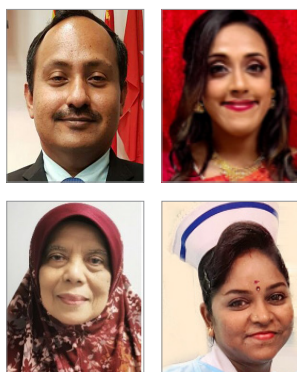


Evaluation of a bioactive microfibre gelling dressing in the management of chronic wounds: a case series



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- Chitosan
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- Hard-to-heal wounds
- Wound dressing

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Managing chronic or hard-to-heal wounds such as diabetic or venous ulcers, or pressure ulcers is difficult as it diverges from its normal healing process. Wound healing is a complicated process that needs a comprehensive environment for proper healing. As wound care is always evolving, Maxiocel, a Bioactive Microfibre Gelling (BMG) dressing was introduced in 2021. It contains chitosan which has distinctive characteristics for pain management, providing comfort, and is highly absorbent. Chitosan also has haemostatic properties to absorb blood which allows accumulation of erythrocytes and platelets at the wound site which then causes activation of the coagulation process. It also stimulates the proliferation of dermal fibroblast and inhibits the proliferation of keratinocytes which causes re-epithelisation. It aids wound healing by protecting the skin in blocking the matrix metalloproteinase-2 expression. **Methods:** After a basic wound cleaning, Maxiocel was applied to the wound bed and dressed according to the standard of care. **Results:** We have recruited 5 patients with chronic wounds. The parameters assessed were wound size, wound bed appearance, periwound condition, exudate level, and patient pain level. All the parameters listed showed improvement within 12-weeks. **Conclusion:** The use of chitosan-based dressing increased granulation, and aided in the management of pain, exudates, and infection, all of which promotes quicker wound healing.

Wound healing is a complex process encompassing four distinct phases: haemostasis, inflammation, proliferation, and remodelling (Guo and DiPietro, 2010; Wang et al 2018). However, chronic or hard-to-heal wounds present a formidable challenge as they deviate from the usual healing trajectory despite appropriate treatment (Han and Ceilley, 2017). This global issue revolves around wounds that remain stuck in the inflammation phase and is particularly associated with conditions like diabetic foot ulcers (DFU), pressure ulcers (PU), and vascular ulcers, including venous and arterial ulcers (Landén et al, 2016; Zhao et al, 2016; Munro, 2017). These persistent wounds not only compromise the patient's quality of life (QoL) but also heighten the risk of severe

health consequences, such as amputations and mortality (Järbrink et al, 2017; Lo et al, 2020). Moreover, individuals suffering from chronic wounds often endure not only physical discomfort but also psychological distress, which can be exacerbated by the delayed healing process (Gouin and Kiecolt-Glaser, 2011; Hopkins, 2011). In cases where wounds produce excessive exudate, patients may experience distress and pain, compounded by concerns about dressing leakage, malodour, and staining of personal belongings like clothing, bedding etc. (Chrisman, 2010; Théorêt and Stashak, 2011).

The primary goal for healthcare providers when managing chronic wounds is to effectively address wound care, control exudate and provide pain relief. This involves the careful selection of appropriate dressing materials,

as well as the implementation of adjunctive therapies tailored to specific wound types, such as offloading techniques for DFUs and compression therapy for venous leg ulcers (VLU) (Richmond et al, 2013; Bowers and Franco, 2020; Rezvani Ghomi et al 2020). Additionally, it is essential to address the patient's underlying health conditions and factors that may impede the healing process, such as smoking, inadequate nutrition, and obesity (Han and Ceilley, 2017; The Wound Pros, 2023). Advanced therapies have emerged to address chronic wounds, such as extracellular matrices, growth factors, chitosan-based wound care dressings and collagen-based dressings. Chronic wounds that struggle to undergo complete re-epithelisation share common characteristics. These characteristics include heightened inflammation due to dysfunctional cells with limited proliferation and secretion capabilities, as well as defective mesenchymal stem cells (Briquez et al, 2015; Okurt et al, 2020; Verdolino et al, 2021; Denget et al, 2022). Contemporary approaches to managing chronic wounds align with the TIME framework, which encompasses tissue management, infection and inflammation control, moisture balance, and edge-of-the-wound considerations. As defined by the European Wound Management Association (EMWA), debridement refers to the removal of non-viable, necrotic tissue, biofilm, slough, scabs, and other impurities found in various types of chronic, infected, and hard-to-heal wounds (European Wound Management Association, 2004; Harries et al, 2016). Debridement is a crucial procedure aimed at preparing the wound bed to optimise subsequent treatments, ultimately leading to enhanced overall wound management outcomes. Effective debridement results in a reduction of biofilm, slough, malodour, improved microcirculation, and the stimulation of wound edges. These improvements contribute to accelerated wound healing, leading to an enhanced QoL for the patient (Leaper et al, 2012; Madhok et al, 2013; Strohal et al, 2013).

Chitosan stands as a natural biopolymer, ranking as the second most prevalent type after cellulose (Dutta et al, 2004; Aranaz et al, 2021). Chitosan is a nontoxic natural antimicrobial polymer and is approved by GRAS (Generally Recognized as Safe by the United States Food and Drug Administration) (Bellich et al, 2016; Leonida et al, 2018). This substance is extracted from chitin, primarily sourced from the shells of crustaceans, including

crabs, shrimp, and lobsters (Kou et al, 2021; Iber et al, 2022). Chitosan boasts a remarkable set of attributes, including biodegradability, hemostatic capabilities, biocompatibility, anti-inflammatory properties, analgesic effects, and the ability to expedite wound closure. In the context of wound healing, Chitosan plays a pivotal role across the initial three phases of wound healing (Khan and Mujahid, 2019; Matica et al 2019; Liu et al, 2021). During the first phase, haemostasis, it actively contributes to preventing excessive bleeding by facilitating platelet and erythrocyte aggregation. The interaction between the negatively charged molecules present on the surface of activated platelets and the positively charged chitosan promotes platelet aggregation. Furthermore, this electrostatic interplay aids in the production of fibrin clots and erythrocyte aggregation. Additionally, Chitosan inhibits the production of plasminogen activators, which, in turn, safeguards fibrin breakdown and prolongs the hemostatic process (Whang et al, 2005; He et al, 2013; Pogorielov and Sikora, 2015).

During the inflammatory phase, chitosan fibres with a positive charge exhibit an affinity for and disrupt the negatively charged bacterial cell wall. This disruption leads to the release of various intracellular substances, including proteins. Additionally, chitosan penetrates the nuclei of bacteria, hindering their ability to synthesize mRNA and proteins. Chitosan and chitosan derivatives can kill microbes by neutralising negative charges on the microbial surface (Goy et al 2009; Kong et al, 2010; Atay et al, 2020). Furthermore, it helps in the conversion of pro-inflammatory macrophages (M1) to anti-inflammatory macrophages (M2) through regulating the interleukin expression level (Oliveira et al, 2012).

Thirdly, in the proliferative phase, chitosan plays a pivotal role in stimulating the formation of granulation tissue, expediting the process of skin cell proliferation. Granulation tissue comprises inflammatory cells, fibroblasts, and capillaries. Chitosan fosters the production of cytokines such as transforming growth factor- β (TGF- β), interleukin-1 (IL-1), and platelet-derived growth factor (PDGF), which are essential for macrophage activity. TGF- β , in particular, aids macrophages in homing to the injury site, promoting fibroblast growth and augmenting collagen synthesis (Kim and Kim, 2006; Periyah et al, 2014; Kiritsi et al, 2018). Consequently, this orchestrated cascade of events contributes to wound repair and skin remodelling, ultimately culminating in the complete healing of the wound.

Table 1. Wound assessment parameters


Parameters	Description
Wound size	Length and width
Wound bed	Tissue Infection/inflammation Moisture balance Edge of wound
Periwound	Healthy/eczematous/ excoriated/ dry/ inflamed/ macerated
Wound exudate	Low, moderate, high
Level of pain	Visual analog score (VAS) 1–10

Chitosan possesses several noteworthy characteristics, including its analgesic properties. This substance has the ability to absorb protein ions that are released at sites of inflammation, thereby reducing the production of bradykinin, gradually breaking down N-acetyl-b-D-glucosamine, decreasing the expression of the TGF- β 1 factor, and inhibiting phospholipase activity. This inhibition, in turn, disrupts the arachidonic acid pathway (Okamoto et al, 2002; Harrison et al, 2020).

MaxiCel is composed entirely of grade A chitosan, derived from shellfish. One of its key advantages is its capacity to transform into a cohesive gel matrix upon contact with wound exudate. As MaxiCel transforms into this soothing gel matrix, it effectively mitigates inflammation, enhances patient comfort, safeguards the periwound area, and most importantly, expedites the wound healing process. This dressing also acts as an autolytic debridement agent, facilitating the removal of

Case 1

- A 59-year-old Malay lady with a left lower limb wound for 5 years. She had underlying diabetes mellitus, hypertension and deep venous thrombosis. Left ankle-brachial systolic index: 0.9
- Medications: oral anti-hyperglycaemia therapy and antihypertensive medications
- Wound treatment: many dressing materials were used before, including UrgoStat (1 month), Kytocel (2 weeks), before using MaxiCel as the primary dressing
- The wound was cleansed with sterile water and MaxiCel was applied with Melolin secondary dressing with calmoseptine as the barrier cream around the periwound and was further covered with gauze and gamgee. The dressing was changed once every 3 days.

Day 1 Size: 6cm x 5cm	Week 4 Size: 6.5cm x 6cm	Week 8 Size: 4cm x 4cm	Week 12 Size: 4cm x 3cm
 <p>Wound assessment: granulation 70%, epithelising: 20% slough 10% No signs of Infection/inflammation exudative with serous discharge advancing edge Periwound healthy Pains score: 4/10</p>	 <p>Wound assessment: granulation 70%, epithelising: 20% slough 10% No signs of Infection/inflammation exudative with serous discharge advancing edge Periwound healthy Pains score: 2/10</p>	 <p>Wound assessment: granulation 50%, epithelising: 45% slough 5% No signs of Infection/inflammation exudative with serous discharge advancing edge Periwound healthy Pains score: 1/10</p>	 <p>Wound assessment: granulation 40%, epithelising: 60% slough none No signs of Infection/inflammation exudative with serous discharge advancing edge Periwound healthy Pains score: 0/10</p>

slough and necrotic tissues, thereby promoting granulation and re-epithelisation. Furthermore, MaxiCel can even remove biofilms if they adhere to the gel matrix, and the matrix is subsequently removed during dressing changes (Nair, 2022; Axio, 2023).

Method

This study is a series of outpatients cases to evaluating the clinical efficacy of MaxiCel in managing chronic, hard-to-heal wounds. Patients with chronic, hard-to-heal wounds of their lower extremities were selected, by random screening, in the Wound Care Unit, at Hospital Kuala Lumpur and were observed for up to 14 weeks. The wound was assessed and documented during each visit, this included wound size, wound bed, level of exudates, periwound skin condition, and level of pain via a validated visual-analogue scale (VAS) 1–10 between dressing changes. Table 1 lists the assessments performed.

All patients were provided information on their treatment and were asked to sign informed

consent before use of the dressing. Patients voluntarily participated and agreed that data could be used for educational purposes.





All dressings were used according to the manufacturer's instructions. Patients' data, medical history, surgical history, treatment, medications, allergy status, and wound assessment using the T. I. M. E. concept were documented and kept on file. Photographs were taken to monitor and record wound status and progression. Details of dressing use were also recorded.

Inclusion criteria

- Pressure ulcers
- Venous leg ulcers
- Diabetic leg ulcers
- Other leg ulcers
- Donor site wounds
- Haemostasis post debridement
- Skin abrasions
- Superficial- and partial-thickness burns
- Surgical or postoperative wound
- Able to comply with the dressing regimen at the hospital.

Case 2

- A 66-year-old Chinese lady with a left lower limb ulcer for 1 year. Underlying diabetes mellitus and hypertension. Left ankle-brachial systolic index :1.0
- Medications: oral antihyperglycemic therapy (T. Metformin 500mg OD, T. Gliclazide 30mg OD) and antihypertensive medications (T. amlodipine 10 mg od, T. Perindopril 4mg od)
- Wound treatment: many dressing materials were used prior such as Hyalo4 (1 month), Kaltostat (3 weeks), and others before using MaxiCel as the primary dressing. The wound was cleansed with sterile water and MaxiCel was applied with Melolin secondary dressing with calomoseptine as the barrier cream around the periwound and was further covered with gauze and gamgee. The dressing was changed once every 3 days.

Day 1 Size: 6.5cm x 4.5cm	Week 4 Size: 6cm x 4cm	Week 8 Size: 6cm x 4cm	Week 12 Size: 5cm x 4cm
			
Wound assessment: granulation 95%, epithelising: 5%. No slough; No signs of Infection/ inflammation; Exudative with serous discharge; Advancing edge Periwound: macerated Pains score: 5/10	Wound assessment: granulation 90%, epithelising: 10% No slough; No signs of Infection/ inflammation; Exudative with serous discharge; Advancing edge Periwound healthy Pains score: 3/10	Wound assessment: granulation 90%, epithelising: 10% No slough; No signs of Infection/ inflammation; Exudative with serous discharge; Advancing edge Periwound healthy Pains score: 2/10	Wound assessment: granulation 80%, epithelising: 20% No slough; No signs of Infection/ inflammation; Exudative with serous discharge; Advancing edge Periwound healthy Pains score: 0/10

Exclusion criteria

- Non-compliant with the dressing regimen.

Protocol for dressing

- The previous dressings were removed from the wound
- The wound was rinsed with sterile water
- Slough and necrotic material were removed via mechanical debridement (rubbing using gauze)
- The wound is dried by dapping
- MaxioCel was applied on the wound, including approximately 1cm margin of the surrounding healthy skin.
- Melolin was applied as the secondary dressing.
- Calmoseptine cream was applied to the periwound skin.
- Gauze and gamgee were applied and the wound was bandaged.
- Wound assessment and pain score were monitored biweekly at the dressing change visit.

Results

We have recruited five female patients with chronic lower limb wounds. At the start

of treatment, some patient's wounds had moderate levels of exudates and slough, which showed improvement over the course of the treatment. The wounds were dressed every 2–3 days depending on the level of exudate. The wound bed improved with a significant decrease in sloughy tissue from 10% at the start of treatment, replaced with healthy granulation and epithelial tissue. The periwound also showed improvement due to the exudate-locking capability of the dressing. The parameters assessed were wound size, wound bed appearance, periwound condition, exudate level and level of pain of the patient. All the parameters listed showed improvement within 4 weeks. The MaxioCel dressing was changed once every three days

In the 14-week evaluation, MaxioCel significantly increased the healing rate, reduced wound area, decreased slough and necrosis, and increased granulation and epithelialisation. MaxioCel also assisted with the reduction of pain as it could be removed easily in one piece. No lasting pain was reported. There was no excessive bleeding in all cases as the haemostatic properties of

Case 3

- A 74-year-old Chinese lady with a right venous leg ulcer for 5 years. Underlying diabetes mellitus and hypertension.
- Medications: oral antihyperglycemic therapy and antihypertensive medications
- Wound treatment: many dressing materials were used prior such as Urgostat (1 month), Anscate (1 month), Kytocell (3weeks), and others before using MaxioCel as the primary dressing. The wound was cleansed with sterile water and MaxioCel was applied with Melolin secondary dressing with calmoseptine as the barrier cream around the periwound and was further covered with gauze and gamgee. The dressing was changed once every 3 days.

Day 1 Size: 6cm x 5cm	Week 4 Size: 5.5cm x 4cm	Week 8 Size: 5.5cm x 3cm	Week 12 Size: 5cm x 3cm
			
Wound assessment: granulation 70%, epithelising: 5% slough 25% No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pains score: 4/10	Wound assessment: granulation 80%, epithelising: 5% slough 15% No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pains score: 2/10	Wound assessment: granulation 80%, epithelising: 10% slough 10% No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pains score: 1/10	Wound assessment: granulation 85%, epithelising: 10% slough 5% No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pains score: 0/10

Case 4

- A 23-year-old Indian lady with left necrotizing fasciitis and completed wound debridement on 1/6/23. Underlying type 1 diabetes mellitus. Left ankle-brachial systolic index: 1.1, Medications: Insulin
- Wound treatment: dressings materials were used such as Anscate over the tendon and MaxiCel as the primary dressing. The wound was cleansed with sterile water. Anscate was applied over the tendon and MaxiCel was applied over it with Melolin secondary dressing with calmoseptine as the barrier cream around the periwound and is further covered with gauze and gamgee and the dressing. The dressing was changed once every 3 days.

Day 1 Size: 6.5cm x 4.5cm (d) 13cm x 6cm (v)	Week 4 Size: 11cm x 8cm (d) 12cm x 3cm (v)	Week 8 Size: 11cm x 5cm (d) 10cm x 3cm (v)	Week 12 Size: 10cm x 5cm (d) 4cm x 1cm (v)
 	 	 	 
<p>Wound assessment: granulation 80%, epithelising: 10% slough 10% tendon exposed. No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound macerated at the ventral Pains score: 5/10</p>	<p>Wound assessment: granulation 70%, epithelising: 20% slough 10% Tendon exposed. No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pains score: 3/10</p>	<p>Wound assessment: granulation 60%, epithelising: 35% slough 5% Tendon exposed. No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pains score: 2/10</p>	<p>Wound assessment: granulation 60%, epithelising: 40% No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pains score: 0/10</p>
<p>(d):dorsal (v): ventral</p>			

MaxiCel were also beneficial as it helps to control bleeding while dressing changes.

Limitations





This is a small observational study with limited number of cases. A more robust study with larger number of patients is required to confirm these preliminary results
Other limitations include the wounds assessed in this study. The cases did not include arterial ulcers. Time taken for full re-epithelisation was not considered assessed.

Conclusion

Wound bed preparation and dressing choice must provide an environment suitable to aid wound healing, protection of the wound and wound closure. To treat chronic hard-to-heal wounds, the ideal wound dressing should be chosen to maintain a suitable moisture level in the wound bed. The dressing chosen should be nontoxic, serve as a bacterial barrier, have a haemostatic characteristic for minor bleeding, and promote wound healing. Additionally, it should also manage pain and decrease

Case 5

- A 59-year-old Malay lady with left necrotising fasciitis completed Extensive wound debridement and Ray amputation of the Left 4th and 5th toe done on 21 April 2023. Underlying diabetes mellitus. Left ankle-brachial systolic index: 0.9
- Medications: oral antihyperglycemic therapy
- Wound treatment: The wound was cleansed with sterile water and MaxioCel was applied with Melolin secondary dressing with calmoseptine as the barrier cream around the periwound and was further covered with gauze and gamgee. The dressing was changed once every 3 days.

Day 1 Size: 19cm x 11cm	Week 4 Size: 16cm x 6cm	Week 8 Size: 12cm x 5cm	Week 12 Size: 10cm x 4.5cm
			
Wound assessment: granulation 80%, epithelising: 10% slough 10% No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound : erythematous and macerated Pain score: 3/10	Wound assessment: granulation 80%, epithelising: 20% no slough No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pain score: 2/10	Wound assessment: granulation 70%, epithelising: 30% no slough No signs of Infection/inflammation Exudative with serous discharge advancing edge Periwound healthy Pain score: 0/10	Wound assessment: granulation 60%, epithelising: 40% No signs of Infection/inflammation Exudative with serous discharge Advancing edge Periwound healthy Pain score: 0/10

scar formation at the site and should be easily removable. In this case, series MaxioCel has achieved positive outcomes through its significant healing capacities as measured by a reduction in wound surface area, improvement to the wound bed and periwound skin, and a reduction in reported pain. Chronic hard-to-heal wounds can improve and progress to healing if the bioburden is eliminated by clearing of necrotic and sloughy tissue. These objectives were achieved with the BMG dressing. The dressing has not only allowed the wound to progress toward healing but also demonstrated pain reduction in patients as it could be easily removed, in one piece.

WAS

Declaration of interest

The authors declare that this study was carried out without any commercial or financial affiliations that could be seen as a possible conflict of interest.

References

Aranaz I, Alcántara AR, Civera MC et al (2021) Chitosan: An overview of its properties and applications. *Polymers (Basel)* 13(19):3256. <https://doi.org/10.3390/polym13193256>

Atay HY (2020) Antibacterial activity of chitosan-based systems. functional chitosan. *Functional Chitosan* 457–89. https://doi.org/10.1007%2F978-981-15-0263-7_15

Axio (2023) BMG Technology based MaxioCel Dressing Properties and Application. <https://tinyurl.com/ma3nwvxv> (accessed 19 September 2023)

Bellich B, D'Agostino I, Semeraro S et al (2016) 'The good, the bad and the ugly' of chitosans. *Mar Drugs* 14(5):99. <https://doi.org/10.3390/md14050099>

Bowers S, Franco E (2020) Chronic wounds: Evaluation and management. *Am Fam Physician* 101(3):159–66

Briquez PS, Hubbell JA, Martino MM (2015) Extracellular matrix-inspired growth factor delivery systems for skin wound healing. *Adv Wound Care* 4(8):479–89. <https://doi.org/10.1089%2Fwound.2014.0603>

Chrisman CA (2010) Care of chronic wounds in palliative care and end-of-life patients. *Int Wound J* 7(4):214–35. <https://doi.org/10.1111/j.1742-481x.2010.00682.x>

Deng X, Gould M, Ali MA (2022) A review of current advancements for wound healing: Biomaterial applications and medical devices. *J Biomed Mater Res Part B Appl Biomater* 110(11):2542–73. <https://doi.org/10.1002/jbm.b.35086>

Dutta PK, Duta J, Tripathi VS (2004) Chitin and Chitosan: Chemistry, properties and applications. *J Sci Ind Res (India)* 63:20–31

European Wound Management Association (EWMA). Position Document: Wound Bed Preparation in Practice. MEP Ltd, 2004

Gouin JP, Kiecolt-Glaser JK (2011) The Impact of Psychological

- Stress on Wound Healing: Methods and Mechanisms. *Immunol Allergy Clin North Am* 31(1):81–93. <https://doi.org/10.1016%2Fj.jiac.2010.09.010>
- Goy RC, De Britto D, Assis OBG (2009) A review of the antimicrobial activity of chitosan. *Polimeros* 19(3):241–7. <https://doi.org/10.1590/S0104-14282009000300013>
- Guo S, DiPietro LA (2010) Factors affecting wound healing. *J Dent Res* 89(3):219–29. <https://doi.org/10.1177/0022034509359125>
- Han G, Ceilley R (2017) Chronic wound healing: a review of current management and treatments. *Adv Ther* 34(3):599–610. <https://doi.org/10.1007/s12325-017-0478-y>
- Harries RL, Bosanquet DC, Harding KG (2016) Wound bed preparation: TIME for an update. *Int Wound J* 13 Suppl 3(Suppl 3):8–14. <https://doi.org/10.1111/iwj.12662>
- Harrison ZL (2020) In Vitro Evaluation of Loaded Chitosan Membranes for Pain Relief and Infection Prevention Major. University of Memphis Digital Commons. <https://tinyurl.com/2p99u26f> (accessed 19 September 2023)
- He Q, Gong K, Ao Q et al (2013) Positive charge of chitosan retards blood coagulation on chitosan films. *J Biomater Appl* 27(8):1032–45. <https://doi.org/10.1177/0885328211432487>
- Hopkins S (2011) Psychological aspects of wound healing. *Nurs Times* 97(48):57
- Iber BT, Kasan NA, Torsabo D, Omuw, JW (2022) A review of various sources of chitin and chitosan in nature. *J Renew Mater* 10(4):1097–123. <http://dx.doi.org/10.32604/jrm.2022.018142>
- Järbrink K, Ni G, Sönnergren H et al (2017) The humanistic and economic burden of chronic wounds: A protocol for a systematic review. *Syst Rev* 6(15):1–7
- Khan MA, Mujahid M (2019) A review on recent advances in chitosan based composite for hemostatic dressings. *Int J Biol Macromol* 124:138–47. <https://doi.org/10.1016/j.ijbiomac.2018.11.045>
- Kim MM, Kim SK (2006) Chitooligosaccharides inhibit activation and expression of matrix metalloproteinase-2 in human dermal fibroblasts. *FEBS Lett* 580(11):2661–6. <https://doi.org/10.1016/j.febslet.2006.04.015>
- Kiritzi D, Nyström A (2018) The role of TGFβ in wound healing pathologies. *Mech Ageing Dev* 172:51–8. <https://doi.org/10.1016/j.mad.2017.11.004>
- Kong M, Chen XG, Xing K, Park HJ (2010) Antimicrobial properties of chitosan and mode of action: A state of the art review. *Int J Food Microbiol* 114(1):51–63. <https://doi.org/10.1016/j.ijfoodmicro.2010.09.012>
- Kou SG, Peters LM, Mucalo MR (2021) Chitosan: A review of sources and preparation methods. *Int J Biol Macromol* 169:85–94. <https://doi.org/10.1016/j.ijbiomac.2020.12.005>
- Landén NX, Li D, Stähle M (2016) Transition from inflammation to proliferation: a critical step during wound healing. *Cell Mol Life Sci* 73(20):3861–85
- Leaper DJ, Schultz G, Carville K et al (2012) Extending the TIME concept: What have we learned in the past 10 years? *Int Wound J* 9 Suppl 2(Suppl 2):1–19. <https://doi.org/10.1111/j.1742-481x.2012.01097.x>
- Leonida M, Ispas-Szabo P, Mateescu MA (2018) Self-stabilized chitosan and its complexes with carboxymethyl starch as excipients in drug delivery. *Bioact Mater* 3(3):334–40. <https://doi.org/10.1016/j.bioactmat.2018.04.001>
- Liu Y, Chen J, Li P, Ning N (2021) The Effect of Chitosan in Wound Healing: A Systematic Review. *Adv Skin Wound Care* 34(5):262–6. <https://doi.org/10.1097/01.asw.0000723128.58588.b5>
- Lo ZJ, Lim X, Eng D et al (2020) Clinical and economic burden of wound care in the tropics: a 5-year institutional population health review. *Int Wound J* 17(3):790–803. <https://doi.org/10.1111/iwj.13333>
- Madhok BM, Vowden K, Vowden P (2013) New techniques for wound debridement. *Int Wound J* 10(3):247–51. <https://doi.org/10.1111%2Fiwj.12045>
- Matica MA, Aachmann FL, Tøndervik A et al (2019) Chitosan as a wound dressing starting material: Antimicrobial properties and mode of action. *Int J Mol Sci* 20(23):5889. <https://doi.org/10.3390/ijms20235889>
- Munro G (2017) Causes and consideration with chronic wounds: A narrative review of the evidence. *Wound Pract Res* 25:88–97
- Nair HK (2022) Evaluation of a novel chitosan wound healing dressing based on bioactive microfibre gelling (bmg) technology: a case series. *Wounds Asia* 5(3):52–58
- Okamoto, Y, Kawakami K, Miyatake K et al (2002) Analgesic effects of chitin and chitosan. *Carbohydr Polym* 49(3):249–52 (2002).
- Okur ME, Karantas ID, Şenyiğit Z et al (2020) Recent trends on wound management: New therapeutic choices based on polymeric carriers. *Asian J Pharm Sci* 15(6):661–84. <https://doi.org/10.1016/j.ajps.2019.11.008>
- Oliveira MI, Santos SG, Oliveira MJ et al (2012) Chitosan drives anti-inflammatory macrophage polarisation and pro-inflammatory dendritic cell stimulation. *Eur Cells Mater* 24:136–52. <https://doi.org/10.22203/ecm.v024a10>
- Periayah MH, Halim AS, Yaacob NS et al (2014) Expression of P-selectin, TXA2, TGF-β1 and PDGF-AB in the presence of bioadhesive chitosan derivatives. *Online Int Interdiscip Res J IV*:5–14
- Pogorielov MV, Sikora VZ (2015) Chitosan as a hemostatic agent: current state. *Eur J Med Ser B* 2(1):24–33. <http://dx.doi.org/10.13187/ejm.s.b.2015.2.24>
- Rezvani Ghomi E, Khalili S, Nouri Khorasani S et al (2019) Wound dressings: Current advances and future directions. *J Appl Polym Sci* 136(27):1–12. <https://doi.org/10.1002/app.47738>
- Richmond N A, Maderal AD, Vivas AC (2013) Evidence-based management of common chronic lower extremity ulcers. *Dermatol Ther* 26(3):187–96. <https://doi.org/10.1111/dth.12051>
- Strohal R, Dissemmond J, Jordan O'Brien J et al (2013) An updated overview and clarification of the principle role of debridement. *J Wound Care* 22 Suppl:51–52. <https://doi.org/10.12968/jowc.2013.22.sup1.s1>
- The Wound Pros (2023) Systemic Factors Affecting Wound Healing. <https://www.thewoundpros.com/post/the-most-important-factors-affecting-wound-healing> (accessed 19 September 2023)
- Théorêt C, Stashak T (2011) Wound dressing: absorbent dressings. *Clin Vet Advis Horse* 15:847–8
- Verdolino DV, Thomason HA, Fotticchia A, Cartmell S (2021) Wound dressings: Curbing inflammation in chronic wound healing. *Emerg Top Life Sci* 5(4):523–37. <https://doi.org/10.1042/etls20200346>
- Wang PH, Huang BS, Horng HC et al (2018) Wound healing. *J Chinese Med Assoc* 81(2):94–101. <https://doi.org/10.1016/j.jcma.2017.11.002>
- Whang HS, Kirsch W, Zhu Y H et al (2005) Hemostatic agents derived from chitin and chitosan. *J Macromol Sci Polym Rev* 45(4):309–23. <https://doi.org/10.1080/15321790500304122>
- Zhao R, Liang H, Clarke E et al (2016) Inflammation in chronic wounds. *Int J Mol Sci* 17(12):1–14. <https://doi.org/10.3390%2Fijms17122085>