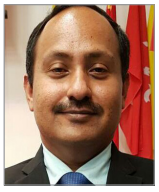
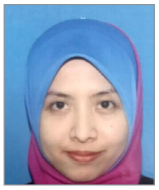
Novel wound debridement using organic acid to desiccate biofilm: a prospective case series in Kuala Lumpur





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Key words:

- *Biofilm*
- *Chronic wounds*
- *Topical dehydrating agent A*
- *Wound healing*

Background: Chronic wounds impact heavily on the patient's quality of life, as well as on the national economy. Biofilm found in chronic wounds can inhibit healing, this makes debridement necessary to disrupt and remove the biolfim to restart the healing process. A topical dehydrating agent A (TDA A) has been developed as a new form of wound debridement. **Methodology:** After basic wound cleansing, TDA A was applied to the wound bed using gloved finger and left on for 60 seconds. The wound bed was rinsed thoroughly and remaining detachable material were rubbed off. The wound bed was dried and dressed according to the standard of care. **Results:** We recruited six patients of different aetiologies, including diabetic foot ulcers (n=4), a carbuncle (n=1) and wound dehiscence (n=1). There were three female and three male patients with a median age of 69 years. The area of the lesions ranged from 30 to 72cm^2 with a median age of 10.5 weeks. The time taken to reach the end-point of the study which was granulation ranged from 2 to 5 weeks. The adverse effect observed with this study is pain, experienced by patient on a range of 2 to 5, according to visual analog scale (VAS) during treatment. The pain resolved within 60 minutes at most and no lasting pain after the treatment was recorded. **Conclusion:** TDA A successfully debrided chronic wounds of different aetiologies and has the potential to serve as an alternative to current available debridement methods.

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Chronic or hard-to-heal wounds are those that fail to progress though the normal phases of healing in an orderly and timely fashion. These can into diabetic foot ulcers (DFU), pressure ulcers (PU), venous leg ulcers (VLU) and arterial ulcers among others (Frykberg et al, 2015). The healing of chronic wounds can be affected by various factors, systematically affected by the age, comorbidities, medications and also including the condition of the wound itself such as size, location, oxygenation level and the presence of infection (Giri, 2018; Kee et al, 2019). Chronic wounds impact heavily on the patient in terms of quality of life due to limb amputations, and even death.

The burden increases with the raising numbers of lifestyle diseases, with diabetes taking the lead. Statistics from the National Health and Morbidity Survey 2019 (2020) in Malaysia show that the prevalence of elevated blood sugar increased significantly from 11.2% in 2011 to 18.3% in 2019, and only half of these patients were diagnosed with diabetes (Institute for Public Health, 2019). Consequently, we are expecting a growth in the prevalence of DFU as a complication of the uncontrolled blood sugar, posing a significant challenge to the healthcare system and economy throughout the nation. A systematic review reveals that the management of a DFU per patient in Malaysia is costing around MYR 6,000 in public setting and about 23% higher in private setting, averaging to MYR 8500 per patient annually (Nair et al, 2017).

About 60–100% of samples from chronic

wound contain biofilm, which under a microscope look like a slimy and translucent layer (World Union of Wound Healing Societies, 2016). Biofilm is an extracellular matrix of polysaccharides secreted by bacteria and encapsulate them making them resistant to antimicrobials and antibiotics (World Union of Wound Healing Societies, 2016; Snyder et al 2017). Although more investigations on biofilm are ongoing, it is widely accepted that their presence is impeding the wound healing progress (Malone et al, 2017; Schultz et al, 2017; Snyder et al 2017) Chronic wounds often have a polymicrobial presences where *Staphylococcus aureus* and *Pseudomonas aeruginosa* maybe predominant. Studies also show that chronic wounds that have a wider bacteria diversity tend to have higher resistance towards antibiotics. (Raja, 2007; Wong et al, 2015). Biofilm is hard to rapidly diagnose, and the healthcare professionals usually decide to debride on the presence of slough, which is a secondary effect of biofilm (Snyder et al, 2017). The current practice for chronic wound management adheres to the TIME framework, which consists of tissue (non-viable), infection and inflammation, moisture balance and edge of wound. According to an overview by European Wound Management Association (EWMA), debridement is defined as the removal of non-viable and/or necrotic tissue, biofilm, slough, scabs and other bioburden in different types of chronically infected, non-healing wounds.

Debridement is a form of wound bed preparation and when done properly, it facilitates the subsequent treatment approaches and improves the overall clinical outcomes of wound management. This then leads to improved quality of life of the patient, reduction in malodour, improved microcirculation, lowered matrix metalloproteinase (MMP) level and stimulated wound edges (Strohal et al, 2013). Typical debridement methods commonly used include mechanical debridement, which includes surgical debridement, sharp debridement, wet-to-dry technique, cleansing sponges, monofilament fibre pad and newer technologies, such as ultrasound debridement and hydrosurgery. Examples of debridement via biotherapy include maggots or sterilised fly larvae that selectively eat away the necrotic tissue only. Enzymatic debridement involves the use of proteinases or collagenases and autolytic debridement makes use of moist wound management strategy, which uses hydrogel, hydrocolloid or transparent film dressings (Strohal et al, 2013; Nowak et al, 2022)

Disadvantages of the current debridement methods are, among others: risk of bleeding, high costs, resources of skilled healthcare professionals, multiple use and risk of infection. To battle these disadvantages, a novel desiccating debridement gel (referred to as topical dehydrating agent [TDA] A) is introduced as a way of debriding wounds. TDA is a gel composition with, among other ingredients, methane sulfonic acid and dimethyl sulfoxide. In an *in vitro* study, TDA A was applied for 30 seconds, and its potent hygroscopic effect eliminated all *Staphylococcus aureus* and *Pseudomonas aeruginosa* on the *in vitro* biofilms (Schwarzer et al, 2021). It is hypothesised that the TDA A is able to penetrate and desiccate the biofilm, thereby achieving its debridement effect within a single application, reducing the need for surgical debridement or even amputation.

Methodology

Patients with non-healing wounds in their lower extremities were selected via random sampling in Wound Care Unit, Hospital Kuala Lumpur and were observed for a period of 2–4 weeks. Ambulatory patients in the outpatient clinic during opening hours Monday to Friday (8am-4pm) were considered. When they match the inclusion criteria they were asked to be enrolled in this study.

Inclusion criteria:

- DFU, wound dehiscence, carbuncle
- Wound surface area of 30cm^2 and above
- Able to comply to twice-weekly visit hospital.

Exclusion criteria:

- Neoplastic ulcers
- Underlying abscesses or fasciitis, which require incision and drainage
- Underlying osteomyelitis

Protocol:

- All previous dressings were removed from the wound
- Any remaining medications were rinsed using sterile water
- The necrotic material or slough were removed by rubbing, with sufficient friction, using a gauze
- The wound was dried
- Patients with a lower pain tolerance a local anesthetic was applied for 10–15 minutes and wiped off before debridement
- Anesthetic used was an Emla cream

Table 1: Demographics of patients and lesion condition

Patient	Gender	Patient age (year)	Type of wound	Wound age (week)	Prior treatments	Wound size at baseline (cm^2)	Wound size at end-point (cm^2)	Wound condition at baseline (%)	Lesion condition at end-point (%)	Time to end-point (weeks)
1	Male	73	Diabetic foot ulcer	16	Hydrogel	30	30	Sloughy: 50% Granulation: 40% Epithelialising: 10%	Granulation: 70% Epitheliaising: 30% Tendon exposed	5
2	Female	72	Wound dehiscence	11	Manuka honey dressing, silver alginate hydrogel	72	64	Sloughy: 60% Granulation: 30% Epitheliaising: 10%	Sloughy:30% Granulation: 60% Epitheliaising:10%	3
3	Female	64	Carbuncle	24	Gelling fibre dressing	63	60	Hypergranulation: 90% Epithealising: 10% Fibrin present	Hypergranulation: 70% Epitheliaising: 30%	4
4	Female	67	Diabetic foot ulcer	5	Manuka honey dressing, hydrogel	47.5	36	Sloughy: 60% Granulation:40%	Sloughy: 40% Granulation: 60%	3
5	Male	63	Diabetic foot ulcer	10	Silver hydrofiber dressing, silver alginate hydrogel	30	30	Sloughy: 70% Granulation: 30%	Sloughy: 40% Granulation: 50% Epitheliaising: 10%	2
6	Male	71	Diabetic foot ulcer	2	NA*	63	58.5	Sloughy: 90% Granulation: 10%	Granulation: 90% Epitheliasing: 10%	2

*NA: not applicable due to patient is applied debridement hydrogel A on day 1 admitted.

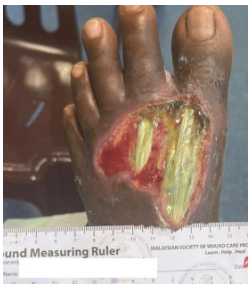
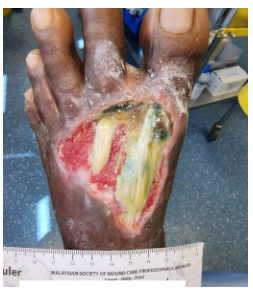
(lidocaine 2.5% and prilocaine 2.5%)

- TDA A was applied directly onto the wound bed and spread evenly using a gloved finger, including approximately 1cm margin of surrounding healthy skin
- TDA A was left on the wound bed for 60 seconds, including the time of application
- TDA A was then rinsed off with sterile water thoroughly
- The lesion was rubbed dry with sterile gauze to remove any detachable material
- The lesion was dressed with primary and secondary dressing, according to standard of care.

The length, width and general condition of the lesion, and side effects were monitored biweekly at the dressing change visit, until granulation.

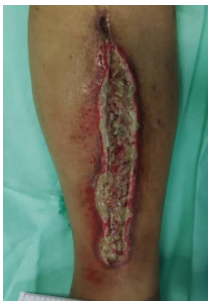
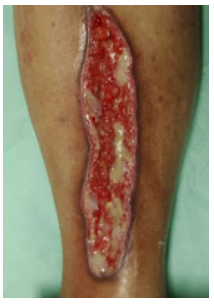
Case 1. Diabetic foot ulcer

- A 73-year-old male with diabetic foot ulcer for 16 weeks. Underlying diabetic mellitus, ischaemic heart disease, hypertension, benign prostatic hyperplasia and chronic limb ischaemia
- Medication: anti-coagulants (dabigatran etexilate and clopidogrel), no bleeding is observed upon application of topical dehydrating agent A.

Before treatment 5 x 6cm Exudate: Moderate (serous)	**After 5 weeks of treatment** 5 x 6cm Exudate: Moderate (serous)
	

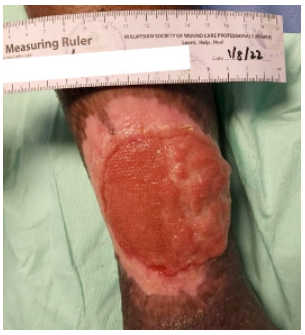
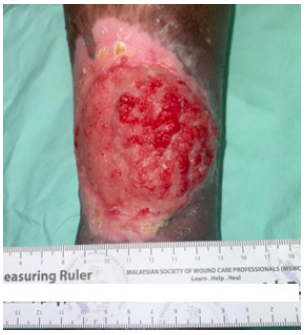
Case 2. Surgical wound dehiscence

- A 72-year-old female with underlying diabetes mellitus for over 10 years
- Wound dehiscence post coronary artery bypass graft surgery in May 2022
- The lesion was presented for 11 weeks before the application of topical dehydrating agent A.

Before Treatment 18 x 4cm Exudate: Moderate (serous)	After 3 weeks of treatment 16 x 4cm Exudate: Moderate (serous)
	

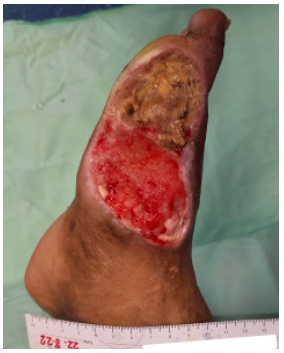
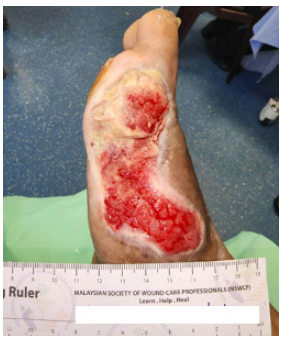
Case 3. Carbuncle on her left leg

- A 64-year-old female with underlying diabetes mellitus, hypertension, chronic kidney disease and dyslipidemia
- She was diagnosed with carbuncle on her left leg and surgical excision was done in February 2022
- After the treatment with topical dehydrating agent A, hypergranulation was observed for a duration of 24 weeks.

Before treatment 9 x 7cm Exudate: Moderate (serous)	After 4 weeks of treatment 7.5 x 8cm Exudate: Moderate (serous)
	

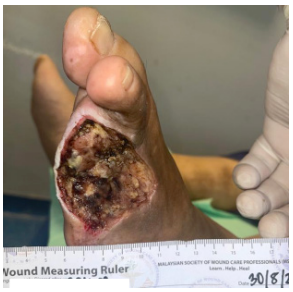
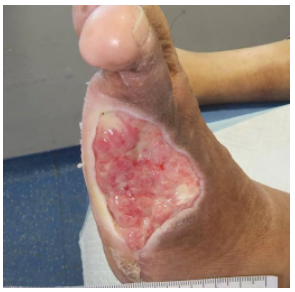
Case 4. Diabetic foot ulcer on the right foot

- A 67-year-old female with underlying diabetes mellitus, hypertension, dyslipidemia and ischaemic heart disease
- Diabetic foot ulcer on the right foot., which underwents sharp debrided and a ray amputation in July 2022
- No bleeding observed during treatment with topical dehydrating agent A, even though the patient was on aspirin.

Before treatment 9.5 x 5cm Exudate: Moderate (serous)	After 3 weeks of treatment 8 x 4.5cm Exudate: Moderate (serous)
	

Case 5. Diabetic foot ulcer on left leg

- A 63-year-old male presented with a diabetic foot ulcer on left leg
- A diabetic foot ulcer on left leg and undergone a ray amputation in June 2022. The wound was present for 10 weeks before the treatment with topical dehydrating agent A

Before treatment 6 x 5cm Exudate: Moderate(serous)	After 2 weeks of treatment 6 x 5cm Exudate: Moderate(serou
	

Case 6. Diabetic foot ulcer on the left leg

- A 71-year-old male with underlying diabetes mellitus was diagnosed with a diabetic foot ulcer on the left leg
- He was admitted for a left foot necrotizing fasciitise, and underwent, sharp wound debridement and a ray amputation in August 2022
- He referred for subsequent wound care and thus received treatment with topical dehydrating agent A.

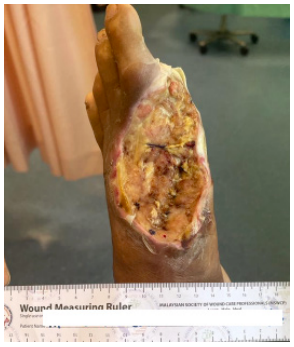
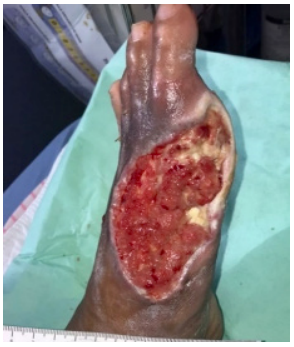
Before treatment 9 x 7cm Exudate: High (serous)	After 2 weeks of treatment 9 x 6.5cm Exudate: High (serous)
	

Table 2. Pain level of patients measure by the visual analogue score (VAS)

Patient	Before treatment	During treatment	Local anesthetic used	Pain duration (minutes)	After treatment
1	2	4	Emla Cream	15	0
2	2	5	Emla Cream	60	0
3	0	0	Nil	NA	0
4	3	0	Nil	NA	0
5	0	0	Nil	NA	0
6	0	2	Nil	30	0

*Emla cream is a local anesthetic agent consisting of lidocaine 2.5% and prilocaine 2.5%.

Results

We recruited six patients to this observational study, there were DFUs (n=4), a wound dehiscence (n=1) and carbuncle (n=1). *Table 1* shows the demographics of the patients and their lesion conditions. There were three males and three females with an age range of 63–73 years (median age: 69 years). All the

patients had underlying diabetes mellitus. The wounds were present for between 2 to 24 weeks before treatment, with a median of 10.5 weeks. The lesion size ranged from 30 to 72cm^2 and the median area is 55.25cm^2. The condition of the wounds of all patients were sloughy at the initial visit. The end-point of the study, to reach granulation, was determined by the healthcare professional. The time taken to reach the end-point ranged from 2 to 5 weeks with a mean of 3.17 weeks.

Adverse events and side effects

Table 2 recorded the pain level of patients before, during and after the debridement with TDA A using a visual analog scale (VAS) score. There were 3/6 patients who reported transient pain with VAS scores ranging from 2 to 5 (median score: 4). The pain lasted for 15 to 60 minutes starting from the first contact with TDA A. No pain was reported on the periwound skin and there was no excessive bleeding in all cases. There were no nodules, boils, burns or rashes reported in all the cases. All cases reported no lasting pain after the treatment, three patients reported an improvement in the pain and the other three had concomitant sensory neuropathy.

Discussion

Wound bed preparation in chronic wounds involves multiple approaches of which debridement is the first step aiming to get rid of bioburden. Bioburden including, biofilm, necrotic tissue and eschar etc, will slow down wound healing (Schultz et al, 2017). TDA A presents a novel chemical debridement method, in this study, all the wounds were successfully debrided. This study was prompted by Cogo et al, where TDA A had successfully treated 10 chronic wounds of different aetiologies, including DFUs, VLUs, revascularised ischaemic ulcers, vasculitis and posttraumatic ulcers (Cogo et al, 2021). This study further strengthens the claim of TDA A as an alternative method of wound debridement, and as a new way to debride the wounds when other methods are contraindicated.

TDA A works by desiccating the biofilm, as well as the bacteria and pathogens residing inside the wound bed, with just 60 seconds of application. The water molecules are instantly drawn out once TDA A comes into contact with the biological material. It is noted that there is minimal damage to the healthy tissue surrounding and underneath the wound bed. The desiccated biofilm then coagulates and precipitates together, detaching itself from the viable tissues over time. The efficacy of TDA A on biofilm is proven by application on the *in vitro* biofilm models consisting of *Staphylococcus aureus* and *Pseudomonas aeruginosa* and the successful elimination in just 30 seconds of topical dehydrating agent A application (Schwarzer e al, 2021). Once the biofilm and bacteria are eliminated, the healing process is able to restart (Cogo et al, 2021).

The application of TDA A, limited within 60 seconds, did not result in any serious side effects, with the most prominent having transient pain lasting from 15 to 60 minutes. The most painful event reported to be 5 out of 10 on a VAS. In addition, the wound pain present before debridement was resolved following the application of TDA A. There are no reported adverse events on the surrounding viable tissues. Even though the desiccating effect of topical dehydrating agent A is not limited to any type of tissue, the viable cells differ from the biofilm. Biofilm has 98% of water content whereas healthy viable tissue is protected by membrane lipids with a lower water content (Malone et al, 2017). Hence, within the 60 seconds of application, TDA A rapidly desiccates the biofilm, denaturing the proteins and extracellular matrix.

TDA A provides an alternative to current practice and at the same time a less complicated debridement technique. The application can be done at bedside, it does not require a sterile environment, such as an operation table and it could reduce the need of specialised healthcare personnel. In the UK, TDA A potentially reduce the overall burden for the National Health System in managing hard-to-heal VLUs if combined with the standard of care (Guest et al, 2022). The decreased number of hospital days that topical dehydrating agent A has the potential to create, also means that topical dehydrating agent A, can at a certain extent, decrease the burden of healthcare prosfessionals, especially in a majority of countries where wound care is a nurse-led discipline (Guest et al, 2015).

Limitation

First and foremost, there is a limited number of inclusions in this study. In addition, the cases did not include PUs and arterial ulcers. A more robust study with a larger number of patients is warranted to validate the results.

Secondly, time limitations are observed in

this study, the endpoint of this study is set at reaching granulation as determined by the HCPs. The time taken to reach full granulation and reepithelisation end points are not taken into account as that would be affected by the subsequent interventions to assist in wound closure. The effectiveness of TDA A is proven in these cases, by being able to clean the chronic wounds thoroughly. The result of this study can act as a basis for a subsequent study design to compare the efficacy of TDA A against the current standard of care, which is surgical debridement.

Thirdly, TDA A is not tested *in vivo* on the antimicrobial activity, the included wounds were also not swabbed to identify microbial species. Previous studies reported that chronic wounds are made up of a blend of bacteria and microbes that are in cases also resistant to antibiotics (Raja, 2007; Wong et al, 2015) Moreover, Schwarzer et al also proved that TDA A can effectively eradicate the viable cells in the *in vitro* biofilms (Schwarzer et al, 2021).

Conclusion

TDA A appeared to have, within the study limitations, successfully debrided a number of chronic wounds, offering a new method of debridement as an alternative to the current standard, surgical debridement. A larger and more robust study is required to further evaluate this new way of debridement. WAS

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Declaration: The second author declares that she works under Auxilto, distributor of Debrichem® in the ASEAN region.

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