



(51) International Patent Classification:

G09B 23/30 (2006.01)

(21) International Application Number:

PCT/GB2024/051544

(22) International Filing Date:

17 June 2024 (17.06.2024)

Published:

— with international search report (Art. 21(3))

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

2308954.3

15 June 2023 (15.06.2023)

GB

(71) Applicant: UNIVERSITY OF HUDDERSFIELD

[GB/GB]; Queensgate, Huddersfield, Yorkshire HD1 3DH (GB).

(72) Inventors: SMITH, Alan; c/o University of Huddersfield, Queensgate, Huddersfield Yorkshire HD1 3DH (GB).

SENIOR, Jessica; c/o University of Huddersfield, Queensgate, Huddersfield Yorkshire HD1 3DH (GB).

(74) Agent: BAILEY WALSH & CO. LLP; Aintree House, 1 York Place, Leeds Yorkshire LS1 2DR (GB).

(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, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, 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,

(54) Title: WOUND MODEL DEVICE AND METHOD

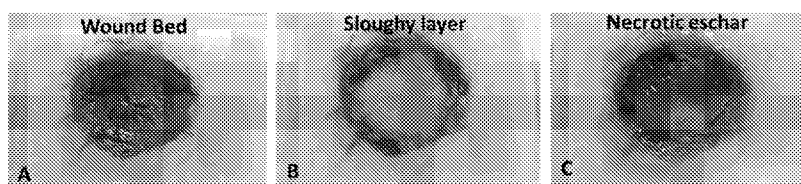


Figure 1 3D Printed wound model A) representing the granulation tissue on the wound bed B) the sloughy layer and C) the necrotic eschar

(57) Abstract: A wound model device and method of preparation. The device comprises at least two layers, at least one of said layers is a base layer that mimics healthy skin wherein the base layer is a biopolymer.



DRAFT**Wound Model Device and Method**

The present invention relates to a wound model for debridement training and other educational purposes. The invention also provides a method for manufacturing such a model. The invention further provides a composition that can be manufactured using natural sustainable materials without the incorporation of animal-based products.

Current wound models that are used for debridement training and educational purposes on today's market are often costly and poorly resemble the appearance and textures of real-life wounds. Current practice involves the use of orange peel or pig's feet. Although, orange peel may superficially resemble the texture of some types of necrotic wound tissue, it does not accurately simulate the complex biological and physiological properties or the variety of wound types that clinicians may encounter in practice. Moreover, using inappropriate materials for wound debridement instruction may convey incorrect or misleading information to learners and ultimately compromise patient safety. Utilising pig's feet is perhaps more realistic anatomically, however, there are several problems associated with their use that include ethical concerns around the use of animal tissue for teaching, infection risk, a limited range of wound types (as pigs feet can only simulate a limited range of wound types), lack of realism and difficulty in sourcing in some regions, limiting their availability and cost - especially if they need to be purchased in large quantities or shipped from a remote location.

There are also synthetic models which look very realistic, but they are not training devices and can't be debrided as they are designed for observational purposes only. The only interactive model for debridement purposes known in the art (see US9972218) uses a

combination of polystyrene foam, clay, paint, leather and glue to create a reusable model [1], however, none of these materials exhibit bulk mechanical properties that are comparable to real tissue.

5

It is therefore an aim of the present invention to provide a wound model that addresses the abovementioned problems.

It is a further aim of the present invention to provide a method
10 of producing and/or assembling a wound model that addresses the abovementioned problems.

It is a yet further aim of the present invention to provide a suitable wound model that better recapitulates chronic wounds as
15 they appear in patients in the clinic.

In a first aspect of the invention there is provided a wound model device, said device comprising at least two layers, at least one of said layers is a base layer that mimics healthy skin wherein the
20 base layer is a biopolymer.

Preferably the device comprises two or more layers wherein the base layer comprises a gel forming biopolymer. Typically the device includes a sloughy layer and/or a necrotic layer.

25

In a preferred embodiment the device includes a base layer, a sloughy layer and a necrotic layer.

In one embodiment the base layer includes a biopolymer and at
30 least one dye or pigment. Typically the base layer is made of biopolymer and can be dyed to match a range of different skin colours and tones.

Further typically the base layer comprises any one or any combination of agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose hydroxypropylmethyl cellulose, chitosan, polysaccharide of tamarind seed, pectin, curdlan, 5 gelatin, furcellaran, agarose sulphate, alginates, guar gum, locust bean gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum, tragacanth gum, karaya gum, arabinan, starch, konjac mannan, galactomannan, funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulan, dextran 10 and dextran sulphate.

Preferably, the gel forming biopolymer substantially forming the base layer is agarose.

15 Typically the amount of agarose used in the base layer is preferably greater than 0.5 wt%, more preferably greater than 1 wt%. The amount of agarose is preferably below 4 wt%, more preferably less than 3 wt%.

20 In one embodiment pink dye paste and/or brown dye paste can be added to agarose. Typically the dye is added to agarose solution prior to solidification to obtain different skin colour tones.

25 In one embodiment the sloughy layer comprises a viscoelastic biopolymer. Typically the sloughy layer is a granular gel.

Further typically the sloughy layer comprises any one or any combination of custard powder, casein, whey protein, gluten, or 30 polysaccharide based granular gels.

Preferably the slough is prepared from custard powder.

Typically the amount of custard powder used in the slough is preferably greater than 5 wt%, more preferably greater than 10 wt%. The amount of custard powder is preferably below 30 wt%, more preferably less than 20 wt%.

5

In one embodiment the sloughy layer is located substantially above the base layer. Typically the sloughy layer is a layer of loosely adherent yellow slough that can be removed using mechanical debridement.

10

In one embodiment the model includes exudate. Typically the exudate is prepared from a fluid gel materials. Further typically the exudate is prepared from any one or any combination of agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose hydroxypropylmethyl cellulose, chitosan, polysaccharide of tamarind seed, pectin, curdlan, gelatin, furcellaran, agarose sulphate, alginates, guar gum, locust bean gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum, tragacanth gum, karaya gum, arabinan, starch, konjac mannan, galactomannan, funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulan, dextran and dextran sulphate. Preferably, exudate gel forming biopolymer is agarose. The amount of agarose used should be greater than 0.1% wt% preferably greater than 0.3% wt%. The amount of agarose is also preferably below 3% and more preferably below 1 %. In this embodiment the concentration of agarose used is 0.5% wt.

25

In one embodiment the uppermost layer is the necrotic layer. Typically the necrotic layer exhibits leathery black necrotic eschar that requires a scalpel to facilitate removal.

30

In one embodiment the necrotic layer comprises any one or any combination of gel forming biopolymer such as agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose

hydroxypropylmethyl cellulose, chitosan. polysaccharide of tamarind seed, pectin, curdlan, gelatin, furcellaran, agarose sulphate, alginates, guar gum, locust bean gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum, tragacanth gum, 5 karaya gum, arabinan, starch, konjac mannan, galactomannan, funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulan, dextran and dextran sulphate.

Preferably, gel forming biopolymer is agarose. Typically the 10 amount of agarose used in the skin base is preferably greater than 0.5 wt%, more preferably greater than 1 wt%. The amount of agarose is preferably below 4 wt%, more preferably less than 3 wt%. Further typically black dye paste is added to agarose solution prior to solidification to obtain deep black colouration.

15

In one embodiment a plasticiser can also be added. Typically the plasticiser can include any one or any combination of glycerol, propylene glycol, propylene glycol, sorbitol, mannitol, sucrose, trehalose, glucose, dextrose, urea, polyethylene glycol, 20 polycarbonates and polyphosphoesters.

In a preferred embodiment the plasticiser is glycerol. Typically the amount of glycerol used is preferably greater than 5% wt%, more preferably greater than 10% wt%. The amount of glycerol is 25 preferably below 50% wt%, more preferably below 30% wt%.

In one embodiment a preservative can also be added. Typically the preservative can be any one or any combination of diazolidinyl urea, sodium benzoate, potassium benzoate, benzoic acid, methyl 30 paraben, propyl paraben, butyl paraben, sodium azide, sodium metabisulphite, sorbic acid, potassium sorbate. Preprepared preservative systems can be used such as Germaben II.

In one embodiment coloured dye paste can be added to agarose solution prior to solidification to obtain different skin colour tones.

- 5 Typically additional appendages can also be added such as hair, tendon, bone blood vessels for a more realistic appearance.

In a second aspect of the invention there is provided a method of forming a wound model device, said device including at least two
10 layers, at least one of said layers is a base layer that mimics healthy skin wherein the base layer is a biopolymer.

In one embodiment the compositions comprising the base layer are prepared from agarose. Typically low EEO grade agarose.
15 Further typically pink and/or brown dye paste is included.

In one embodiment the agarose powder was dispersed in a small amount of cold deionised water. Typically around 10% of water content. Further typically once dispersed, the rest of the
20 deionised water was added was added hot ($>80^{\circ}\text{C}$) to create a 2% w/w agarose solution.

In one embodiment 20 % glycerol is added followed by the remaining deionised water.
25

In one embodiment the mixture was stirred and heated to $\sim 85^{\circ}\text{C}$ and a homogenous solution was evident. Typically the solution is then cooled to around 50°C and a preservative system added. In one embodiment Germaben II was used at a concentrations
30 between 0.5% and 1% w/v.

Typically a sufficient quantity of dye paste is added until solution became opaque. For different skin tones different quantities and

colours can be added. This provided the healthy skin base material.

Typically the hot agarose solution was then poured into a mould
5 that defines the shape and dimensions of the required wound.
Further typically the mould is a 3D printed mould.

The composition is then allowed to set at room temperature.

10 Additional appendages such as hair can be added prior to the
biopolymer or agarose fully setting.

In one embodiment the sloughy layer is produced by weighing the
appropriate quantity of custard powder for a 15% w/w solution
15 then was added to a beaker of cold deionised water. Typically the
solution is heated to fully solubilise the custard powder. The
composition is typically allowed to thicken and solidify.

In one embodiment, once solidified the sloughy layer composition
20 is placed at 4 °C to cool. Once cooled prior to use, the gelled
custard was stirred to produce a granular material that was used
as the slough in the wound model.

In one embodiment artificial exudate is prepared by dispersing
25 agarose in deionised water. Typically artificial exudate is prepared
by dispersing 0.5% wt agarose in deionised water at around 90°C
and then once fully dissolved cooling to 20 °C under a shear.
Further typically the shear is constant at around 700 rpm.

30 In one embodiment the necrotic eschar layer composition is
prepared from agarose and a dye. Typically the dye is black dye
paste.

In one embodiment the agarose powder is dispersed in a small amount of cold deionised water, typically around 10% of water content. Further typically once dispersed, the rest of the deionised water is added hot ($>80^{\circ}\text{C}$) to create a 2% w/w agarose solution.

Typically the mixture is stirred and heated to $\sim 85^{\circ}\text{C}$ until the material was fully hydrated and a homogenous solution was evident.

Further typically a sufficient quantity of black dye paste is added until solution is opaque. This provides the necrotic eschar material.

In one embodiment the hot agarose solution was then poured into a mould that contains the shape and dimensions of the required necrotic eschar. This was then allowed to set at 4°C . The remaining black agarose solution can then be stored in the fridge at 4°C and reused.

Typically to reuse once cooled, the material is heated in a microwave for ~ 30 seconds until the agarose gel has melted and can be poured.

In one embodiment the wound model device is assembled by removing the base layer from the mould and any imperfections trimmed away around the edges using a scalpel.

Typically a drop of red food colouring is added to the wound cavity and carefully spread evenly taking care to prevent 'bleed' into the small channels at the edges of the cavity.

Further typically a second drop of red food colouring was added into the centre of the wound cavity to make a darker red colour at the centre.

- 5 In one embodiment the slough layer is then added to fill the cavity. Typically the slough layer is added until flush with the base layer or healthy skin region.

10 In one embodiment the necrotic layer or gelled agarose eschar is removed from the mould and placed on the artificial slough. Typically the layer is cut in half before being placed on the slough layer and gently pressed into the slough until flush with the healthy skin region base layer.

15 In one embodiment artificial exudate is added onto the surface of the slough. Typically then the gelled agarose eschar is then removed from the mould and cut in half and placed on the artificial slough and exudate. Further typically the eschar is gently pressed into the slough until flush with the healthy skin region.

20

In one embodiment the top of the necrotic layer eschar is then cauterized from the edge towards the centre until a thin film is visible on the surface and the edges are bound to the healthy skin region of the base layer.

25

In a further aspect of the invention there is provided a wound model based on a composition containing a biopolymer gel base and a viscoelastic biopolymer for the sloughy tissue. Typically a solid leathery biopolymer necrotic eschar is included. Further
30 typically other minor ingredients such as colouring agents, plasticisers and/or preservatives can be included.

Typically the remainder of the composition is water.

Specific embodiment of the invention are now described with reference to the following figures wherein:

Our preliminary work has demonstrated the feasibility of upscaling and automating chronic wound model production, using relatively cheap materials and robust 3D printing technologies.

Initially, a 3D printed mould is used to cast the base of the skin mimic, within which the wound void is situated. The base layer is made of biopolymer and can be dyed to match a range of different skin colours and tones. It features a smooth, skin-like appearance at the surface that surrounds a wound void with red, rough granulation tissue lining the wound bed (Fig 1A). Above the granulation tissue is a layer of loosely adherent yellow slough that can be removed using mechanical debridement (Fig 1B). The uppermost layer of the wound region exhibits leathery black necrotic eschar that requires a scalpel to facilitate removal (Fig 1C) - as is often the case in real-life wounds.

The mechanical properties of the model layers have been matched to be similar to those in human tissue. There is also further scope and potential to incorporate additional apparatus to make these models even more life-like to better aid in debridement training and demonstrations, featuring bone, tendon, muscle and blood vessels within the underlying layers as well as offering a range of wound dimensions.

The present invention relates to a wound model based on a composition containing a biopolymer gel base, viscoelastic biopolymer for the sloughy tissue, a solid leathery biopolymer necrotic eschar and other minor ingredients such as colouring agents plasticisers and preservatives. The remainder of the composition being water.

Skin Base composition

The skin base polymer can be a gel forming biopolymer, such as agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose hydroxypropylmethyl cellulose, chitosan, polysaccharide of tamarind seed, pectin, curdlan, gelatin, furcellaran, agarose sulphate, alginates, guar gum, locust bean gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum, tragacanth gum, karaya gum, arabinan, starch, konjac mannan, galactomannan, funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulan, dextran and dextran sulphate. Preferably, gel forming biopolymer is agarose. The amount of agarose used in the skin base is preferably greater than 0.5 wt%, more preferably greater than 1 wt%. The amount of agarose is preferably below 4 wt%, more preferably less than 3 wt%.

15

A plasticiser can also be added such as glycerol, propylene glycol, propylene glycol, sorbitol, mannitol, sucrose, trehalose, glucose, dextrose, urea, polyethylene glycol, polycarbonates and polyphosphoesters. In this embodiment glycerol is preferred. The amount of glycerol used is preferably greater than 5% wt%, more preferably greater than 10% wt%. The amount of glycerol is preferably below 50% wt%, more preferably below 30% wt%.

20

A preservative can also be added such as diazolidinyl urea, sodium benzoate, potassium benzoate, benzoic acid, methyl paraben, propyl paraben, butyl paraben, sodium azide, sodium metabisulphite, sorbic acid, potassium sorbate. Or preprepared preservative systems can be used such as Germaben II.

25

Coloured dye paste can be added to agarose solution prior to solidification to obtain different skin colour tones Fig 2A.

30

Additional appendages can also be added such as hair, tendon, bone blood vessels for a more realistic appearance. In this

embodiment artificial hair was added to the surface of the agarose prior to gelation. (Fig 2B)

Sloughy tissue composition

- 5 The sloughy tissue can be prepared from materials such as custard powder, casein, whey protein, gluten, or polysaccharide based granular gels. Preferably the slough is prepared from custard powder. The amount of custard powder used in the slough is preferably greater than 5 wt%, more preferably greater than 10
10 wt%. The amount of custard powder is preferably below 30 wt%, more preferably less than 20 wt%.

Exudate Composition

- Exudate can be prepared from a fluid gel materials such as
15 agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose hydroxypropylmethyl cellulose, chitosan. polysaccharide of tamarind seed, pectin, curdlan, gelatin, furcellaran, agarose sulphate, alginates, guar gum, locust bean gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum,
20 tragacanth gum, karaya gum, arabinan, starch, konjac mannan, galactomannan, funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulan, dextran and dextran sulphate. Preferably, gel forming biopolymer is agarose. The amount of agarose used should be greater than 0.1% wt%
25 preferably greater than 0.3% wt%. The amount of agarose is also preferably below 3% and more preferably below 1 %. In this embodiment the concentration of agarose used is 0.5% wt.

Necrotic Layer composition

- 30 The necrotic layer can be prepared from a gel forming biopolymer such as agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose hydroxypropylmethyl cellulose, chitosan. polysaccharide of tamarind seed, pectin, curdlan, gelatin, furcellaran, agarose sulphate, alginates, guar gum, locust bean

gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum, tragacanth gum, karaya gum, arabinan, starch, konjac mannan, galactomannan, funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulan, dextran and dextran sulphate. Preferably, gel forming biopolymer is agarose. The amount of agarose used in the skin base is preferably greater than 0.5 wt%, more preferably greater than 1 wt%. The amount of agarose is preferably below 4 wt%, more preferably less than 3 wt%. Black dye paste should be added to agarose solution prior to solidification to obtain deep black colouration.

Example 1: Wound Model Assembly

Preparation of Healthy Skin Wound Base: Skin base compositions were prepared from agarose (low EEO grade) and pink dye paste. The agarose powder was dispersed in a small amount of cold deionised water (10% of water content) and once dispersed, 20% glycerol was added followed by the remaining deionised water added hot ($>80^{\circ}\text{C}$) to create a 2% w/w agarose solution. The mixture was stirred and heated to $\sim 85^{\circ}\text{C}$ using a heated magnetic stirrer set to ~ 700 rpm until the material was fully hydrated and a homogenous solution was evident. The solution was then cooled to 50°C and the preservative system was added. In this embodiment Germaben II was used at a concentrations between 0.5% and 1% w/v. A sufficient quantity of pink dye paste was gently added until solution became opaque. For different skin tones different quantities and colours can be added. This provided the healthy skin base material. The hot agarose solution was then poured into a 3D printed mould that contains the shape and dimensions of the required wound. This was then allowed to set at room temperature. Additional appendages such as hair could be added prior to the agarose fully setting.

Preparation of Artificial Sloughy Tissue: The artificial sloughy tissue composition was prepared by weighing the appropriate

quantity of custard powder for a 15% w/w solution then was added to a beaker of cold deionised water ~25 ml per model. The solution was heated to fully solubilise the custard powder, then it was allowed to thicken and solidify. Once solidified it was placed
5 at 4 °C to cool. Once cooled prior to use, the gelled custard was stirred to produce a granular material that was used as the slough in the wound model.

Preparation of Artificial Exudate: Artificial exudate was prepared
10 by dispersing 0.5% wt agarose in deionised water at 90 °C and then once fully dissolved cooling to 20 °C under a constant shear of 700 rpm.

Preparation of Artificial Necrotic Eschar Solution: The necrotic
15 eschar compositions were prepared from agarose (low EEO grade) and black dye paste. The agarose powder was dispersed in a small amount of cold deionised water (10% of water content) and once dispersed, the rest of the deionised water was added was added hot (>80 °C) to create a 2% w/w agarose solution. The
20 mixture was stirred and heated to ~85 °C using a heated magnetic stirrer set to ~700 rpm until the material was fully hydrated and a homogenous solution was evident. A sufficient quantity of black dye paste was gently added until solution became opaque. This provided the necrotic eschar material. The hot black agarose
25 solution was then poured into a 3D printed mould that contains the shape and dimensions of the required necrotic eschar. This was then allowed to set at 4 °C. The remaining black agarose solution can then be stored in the fridge at 4 °C and reused (to reuse once cooled, the material should be heated in a microwave
30 for ~30 seconds until the agarose gel has melted and can be poured).

Wound Model Assembly: The wound bed was gently removed from the mould and any imperfections trimmed away around the

edges using a scalpel. A drop of red food colouring was added to the wound cavity and carefully spread evenly taking care to prevent 'bleed' into the small channels at the edges of the cavity. A second drop of red food colouring was added into the centre of the wound cavity to make a darker red colour at the centre, then was left for 5 min (Fig 3A). Artificial slough was then added to fill the cavity using a spatula, until flush with the healthy skin region. Artificial exudate was then added onto the surface of the slough and then the gelled agarose eschar was then removed from the mould and cut in half and placed on the artificial slough and exudate and gently pressed into the slough until flush with the healthy skin region. The top of the eschar was then cauterized from the edge towards the centre using a blow torch until a thin film is visible on the surface and the edges are bound to the healthy skin region (Fig 3B).

Example 2: Rheological analysis

Rheological analysis of the skin base and the sloughy tissue was carried out using small deformation oscillatory measurements with a 40 mm parallel plate geometry mounted on a Malvern Gemini Rheometer (Malvern Instruments, UK) fitted with peltier plate thermal control. Amplitude sweeps were performed first to determine the elasticity of the materials where changes in G' (elastic modulus) as a function of strain were measured. The skin base was shown to have a similar elastic behaviour to full thickness adult healthy skin [2] with a linear viscoelastic region (LVR) lying between 0.1% - 1% strain (Fig 4A). The frequency sweeps of the skin base (Fig 4B) showed strong gel behaviour with $G' > G''$ across all frequencies measured with values in the same order of magnitude of full thickness healthy skin. The strain sweeps for the sloughy tissue (Fig 4C) showed that the LVR extended to almost 10% strain highlighting the elastic behaviour of the slough. Moreover, the frequency sweep data showed solid-like behaviour with $G' > G''$ across all frequencies measured,

however, at higher frequencies G'' (viscous modulus) began to increase indicating break down of polymer interactions (Fig 4D). This solid like behaviour at low frequencies and the onset of more viscous behaviour at higher frequencies allows the slough to remain within the wound void at rest but when debriding will have increased viscous behaviour, similar to that of native sloughy tissue.

To quantify the mechanical properties of the eschar layer, a texture analyser was used to perform elongation measurements to generate force deformation curves. Dog bone shaped eschar material was secured with clamps on the texture analyser. Strain was then measured as a function of stress and mechanical properties were calculated from the resulting force deformation curve, which showed characteristic brittle fracture behaviour (Fig 5). In this embodiment the material had an average Youngs modulus of 0.78 kPa and a tensile strength of 34.49 MPa. Although this was relatively low in stiffness and strength, the mechanism of fracture and realistic organoleptic properties demonstrates how eschar will likely behave during debridement as real eschars have previously been described to be brittle in nature [3]. Moreover, the tailorable nature of the material used for the eschar provides scope to further optimise the mechanical properties if required.

References:

References:

[1] Normand CA, (2018) Wound Debridement Model, US Patent US9972218

[2] Malhotra, et al., (2019) Linear viscoelastic and microstructural properties of native male human skin and in vitro 3D reconstructed skin models, J. Mech. Behav. Biomed. Mater.90, pp.644-654

[3] Szycher M, Lee SJ. Modern wound dressings: a systematic approach to wound healing. J. Biomater. Appl. 1992 Oct;7(2):142-213.b

Claims

1. A wound model device, said device comprising at least two layers, at least one of said layers is a base layer that mimics healthy
5 skin wherein the base layer is a biopolymer.
2. A wound model device according to claim 1 wherein the device comprises two or more layers wherein the base layer comprises a gel forming biopolymer.
- 10 3. A wound model device according to claim 2 wherein the device includes a sloughy layer and/or a necrotic layer.
4. A wound model device according to claims 1-3 wherein the
15 base layer includes a biopolymer and at least one dye or pigment.
5. A wound model device according to claims 1-4 wherein the base layer comprises any one or any combination of agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose
20 hydroxypropylmethyl cellulose, chitosan, polysaccharide of tamarind seed, pectin, curdlan, gelatin, furcellaran, agarose sulphate, alginates, guar gum, locust bean gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum, tragacanth gum, karaya gum, arabinan, starch, konjac mannan, galactomannan,
25 funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulnan, dextran and dextran sulphate.
6. A wound model device according to claim 5 wherein the gel forming biopolymer substantially forming the base layer is
30 agarose.
7. A wound model device according to claim 6 wherein agarose used in the base layer is between 0.5 wt% and 3 wt%.

8. A wound model device according to claim 7 wherein dye paste is added to the agarose.

9. A wound model device according to claim 3 wherein the sloughy layer comprises a viscoelastic biopolymer.

10. A wound model device according to claim 9 wherein the sloughy layer is a granular gel.

11. A wound model device according to claim 10 wherein the sloughy layer comprises any one or any combination of custard powder, casein, whey protein, gluten, or polysaccharide based granular gels.

12. A wound model device according to claim 11 wherein the amount of custard powder used in the slough is between 5 wt% and 30 wt%.

13. A wound model device according to claims 3-12 wherein the sloughy layer is located substantially above the base layer.

14. A wound model device according to claim 13 wherein the model includes exudate prepared from a fluid gel materials.

15. A wound model device according to claim 14 wherein the exudate is prepared from any one or any combination of agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose hydroxypropylmethyl cellulose, chitosan, polysaccharide of tamarind seed, pectin, curdlan, gelatin, furcellaran, agarose sulphate, alginates, guar gum, locust bean gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum, tragacanth gum, karaya gum, arabinan, starch, konjac mannan, galactomannan, funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulan, dextran and dextran sulphate.

16. A wound model device according to claim 15 wherein the exudate gel forming biopolymer is agarose in an amount 0.1 wt%-3 wt%.

5

17. A wound model device according to claims 3-16 wherein the uppermost layer is the necrotic layer.

18. A wound model device according to claim 17 wherein the
10 necrotic layer comprises any one or any combination of gel forming biopolymer such as agarose, agar, gellan gum, xanthan gum, carrageenan, methylcellulose hydroxypropylmethyl cellulose, chitosan, polysaccharide of tamarind seed, pectin, curdlan, gelatin, furcellaran, agarose sulphate, alginates, guar
15 gum, locust bean gum, tara gum, gum Arabic, ghatti gum, Khaya grandifolia gum, tragacanth gum, karaya gum, arabinan, starch, konjac mannan, galactomannan, funoran, acetan, welan, rhamsan, succinoglycan, scleroglycan, schizophyllan, pullulan, dextran and dextran sulphate.

20

19. A wound model device according to claim 18 wherein the gel forming biopolymer is agarose of the amount 0.5-3 wt%.

20. A wound model device according to claim 19 wherein black
25 dye paste is added to agarose solution.

21. A wound model device according to any preceding claim wherein a plasticiser is added.

30 22. A wound model device according to claim 21 wherein the plasticiser can include any one or any combination of glycerol, propylene glycol, propylene glycol, sorbitol, mannitol, sucrose, trehalose, glucose, dextrose, urea, polyethylene glycol, polycarbonates and polyphosphoesters.

23. A wound model device according to any preceding claim wherein a preservative is added.

5 24. A wound model device according to claim 23 wherein the preservative can be any one or any combination of diazolidinyl urea, sodium benzoate, potassium benzoate, benzoic acid, methyl paraben, propyl paraben, butyl paraben, sodium azide, sodium metabisulphite, sorbic acid, potassium sorbate.

10

25. A wound model device according to any preceding claim wherein additional appendages are added such as hair, tendon, bone blood vessels.

15 26. A method of forming a wound model device according to claim 1, said device including at least two layers, at least one of said layers is a base layer that mimics healthy skin wherein the base layer is a biopolymer said method including the step of dispersing the biopolymer in an amount of water.

20

27. A method according to claim 26 wherein the base layer is prepared from agarose dispersed in a small amount of cold deionised water.

25 28. A method according to claim 27 wherein once dispersed, the rest of the deionised water was added was added hot ($>80^{\circ}\text{C}$) to create a 2% w/w agarose solution.

29. A method according to claim 28 wherein the hot agarose
30 solution is then poured into a mould that defines the shape and dimensions of the required wound.

30. A method according to claim 28 or 29 wherein composition is then allowed to set at room temperature.

31. A method according to claim 30 wherein the sloughy layer is produced by weighing the appropriate quantity of custard powder for a 15% w/w solution then was added to deionised water.

Figures

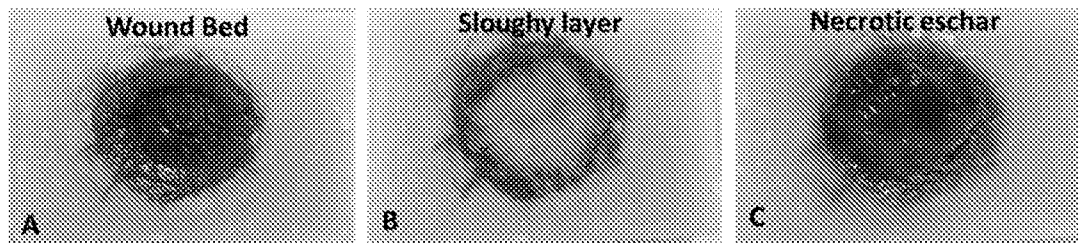


Figure 1 3D Printed wound model A) representing the granulation tissue on the wound bed B) the sloughy layer and C) the necrotic eschar

5

Figure 2: Healthy wound bed in A) different skin tones and B) with hair as an additional appendage

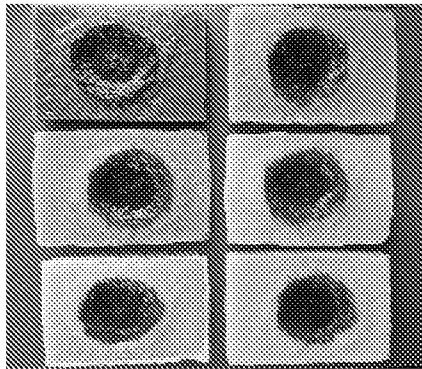


Figure 2A

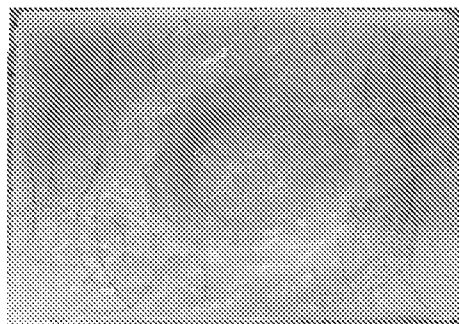


Figure 2B

10

Figure 3 A) Healthy wound bed and B) the finished model containing slough exudate and eschar.

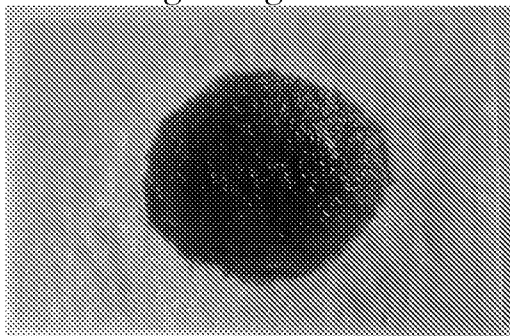


Figure 3A

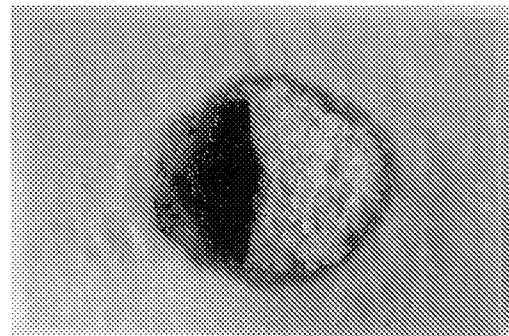


Figure 3B

15

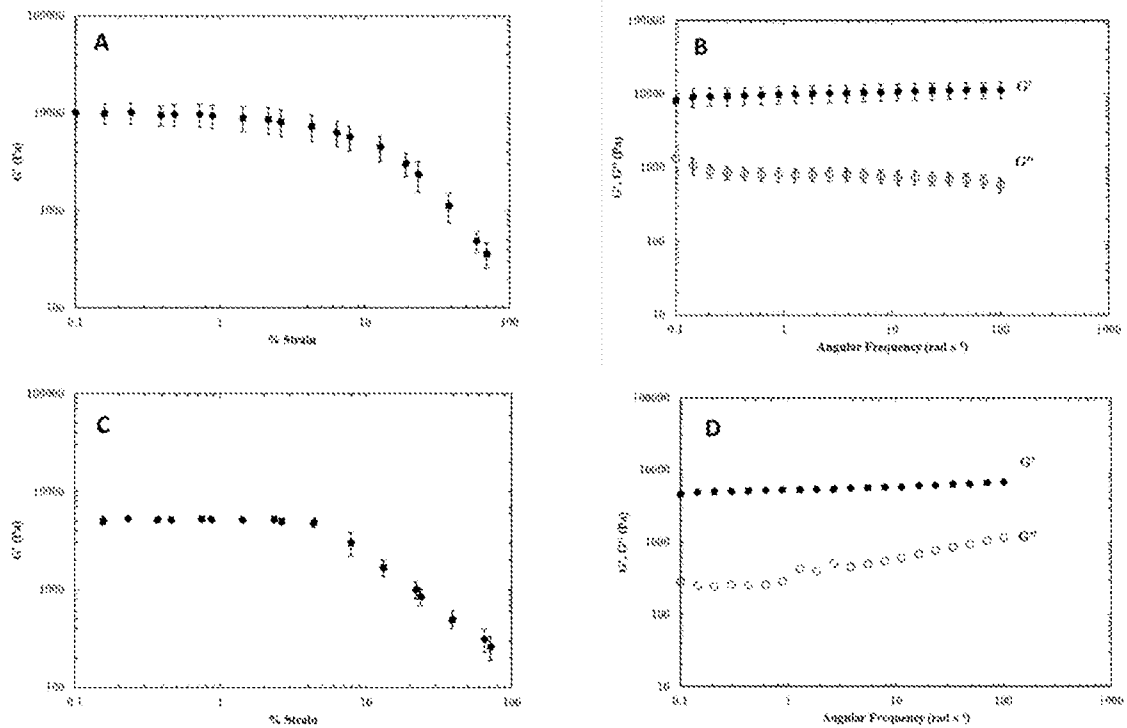


Figure 4 Rheological behaviour of the healthy skin base (A-B) and the sloughy tissue (C-D). A) Strain sweep of the healthy skin base showing strain independent values of elastic modulus G' between 0.1% and 1% strain. B) Frequency sweep of the skin base showing strong gel like behaviour with $G' > G''$ across all frequencies measured. C) Strain sweep of the sloughy tissue showing a LVR between 0.1 and 5% strain. D) Frequency sweep of the slough showing solid gel like behaviour at low frequencies with a gradual increase in viscous modulus at higher frequencies indicating an onset of viscous behaviour.

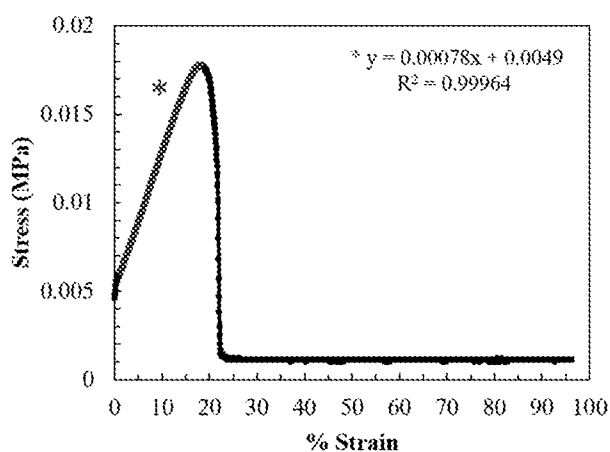


Figure 5 Stress-strain curves demonstrating the brittle fracture failure of artificial eschar

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2024/051544

A. CLASSIFICATION OF SUBJECT MATTER INV. G09B23/30 ADD.		
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) G09B G09D		
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	TW 200 918 109 A (IND TECH RES INST [TW]) 1 May 2009 (2009-05-01) paragraph [0005] - paragraph [0030] -----	1 - 31
X	US 2017/345339 A1 (NORMAND CARI JOANN [US]) 30 November 2017 (2017-11-30) paragraph [0006] - paragraph [0016] paragraph [0023] - paragraph [0043] ----- - / - -	1 - 31
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 13 September 2024		Date of mailing of the international search report 30/09/2024
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Kraska, Nora

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2024/051544

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	SENIOR JESSICA J. ET AL: "Development of a bio-inspired wound model for debridement training", IN VITRO MODELS, 29 April 2024 (2024-04-29), pages 81-89, XP093203914, ISSN: 2731-3441, DOI: 10.1007/s44164-024-00071-6 Retrieved from the Internet: URL:https://pure.hud.ac.uk/en/publications/development-of-a-bio-inspired-wound-model-for-debridement-trainin [retrieved on 2024-09-11] the whole document	1-31
A	CA 2 882 131 A1 (CHD BIOSCIENCE INC [US]) 20 February 2014 (2014-02-20) paragraph [0035] - paragraph [0050] paragraph [0082] - paragraph [0097] claim 8	1-31
A	NOSRATI HAMED ET AL: "Cationic, anionic and neutral polysaccharides for skin tissue engineering and wound healing applications", INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES, ELSEVIER BV, NL, vol. 192, 9 October 2021 (2021-10-09), pages 298-322, XP086848640, ISSN: 0141-8130, DOI: 10.1016/J.IJBIOMAC.2021.10.013 [retrieved on 2021-10-09] sections 5, 6	1-31
A	ZHANG MENGDE ET AL: "Advances in 3D skin bioprinting for wound healing and disease modeling", RESEARCH CENTER FOR TISSUE REPAIR AND REGENERATION AFFILIATED TO THE MEDICAL INNOVATION RESEARCH DEPARTMENT, PLA GENERAL HOSPITAL AND PLA MEDICAL COLLEGE , 28 FU XING ROAD , BEIJING 100853, CHINA, 17 January 2023 (2023-01-17), pages 1-20, XP093203920, ISSN: 2056-3426, DOI: 10.1093/rb/rbac105 Retrieved from the Internet: URL:https://watermark.silverchair.com/rbac105.pdf?token=AQECAHi208BE49Oan9kKhW_Ercy7Dm3ZL_9Cf3qfKAc485ysgAAA20wggNpBgkqhkiG9w0BBwagggNaMIIDVgIBADCCA08GCSqGSib3DQEHATAeBgqlghkgBZQMEAS4wEQQMIn9H3zno_R6UHF3AAgEQgIIDII06bMusv7xe_hMCxMb6L-cv7iP6D4nXzNPzxbosmDyGCKbhzyEEZX2k6YHToLZwKgaoflZ-5wGv77JTZZcyZrLvr96Q [retrieved on 2024-09-11] the whole document	1-31

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2024/051544

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
TW 200918109 A	01-05-2009	TW 200918109 A	01-05-2009
		US 2009098521 A1	16-04-2009
US 2017345339 A1	30-11-2017	NONE	
CA 2882131 A1	20-02-2014	AU 2013302680 A1	19-03-2015
		BR 112015003403 A2	04-07-2017
		CA 2882131 A1	20-02-2014
		CN 104902954 A	09-09-2015
		EP 2885046 A1	24-06-2015
		ES 2753125 T3	07-04-2020
		JP 2015530994 A	29-10-2015
		KR 20150041047 A	15-04-2015
		NZ 705535 A	27-05-2016
		RU 2015108941 A	10-10-2016
		WO 2014028633 A1	20-02-2014