

Evaluation of a novel chitosan wound healing dressing based on bioactive microfibre gelling (bmg) technology™: a case series



Authors:
Harikrishna KR Nair

Abstract: Health professionals can be overwhelmed by the number of wound dressings currently available. Their choice is based on clinical evidence and also on their clinical expertise and experiences. Chitosan is a natural cationic polysaccharide that is the partially- to fully-deacetylated form of chitin. There is great interest in the use, as this biopolymer is the second most abundant after cellulose. Chitosan has been reported to have a number of useful properties in the management of wound healing. Here we share our experience regarding the management of five complex wounds treated with a novel Chitosan dressing. The outcomes of all cases were very encouraging, and the clinician feedback was positive.

Key words:

- Chitosan
- Diabetic foot ulcer
- Polymer films
- Wound Healing

The clinical requirement of a wound dressing, aside from protecting the wound and absorbing exudate, has shifted towards having the ability to encourage healing (Sinha, 2018). Currently, a wide range of absorbent dressings are available in the market for wound care, claiming to have the ability to manage exudate while also encouraging healing (Sinha, 2018). However, it is becoming clear, that some of these dressings are not meeting their expectations when applied in a clinical setting (Sinha, 2018). Moreover, understanding the interventions that effectively promote and support healing and wound repair is essential for health professionals working in wound care (Tayyib and Ramaiah, 2021). The efficient management of wounds requires the health care professionals involved in wound management to have the appropriate knowledge and skills to maximize positive health outcomes (Welsh, 2018).

Hard-to-heal wounds are defined as wounds that fail to heal with standard therapy, in an orderly and timely fashion (Troxler et al, 2006; Milne et al, 2020). Delayed healing can occur in a variety of wound types, and, although delayed healing is common, it is frequently not recognised early enough and can pose a major problem that increases the burden on health care

professionals and hospitals (Troxler et al, 2006). It is therefore essential for healthcare professionals to differentiate between a wound that is likely to heal with a standard treatment, and a non-responding wound, that would require and justify a different treatment approach (White, 2011).

Novel wound dressing in wound management

Chitosan is a natural cationic polysaccharide which is the partially- to fully-deacetylated form of chitin (Hosseinnejad and Jafari, 2016) that has generated great interest in the use of chitin since this biopolymer is the second most abundant after cellulose (Abdel-Rahman et al, 2015). Chitosan has been reported to possess a lot of excellent properties, such as biocompatibility, biodegradability, haemostatic property, anti-inflammatory effects and capability to accelerate wound closure (Matica et al, 2019). The roles of Chitosan in wound healing include haemostasis, pain reduction, initial macrophage activation followed by the anti-inflammatory response, antimicrobial, inhibition of matrix metalloproteinase-2 (MMP-2), and re-epithelialisation (Dai et al, 2011; Liu et al, 2018). Haemostasis is achieved through the absorption of blood plasma that leads to the concentration of erythrocytes and platelets, adhesion, aggregation and activation of platelets, and promotion of erythrocyte coagulation and activation due to a charge-

Harikrishna KR Nair, Professor and Head of the Wound Care Unit, Department of Internal Medicine, Hospital Kuala Lumpur Malaysia

Case 1. Left limb ulcer

- A 39-year-old female with underlying diabetic mellitus. The wound size was 17cm x 3cm
- The wound was flushed with sterile water and the Chitosan dressing was applied with a foam secondary dressing
- By day 12, the wound had improved with wound size now reduced to 11.3cm x 1.9cm
- Complete wound closure was achieved by 19th January 2022.

8/11/2021: Chitosan dressing regime started	22/11/2021 Showing improvement and wound size reduction	19/1/2022 Wound completely healed
		

based interaction (He et al, 2013; Maksym and Vitali, 2015; Chen et al 2017). Promotion of re-epithelialisation occurs through the stimulation of the dermal fibroblasts, interaction with the growth factors and metal ions and inhibition of keratinocyte proliferation (Hamilton et al, 2006; Howling et al, 2001). The antimicrobial activity occurs as cationic Chitosan binds to the negatively charged cell wall of microorganisms, resulting in the leakage of proteinaceous and other intercellular constituents; inhibition of the mRNA and protein synthesis via the penetration of Chitosan into the nuclei, and provocation of cell osmolytic of microorganisms (Goy et al, 2009; Orgaz et al, 2011).

The analgesic effect is achieved through the capacity of Chitosan to absorb the protein ions released at the inflammatory sites, together with chitin lowering the bradykinin production at inflammatory sites (among the major pain mediators during inflammation), as well as inhibition of Phospholipase (PLA-2) activity, in turn blocking the arachidonic acid pathway (Okamoto et al, 2002; Mo et al, 2015; Choi et al, 2018). The anti-inflammatory properties of Chitosan are achieved through the inhibition of inflammatory mediators (e.g., Interleukin), reduction of pro-inflammatory cytokines (e.g., TNF- α) and down-regulation of NF- κ B expression and AP-1 activation (Oliveira et al, 2012; Chang et al, 2019). Chitosan has also been shown to inhibit the activation and expression of MMP-2 in human dermal fibroblasts (Kim and Kim, 2006).

Scar minimisation is achieved through the gradual degradation of N-acetyl-b-D-

glucosamine, which initiates hyaluronic acid at the wound site, thus helping in faster scar improvement (Anjum et al, 2016). Moreover, in the presence of Chitosan, type IV collagen produced is in the form of fine reticulin-like fibres rather than mature bands of dense collagen. In addition, it significantly minimises scarring by decreasing the expression of TGF- β 1 factor by blocking the cyclooxygenase and arachidonic acid pathways (Lv et al, 2012; Anjum et al, 2016).

In a randomised control trial (RCT) comparing the effect of Chitosan to standard treatment, pressure ulcers managed with the Chitosan dressing (29 out of the 34) healed within 21 days of the trial period and none became infected, compared to only four wounds healed in the control group. The authors concluded that the Chitosan based bioactive dressing significantly increases healing rates which equates to significant cost savings (Kordestani et al, 2008).

Dressing evaluation

The evaluated novel wound dressing (MaxiCel, which uses Bioactive Microfiber Gelling Technology™) is a highly absorbent antimicrobial wound dressing, designed to heal patients suffering from chronic wounds by effectively managing exudate, pain, and scarring (Ray et al, 2021).






RESULTS

Case 1

A 39-year-old female working as a housewife with a history of diabetes mellitus type 2 for

Case 2. Plantar and lateral wound

- A 42-year-old unemployed Malay lady with underlying diabetic melitus
- Right a plantar diabetic foot ulcer present for 2 months. The Patient had a history of right lower leg necrotising fasciitis and wet gangrene of right big toe
- The wound was flushed with sterile water and the Chitosan dressing was applied with a foam secondary dressing and offloading pad
- The post-amputation (lateral) wound had healed by the 26/11/2021 and the plantar wound healed by 7/2/2022.

Plantar wound on 8/11/2021- Chitosan dressing regime started	Lateral wound on 8/11/21- Chitosan dressing regime started	Plantar wound reduced in size by 26/11/2021	Lateral wound healed 26/11/2021	Plantar wound healed 7/2/2022
				

five years presented with a left limb ulcer which was non-healing for the past month. Wound debridement was conducted by Orthopaedics on 6/10/21. The wound was previously managed with a matrix metalloproteinase inhibiting foam dressing for two weeks. On presentation, wound serous exudate was high, however, healthy granulating tissue was present. The wound size was 17cm x 3cm. The wound was flushed with sterile water and the new regimen with Chitosan

dressing was initiated on 8/11/20 (Figure 1A). A foam was applied as a secondary dressing. On day 12, the wound continued to improve with wound size now reduced to 11.3cm x 1.9cm (Figure 1B). Complete wound closure was achieved by 19th January 2022 (Figure 1C).

Case 2

A 57-year-old male working as a Barista with a 10 years history of diabetes mellitus type 2,

Case 3. Shin wound after traumatic injury

- A 29-year-old male working as a foreaen came to the hospital on 15/9/2021 with a wound over the shin that was sustained during a motorcycle accident a couple of weeks previously
- The wound was flushed with sterile water and the Chitosan dressing was applied with a foam secondary dressing
- The wound healed by 20/12/2021.

15/9/2021: 9.3cm x 2.9cm	25/11/2021 Wound showing signs of healing, 4.3cm x 1.7cm	20/12/2021 Wound healed
		

presented with a right plantar diabetic foot ulcer (4cm x 3cm) (Figure 2A) and a post-Ray's amputation of 3rd, 4th and 5th toes (6cm x 1.1cm) (Figure 2B) on 8th November 2021. The wounds were previously managed with a sodium hyaluronate gel and a secondary foam dressing together with offloading pad for two months. After wound flushing with sterile water cleansing solution, Chitosan dressing was applied, with the same secondary foam dressing and offloading pad. The patient visited the clinic twice a week. By the 26th November, the plantar wound was reduced to 3.4cm x 2.2cm (Figure 2C), while the post-amputation (lateral) wound had completely healed (Figure 2D). Wound closure for the plantar wound was achieved by 7th November 2022 (Figure 2E).

Case 3

A 29-year-old male working as a foreman came to the hospital on 15th September 2021 with a wound over the shin that was sustained during a motorcycle accident a couple of weeks previously. Up to that point, the wound was being managed with honey gel. The wound was debrided by Orthopaedics and then referred to the wound clinic. The initial wound size was 9.3cm x 2.9cm (Figure 3A). After wound flushing with sterile water cleansing solution, the Chitosan dressing was applied and covered with a foam as a secondary dressing. The dressing was changed twice weekly. By the 25th November, the wound was showing evidence of healing, with healthy granulating tissues and

wound area reduction (Figure 3B), with the wound size reduced to 4.3cm x 1.7cm. The wound healed by 20th December (Figure 3C).

Case 4


A 64-year-old male driver with known type 2 diabetes mellitus and hypertension for 30 years, was referred on 8th November 2021 for management of a long-standing ulcer on the left lateral aspect (malleolar region) (Figure 4A). The wound measured 8cm x 3.5cm, was mostly covered with slough and had high levels of serous exudate. The wound was previously managed with an organic healing ointment for two weeks, which was then changed to a collagen foam dressing for another two weeks. After wound flushing with sterile water cleansing solution, the Chitosan dressing was applied under a foam, with dressing changed twice a week. After one dressing change (12th November), the wound bed was clean and showed signs of granulation (Figure 4B) and by the 25th of November, the wound showed great improvement with wound area reduction to 7.9cm x 3.7cm and reduced levels of exudate (Figure 4C).

Case 5

A 57-year-old female pensioner was referred on 5th November 2021 for a venous leg ulcer on the left medial aspect malleolar region. Measuring 6.6cm x 7.1cm, the wound had been present for the past 3 years

Case 4. Shin wound after traumatic injury

- A 64-year-old male with known type 2 diabetes mellitus and hypertension for 30 years
- Presented with a long-standing ulcer on the left lateral aspect of the foot
- The wound was flushed with sterile water and the Chitosan dressing was applied with a foam secondary dressing. Dressing changed twice a week
- Wound area reduced to 7.9cm x 3.7cm and reduced levels of exudate by 25/11/2021.

8/11/2021: 8cm x 3.5cm	12/11/2021 Wound bed improvement after 1 dressing change,	25/11/2021 Condition of the wound is further improved 7.9cm x 3.7cm
		

Case 5. Venous leg ulcer

- A 57-year-old female pensioner with a venous leg ulcer on the left medial aspect malleolar region
- The patient had a history of diabetes mellitus and hypertension, both treated with the appropriate medications
- The wound was flushed with sterile water and the Chitosan dressing was applied with a foam secondary dressing and a compression bandage
- The wound healed by 21/1/2022.

5/11/2021 wound at presentation 6.6cm x 7.1cm	24/11/2021 reduce size and exudate levels 3.4cm x 4.9cm	4/12/2021 healthy granulation tissue 3.5cm x 0.5cm	21/1/2022 healed
			

(Figure 5A) with high levels of serous exudate. The patient had a history of diabetes mellitus and hypertension, which were both treated with the appropriate medications. The wound was recently treated with a polyether foam with Methylene Blue, Gentian Violet, Silver Sodium Zirconium Phosphate and a compression bandage. After wound flushing with sterile water cleansing solution, the Chitosan dressing was applied with foam as a secondary dressing and a compression bandage. The dressing was changed twice a week. By the 24th of November, the wound size was decreased to 3.4cm x 4.9cm and exudate level was reduced (Figure 5B). Further improvement of the wound bed, with healthy granulation tissues was noted by 4th December (Figure 5C) and the wound was healed by 21st January 2022 (Figure 5D).

CONCLUSION

Wound dressings aim to restore the environment required for healing as well as protect the wound from environmental threats, such as infection (Elsner et al, 2010). Moreover, the dressings should be easy to apply and remove and maintain a moist healing environment (Elsner et al, 2010). When selecting a dressing, the health care professional must remember to consider wound size and depth, exudate amount, dressing frequency, and any patient-related factors (Dabiri et al, 2016). Dressings should also have the conformability to keep direct contact with the wound bed.

The evaluated dressing was tried initially in five difficult-to-heal cases. The wounds were challenging due to their complexity. The results achieved with the novel Chitosan

wound dressing in these cases are highly promising and provided good results for the wound healing process and received excellent feedback from the clinicians.

However, the cohort of this evaluation is quite small, and therefore, further evaluations will continue to be conducted in this wound care centre in Malaysia. WAS

References

- Abdel-Rahman RM, Hrdina R, Abdel-Mohsen AM et al (2015) Chitin and chitosan from Brazilian Atlantic Coast: Isolation, characterization and antibacterial activity. *International Journal of Biological Macromolecules*. 80:107–20. <https://doi.org/10.1016/j.ijbiomac.2015.06.027>
- Anjum S, Arora A, Alam MS, Gupta B (2016) Development of antimicrobial and scar preventive chitosan hydrogel wound dressings. *Int J Pharm* 508(1–2):92–101.
- Chang SH, Lin YY, Wu GJ et al (2019) Effect of chitosan molecular weight on anti-inflammatory activity in the RAW 264.7 macrophage model. *Int J Biol Macromol* 131:167–75.
- Chen Z, Yao X, Liu L, Guan J et al (2017) Blood coagulation evaluation of N-alkylated chitosan. *Carbohydrate polymers*. 173:259–68. <https://doi.org/10.1016/j.carbpol.2017.05.085>
- Dai T, Tanaka M, Huang YY, Hamblin MR (2017) Chitosan preparations for wounds and burns: antimicrobial and wound-healing effects. *Expert Rev Anti Infect Ther* 9(7):857–79. <https://doi.org/10.1586%2Feri.11.59>
- Choi SI, Hwang SW (2018) Depolarizing effectors of bradykinin signalling in nociceptor excitation in pain perception. *Biomol Ther (Seoul)* 26(3):255–267. <https://doi.org/10.4062%2Fbiomolther.2017.127>
- Dabiri G, Damstetter E, Phillips T (2016) Choosing a wound dressing based on common wound characteristics. *Adv Wound Care (New Rochelle)* 5(1):32–41. <https://doi.org/10.1089%2Fwound.2014.0586>
- Elsner JJ, Shefy-Peleg A, Zilberman M (2010) Novel biodegradable composite wound dressings with controlled release of antibiotics: microstructure, mechanical and physical properties. *J Biomed Mater*

- Res B Appl Biomater* 93(2):425–35. <https://doi.org/10.1002/jbm.b.31599>
- Goy RC, Britto DD, Assis OB (2009) A review of the antimicrobial activity of chitosan. *Polimeros* 19:241–7. <https://doi.org/10.1590/S0104-14282009000300013>
- Hamilton V, Yuan Y, Rigney DA et al (2006) Characterization of chitosan films and effects on fibroblast cell attachment and proliferation. *J Mater Sci Mater Med* 17(12):1373–81. <https://doi.org/10.1007/s10856-006-0613-9>
- 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>
- Hosseinnejad M, Jafari SM (2016) Evaluation of different factors affecting antimicrobial properties of chitosan. *Int J Biol Macromol* 85:467–75. <https://doi.org/10.1016/j.ijbiomac.2016.01.022>
- Howling GI, Dettmar PW, Goddard PA et al (2001) The effect of chitin and chitosan on the proliferation of human skin fibroblasts and keratinocytes in vitro. *Biomaterials* 22(22):2959–66. [https://doi.org/10.1016/S0142-9612\(01\)00042-4](https://doi.org/10.1016/S0142-9612(01)00042-4)
- Kordestani S, Shahrezaee M, Tahmasebi MN et al (2008) A randomised controlled trial on the effectiveness of an advanced wound dressing used in Iran. *Journal of wound care*. 2008 Jul;17(7):323–7.
- Liu H, Wang C, Li C, Qin Y et al (2018) A functional chitosan-based hydrogel as a wound dressing and drug delivery system in the treatment of wound healing. *RSC Adv* 8(14):7533–49. <https://doi.org/10.1039/C7RA13510F>
- Lv C, Dai H, Xing X, Zhang J (2012) The systematic effects of chitosan on fibroblasts derived from hypertrophic scars and keloids. *Indian J Dermatol Venereol Leprol* 78(4):520. <https://doi.org/10.4103/0378-6323.98098>
- Kim MM, Kim SK (2006) Chitoooligosaccharides 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>
- Maksym PV, Vitali S (2015) Chitosan as a hemostatic agent: current state. *European journal of medicine. Series B*. 2015; 2(1):24–33
- 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>
- Milne J, Searle R, Styche T (2020) The characteristics and impact of hard-to-heal wounds: results of a standardised survey. *J Wound Care* 29(5):282–8. <https://doi.org/10.12968/jowc.2020.29.5.282>
- Mo X, Cen J, Gibson E, Wang R, Percival SL (2015) An open multicenter comparative randomized clinical study on chitosan. *Wound Repair and Regeneration* 23(4):518–24.
- Okamoto Y, Kawakami K, Miyatake K et al (2002) Analgesic effects of chitin and chitosan. *Carbohydrate Polymers* 49(3):249–52. [https://doi.org/10.1016/S0144-8617\(01\)00316-2](https://doi.org/10.1016/S0144-8617(01)00316-2)
- Oliveira MI, Santos SG, Oliveira MJ et al (2012) Chitosan drives anti-inflammatory macrophage polarisation and pro-inflammatory dendritic cell stimulation. *Eur Cell Mater* 24(136):133–6. <https://doi.org/10.22203/ecom.v024a10>
- Orgaz B, Lobete MM, Puga CH, Jose CS (2011) Effectiveness of chitosan against mature biofilms formed by food related bacteria. *Int J Mol Sci* 12(1):817–28. <https://doi.org/10.3390/2Fijms12010817>
- Ray PG, Rajasekaran R, Roy T et al. Engineered surfaces: A plausible alternative in overcoming critical barriers for reconstructing modern therapeutics or biomimetic scaffolds. In Sharma CP (ed) *Regenerated Organs*. Academic Press, 2021
- Sinha M. Advance measures and challenges of wound healing. *J Pharmacol Ther Res* 2018;2(1):1–3.
- Tayyib NA, Ramaiah P (2021) Nurses' challenges in wound care management—a qualitative study. *Journal of Clinical & Diagnostic Research* 1;15(3).
- Troxler M, Vowden K, Vowden P. Integrating adjunctive therapy into practice: the importance of recognising 'hard-to-heal' wounds. *World wide wounds*. 2006 Dec;32(1):99–105.
- Welsh L (2018) Wound care evidence, knowledge and education amongst nurses: a semi-systematic literature review. *Int Wound J* 15(1):53–61. <https://doi.org/10.1111/iwj.12822>
- White R (2011) Hard-to-heal wounds: results of an international survey. *Wounds UK* 7(4):22–31. <https://tinyurl.com/mr3nxvr7> (accessed 4 October 2022)