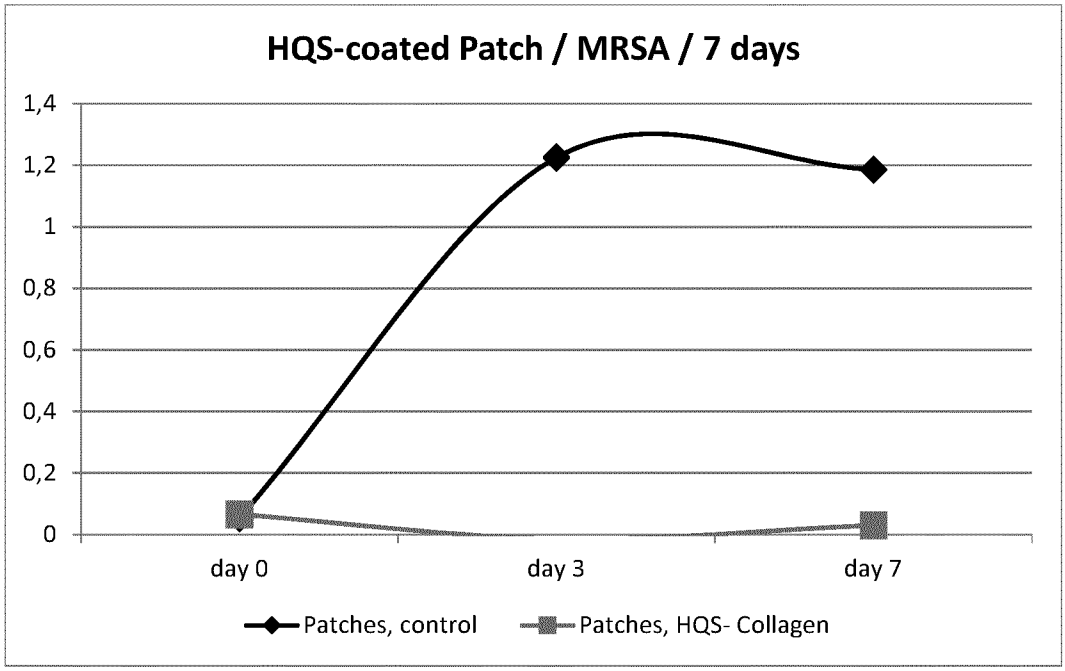


Figure 7

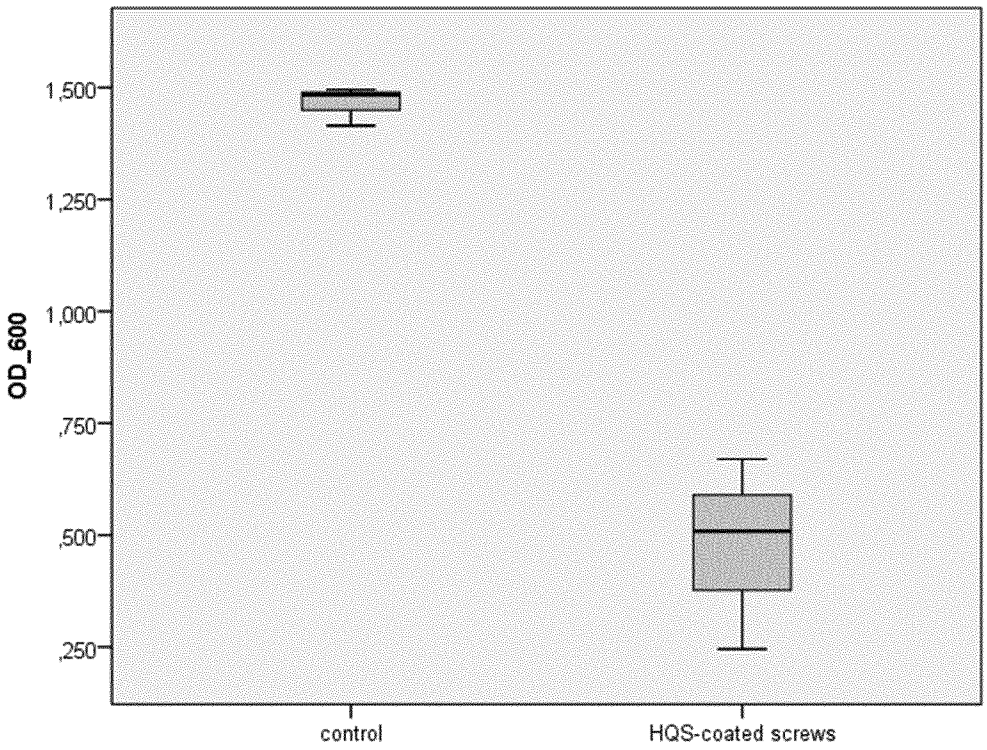


Figure 8

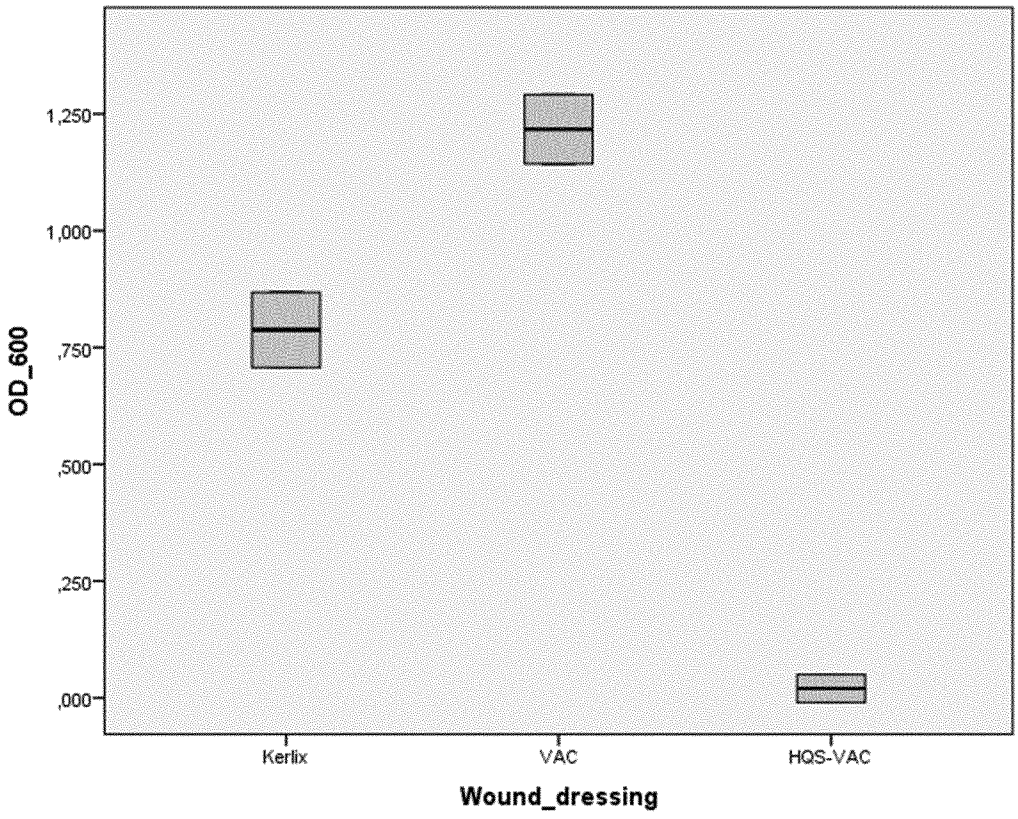


Figure 9

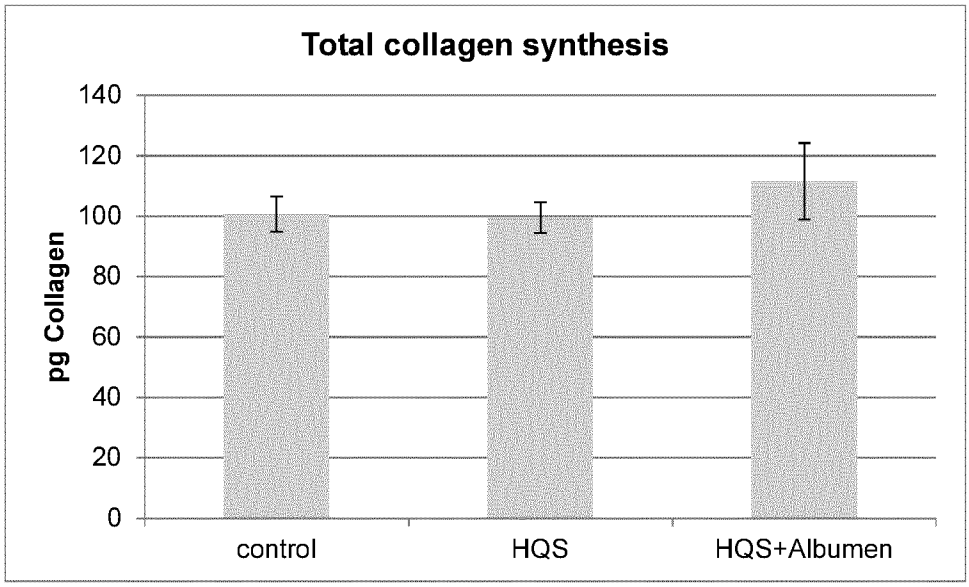


Figure 10

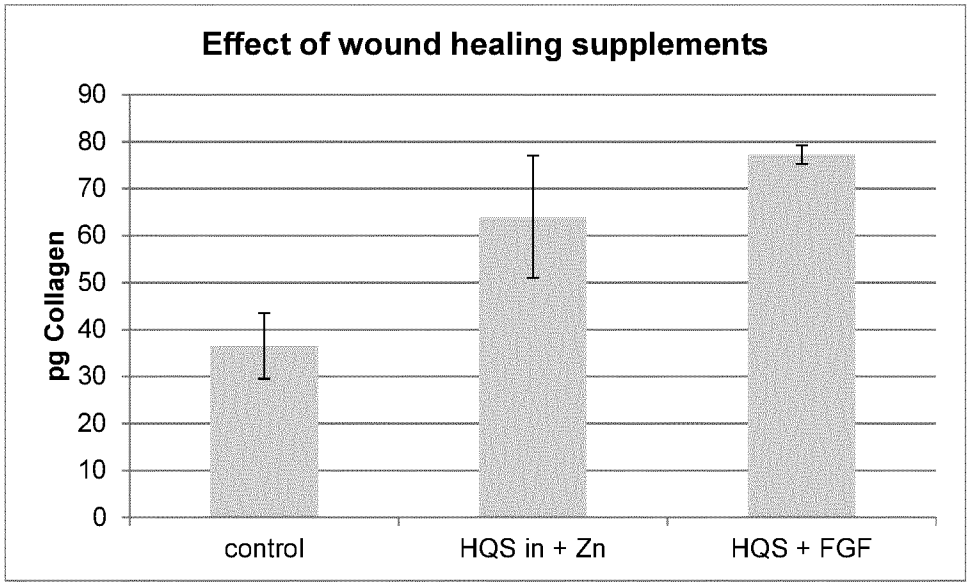


Figure 11

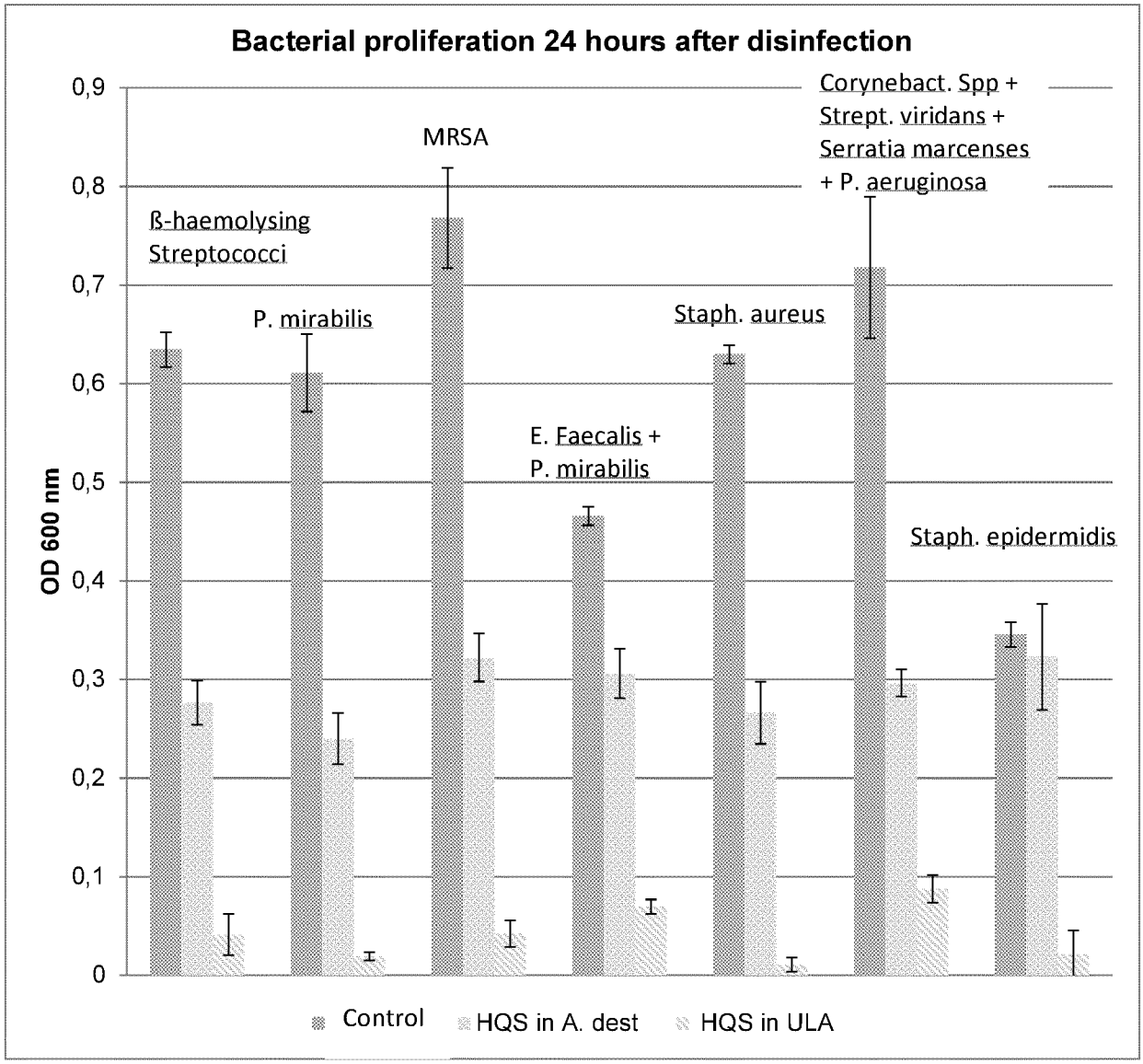

Bacterial proliferation 24 hours after disinfection
OD 600 nm
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0
ß-haemolysing Streptococci
P. mirabilis
MRSA
E. Faecalis + P. mirabilis
Staph. aureus
Corynebact. Spp + Strept. viridans + Serratia marcenses + P. aeruginosa
Staph. epidermidis
Control
HQS in A. dest
HQS in ULA

Figure 12

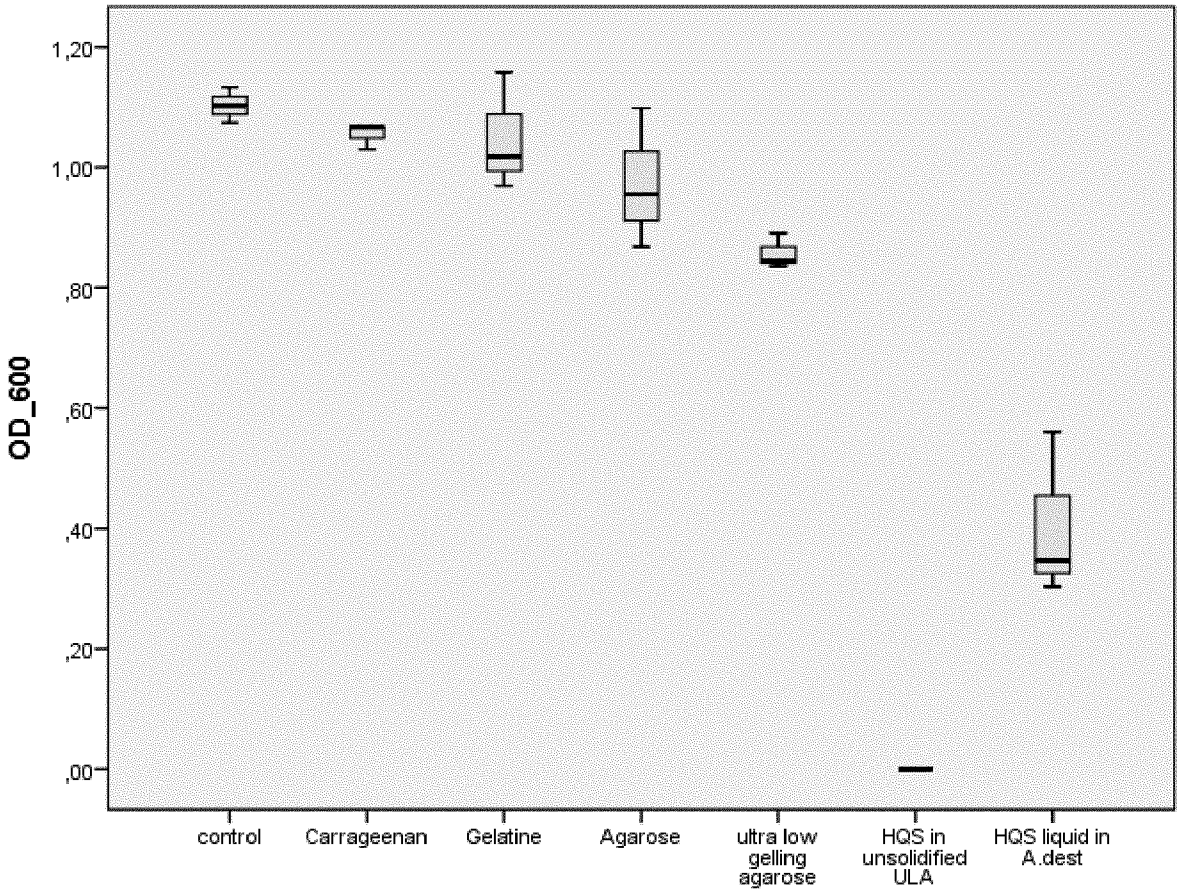


Figure 13

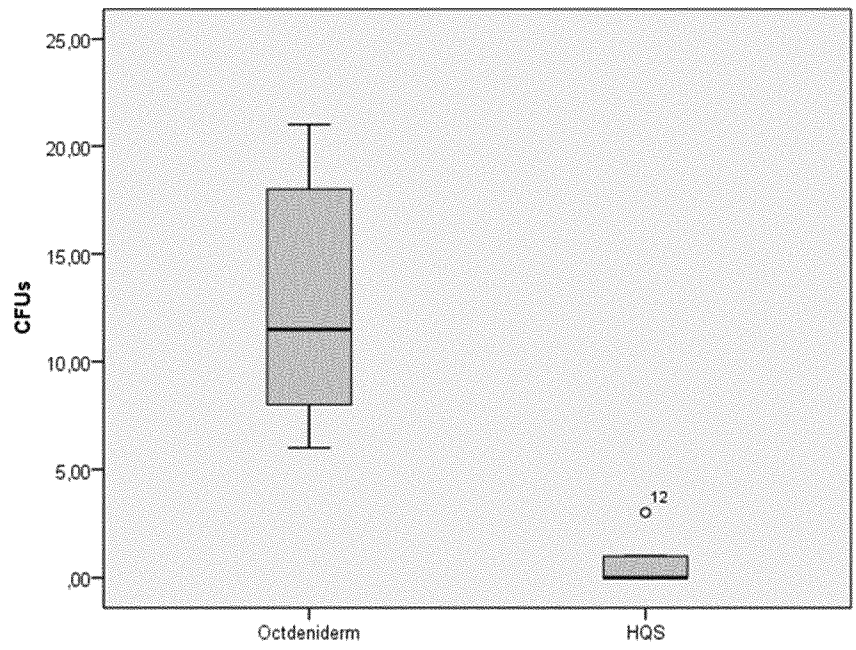
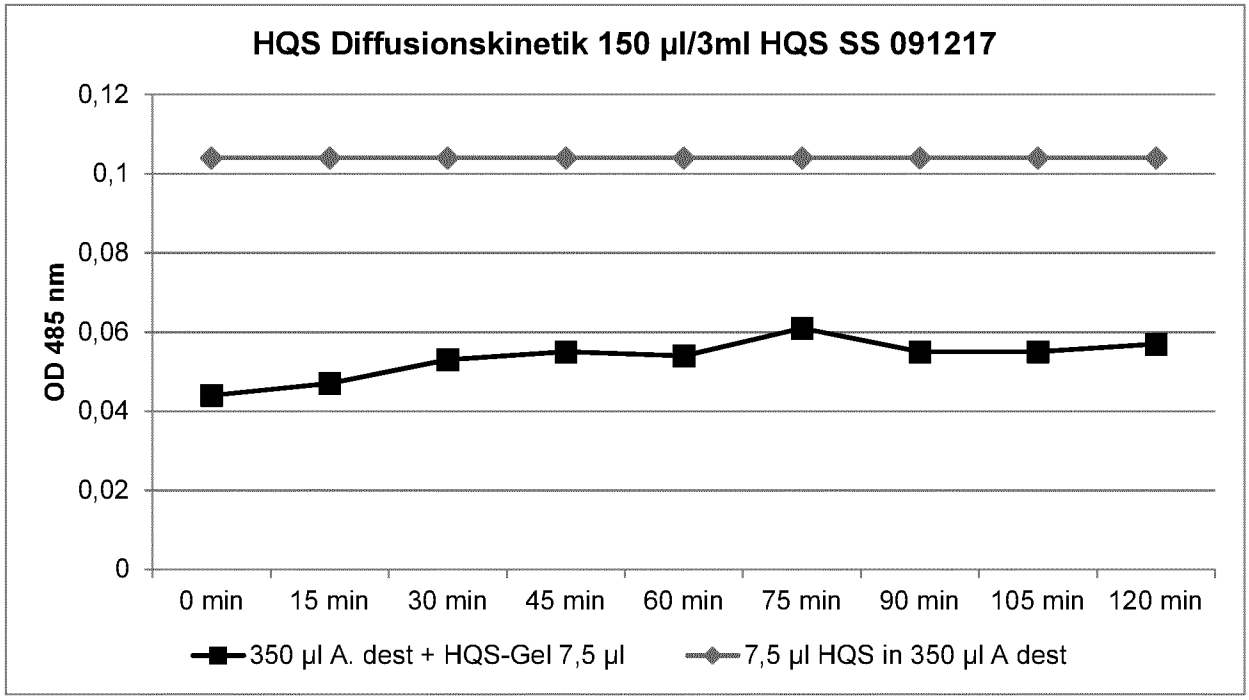


Figure 14


HQS Diffusionskinetik 150 µl/3ml HQS SS 091217
OD 485 nm
0,12
0,1
0,08
0,06
0,04
0,02
0
0 min
15 min
30 min
45 min
60 min
75 min
90 min
105 min
120 min
350 µl A. dest + HQS-Gel 7,5 µl
7,5 µl HQS in 350 µl A dest

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2019/072717

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61L15/42 A61L15/44 A61L15/46 A61L15/60 A61L24/00
A61L24/04 A61L24/10 A61L31/10 A61L31/14 A61L31/16
A61F13/00

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)
A61L A61F

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 practicable, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/091551 A1 (BAUR BORIS [DE] ET AL) 21 April 2011 (2011-04-21) claims 1, 4-6, 9 paragraphs [0004], [0009] paragraphs [0015], [0013] paragraph [0026] - paragraph [0027] paragraph [0038] paragraph [0025] -----	1-4,6, 10-14
X Y	US 2015/157758 A1 (BLÜCHER HASSO VON [DE] ET AL) 11 June 2015 (2015-06-11) claims 16, 18, 21, 37 paragraphs [0037], [0142] paragraph [0117] - paragraph [0132] paragraph [0186] - paragraph [0212] paragraph [0104] - paragraph [0107] paragraphs [0152], [0157] ----- -/--	1,4-9, 11-15, 19,20 16

[X] Further documents are listed in the continuation of Box C.

[X] 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
19 November 2019	23/01/2020

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Guazzelli, Giuditta

1

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2015/118283 A1 (VON BLÜCHER HASSO [DE] ET AL) 30 April 2015 (2015-04-30) claims 1, 4, 7, 17-19, 23, 29 paragraph [0037] paragraph [0117] - paragraph [0119] paragraph [0168] - paragraph [0206] paragraph [0148]	1,4-7,9, 11-15
A	US 5 578 317 A (MULDER GERIT D [US]) 26 November 1996 (1996-11-26) claim 1 column 1, line 45 - column 2, line 24	1-16,19, 20
A	MORITZ SEBASTIAN ET AL: "Active wound dressings based on bacterial nanocellulose as drug delivery system for octenidine", INTERNATIONAL JOURNAL OF PHARMACEUTICS, ELSEVIER, NL, vol. 471, no. 1, 2 May 2014 (2014-05-02), pages 45-55, XP028872225, ISSN: 0378-5173, DOI: 10.1016/J.IJPHARM.2014.04.062 abstract	1-16,19, 20
Y	MARIAM MIR ET AL: "Synthetic polymeric biomaterials for wound healing: a review", PROGRESS IN BIOMATERIALS, BIOMED CENTRAL LTD, LONDON, UK, vol. 7, no. 1, 14 February 2018 (2018-02-14), pages 1-21, XP021253939, ISSN: 2194-0509, DOI: 10.1007/S40204-018-0083-4	16
A	page 15, column 1, lines 3-18	1-15,19, 20

1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2019/072717

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:

see additional sheet

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 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.:

1-16, 19, 20

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-16, 19, 20

   Medical dressings coated with a composition comprising 8-hydroxyquinoline or octenidine, and a biocompatible gelling agent, preparation thereof and said dressings for use in skin disinfection

   ---

2. claims: 17, 18

   Implants coated with a composition comprising 8-hydroxyquinoline and a gelling agent selected from the group consisting of collagen, agarose, carrageenan, fibronectin and methylcellulose

   ---

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2019/072717

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2011091551 A1	21-04-2011	DE 102009049506 A1	21-04-2011
		EP 2311504 A2	20-04-2011
		EP 3150234 A1	05-04-2017
		ES 2706648 T3	29-03-2019
		PL 2311504 T3	31-05-2019
		US 2011091551 A1	21-04-2011
US 2015157758 A1	11-06-2015	CA 2846682 A1	07-03-2013
		CN 103889468 A	25-06-2014
		DE 102011120491 A1	07-03-2013
		DE 202011108805 U1	03-09-2012
		EP 2736542 A1	04-06-2014
		ES 2544106 T3	27-08-2015
		IL 231189 A	31-10-2017
		JP 5827408 B2	02-12-2015
		JP 2014529449 A	13-11-2014
		PL 2736542 T3	30-10-2015
		US 2015157758 A1	11-06-2015
		WO 2013029796 A1	07-03-2013
US 2015118283 A1	30-04-2015	CA 2846447 A1	07-03-2013
		CN 103889469 A	25-06-2014
		DE 102011120487 A1	07-03-2013
		DE 202011108802 U1	03-09-2012
		EP 2734245 A1	28-05-2014
		ES 2539614 T3	02-07-2015
		IL 231245 A	31-07-2017
		JP 6067018 B2	25-01-2017
		JP 2014527535 A	16-10-2014
		PL 2734245 T3	30-10-2015
		US 2015118283 A1	30-04-2015
		WO 2013029797 A1	07-03-2013
US 5578317 A	26-11-1996	NONE	