Maggot Debridement Therapy (MDT)

Effective and Accessible Bio Therapeutic Solutions

Company Profile

Cuprina Pte Ltd is a Singapore-based MedTech company. Our first products to market were bio-dressings made of live, sterile maggots.

We launched our MEDIFLY product range in 2020 and they are used across hospitals and veterinary clinics in Singapore to treat chronic wounds.

The MEDIFLY products are specifically used to effectively debride and manage infections associated with chronic wounds.

What is Maggot Debridement Therapy?

Maggot Debridement Therapy (MDT) is the use of sterile, medical-grade maggots (fly larvae) to clean and disinfect chronic wounds. MDT can be used for the removal of necrotic tissue, biofilm, or slough and on bacteria-infested wounds which may be antibiotic-resistant (i.e.: MRSA).

How Maggots Work?

- Maggots are living creatures which require oxygen and liquefied food to survive
- Maggots have no teeth…. only “sucking” parts,
- As the maggots crawl on the wound bed, the exo-spines of the maggot work like “mini scalpels” which mimics the action of surgical debridement.
- Maggots are chemical factories - secreting a powerful mixture of proteolytic enzymes which break down dead tissue, liquidizing it as they move on the surface of the wound.
- Maggots then ‘suck’ up this liquidized tissue, ingesting it and digesting it.
- Maggot Enzymes only liquefy devitalized tissue including MRSA and leave healthy tissue undisturbed.
- Maggots also ingest and digest bacteria within the devitalized tissue from the wound, this is done in their gut.
- Secrete chemicals with inherent antimicrobial activity which help combat infections.
- Reduce infections decreases inflammation and promotes wound healing.

Treatment of

ANY CHRONIC ULCER: Pressure Sores, Diabetic Foot Ulcers, Venous, Ischemic, Malignant, Burns….

Methicillin-resistant Staphylococcus aureus (MRSA)

Devitalized tissue – slough, necrosis, gangrene

Non-aggressive & quick debridement

Biofilm formation

Painful adhered Slough

Diabetic Foot Ulcers

Pressure Sores

Slough Wound

Gangrene

MEDiFLY

Superiority On the 3 Aspects

1. Proven Effectiveness (TIME)

2. Safe & Easy

3. Cost-effective

Wound Bed Preparation (WBP)

The concept of wound bed preparation (WBP) as a clinical approach to the treatment of chronic wounds has been adopted and established as an integral part of the treatment of chronic wounds.

WBP is a holistic concept, which addresses the factors that contribute to the chronicity of wounds, including underlying diseases, and identifies measures to remove barriers to healing.

These measures aim to remove dead tissue and slough, normalise inflammation, re-establish moisture balance and support the movement and migration of cells essential for wound repair.

Effectiveness of MDT (TIME Principles)

T	Tissue: non-viable or deficient	1. Debridement and concomitant loss of bacterial bioburden; 2. Removal of biofilm; 3. Removal of tissue docking sites for bacteria, and effects on bacterial adhesins.
I	Infection or Inflammation	1. Raised wound pH; 2. Antibacterial and antifungal effects; 3. Inhibition of the complement system, and inflammatory cell migration and activation
M	Moisture imbalance	1. larval feeding is facilitated by the liquefaction of tissues resulting from the action of digestive enzymes, which in turn can contribute to the moisture profile of the wound.
E	Edge of wound: non-advancing or undermining	1. Promotion of cell motility and angiogenesis

Tissue - Targeted Debridement

Maggots perform debridement by physically feeding on dead tissue, cellular debris and exudate present in sloughy wounds. Their feeding action physically breaks up necrotic or sloughy tissue, which is then consumed and digested.

This process is mediated by proteolytic enzymatic digestion through a process of extracorporeal digestion. Collagenases, trypsin-like and chymotrypsin-like enzymes are secreted which breakdown devitalised tissue into a semiliquid form which the larvae can ingest.

The larvae of Lucilia sericata do not digest living human tissue. This selective process is one of the major advantages of larval debridement therapy as it spares the healthy tissues necessary for healing (Gottrup and Jørgensen, 2011; Fforwm and Meinwe, 2013).

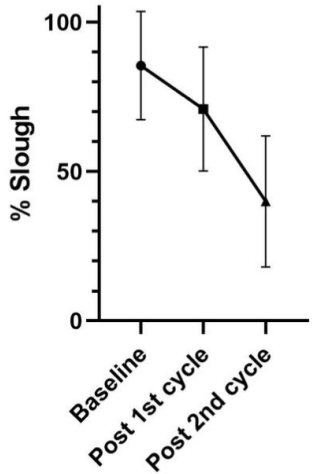

Figure 1. The mean percentage slough pre, during and post MDT (n=11). Error bars indicate standard deviation. There was 45% reduction in slough following the 2nd cycle of MDT compared with baseline ($p<0.001$).

Infection - Antimicrobial Effect

Additional mechanisms of action include an antibacterial effect within the wound as bacteria contained in liquefied material is ingested and digested, reducing the bioburden within the wound and larval secretions that prevent the formation of, and reduce pre-formed biofilms (Harris et al, 2007; Cazander et al, 2009).

One clinical trial reported that the number of infected wounds decreased between days 1 and 15 with MDT, but not conventional treatment (Mudge et al., 2014). Infections cure faster, and patients remain infection-free for a longer period with MDT (Shi & Shofler, 2014)

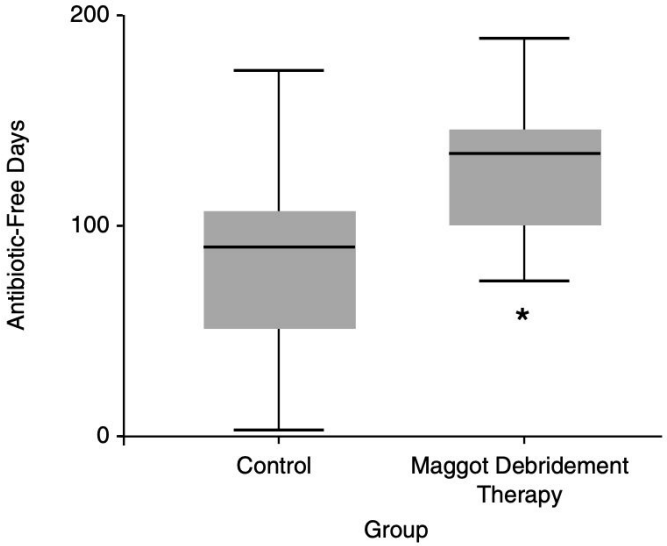

Figure 1*. Antibiotic-free days in the maggot debridement therapy and control groups. Horizontal lines represent mean; error bars, SEM; shaded boxes, first to third quartiles. *P = .0001.

*Source: * Armstrong et al.. 2005. Maggot therapy in "LowerExtremity Hospice" Wound care. Journal of the American Podiatric Medical Association 95 (3), 254 - 257*

Moisture - Rebalance of Humidity

As maggot feeding is facilitated by the liquefaction of tissues resulting from the action of digestive enzymes, this in turn can contribute to the moisture profile of the wound.

At the initiation of MDT, the production of exudate is often enhanced, which is probably a result of the degradation of necrotic and infected material.

As maggots also require a balance of moisture and humidity, they have the potential to act as visual bio-indicators of the wound environment, as they can drown or desiccate in conditions adverse to their survival.

Epithelial Edge - Healing Progression

Two studies [1,2] suggested that MDT hastens the growth of granulation tissue. Sherman reported that ulcers treated with MDT attained at least 50% of granulation tissue within three weeks, whereas Sherman found that the amount of healthy granulation tissue was statistically significant after complete debridement was achieved in four weeks.

Ulcer healing rates are seven times higher with MDT than with conventional therapy (Wilasrusmee et al., 2014)

MDT achieved significantly better granulation rates and shorter healing times than traditional dressings in pressure ulcers and diabetic foot ulcers (Shi & Shofler, 2014)

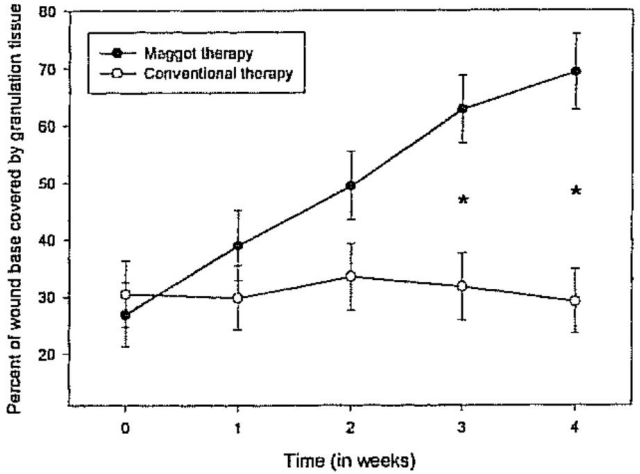

FIGURE 3. Average percentage of wound base covered by granulation tissue during MDT ($N = 43$) or conventional therapy only ($N = 49$). Error bars indicate standard error; asterisks indicate significant differences in mean percentage of granulation tissue ($p < 0.05$).

Source: [1] Sherman R.A. Maggot versus conservative debridement therapy for the treatment of pressure ulcers. Wound Repair Regen. 2002;10:208–214. doi: 10.1046/j.1524-475X.2002.10403.x.
[2] Sherman R.A. Maggot Therapy for treating diabetic foot ulcers unresponsive to conventional therapy. Diabetes Care. 2003;26:446–451. doi: 10.2337/diacare.26.2.446.

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Amputation Prevention

Maggot Debridement Therapy is associated with a 3 x lower rate of amputation.[1]

Studies show that when compared to standard therapies. Maggot Debridement Therapy was not only associated with lower amputation rates but also increased healing rates and in some cases patients avoided imminent amputation. [2, 3]

Another case report done in Singapore showed that the limb salvage rate was 90.9% (10/11), while the wound closure rate was 45.5% (5/11) in this challenging patient population. [4]

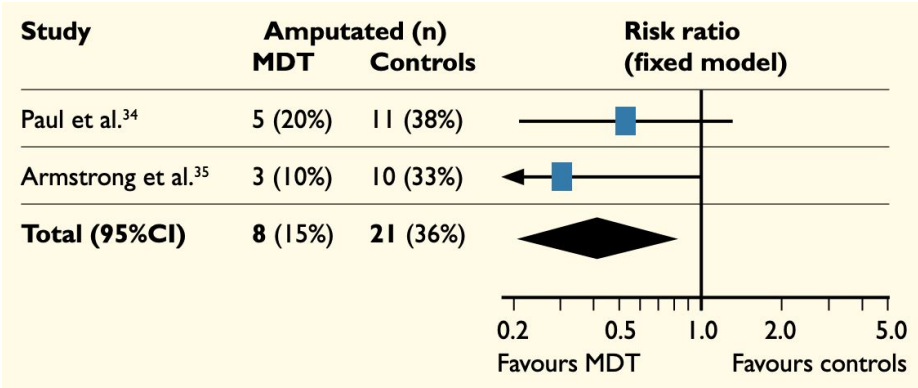

Figure 1. Comparison of amputation rates [3]

Source: [1] Armstrong et al.. 2005. Maggot therapy in "Lower Extremity Hospice" Wound care. Journal of the American Podiatric Medical Association 95 (3), 254 - 257
[2] Gilead L, Mumcuoglu KY, Ingber A. 2012. The use of maggot debridement therapy in the treatment of chronic wounds in hospitalized and ambulatory patients. J Wound Care; 21(2):78–85.
[3] Tian X et al. 2013. Maggot debridement therapy for the treatment of diabetic foot ulcers: a metaanalysis. Journal of Wound care; 22(9): 462-9.
[4] Reintroduction of maggot debridement therapy in the treatment of diabetic foot ulcers in Singapore: a single institution's initial experience

Safe & Easy

MDT is relatively safer and has lower side effects. The results [1] were promising with minimal side effects besides discomfort and mean visual analogue pain score was 3.3.

Food & Drug Administration (FDA) of the United States has confirmed the prescription and use of Maggot therapy and enacted regulations for it. Also, in other countries, MDT has been used as a kind of drug and at least 24 laboratories in more than 30 countries in the world in 2009 have worked to prepare therapeutic maggots [2].

The MDT application of the takes the same length of time as a standard wound care dressing and can be removed from the wound quickly and easily [3].

Mr William Teo (left) underwent five cycles of maggot debridement therapy at the National University Hospital. Photo: Ili Nadhirah Mansor/TODAY

Source: [1] Wounds Asia 2022 | Vol 5 Issue 2 | ©Wounds Asia 2022 | www.woundsasia.com
[2] Sherman RA. Maggot therapy takes us back to the future of wound care: new and improved maggot therapy for the 21st century. Journal of diabetes science and technology 2009;3(2):336-44.
[3] Bültemann. 2015. Anleitung zur Applikation medizinischer Fliegenlarven (Lucilia sericata) bei der Behandlung chronischer Wunden. Wund Management 2015; 9 (3), S. 100-106

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Cost-effective

The median cost of Maggot Debridement Therapy (6,700 Baht) was even less than half of the expenditure for conventional therapy (16,800 Baht). [1]

The cost saving by the use of MDT was due to its shorter curing duration, about half of the curing duration for conventional therapy. [1]

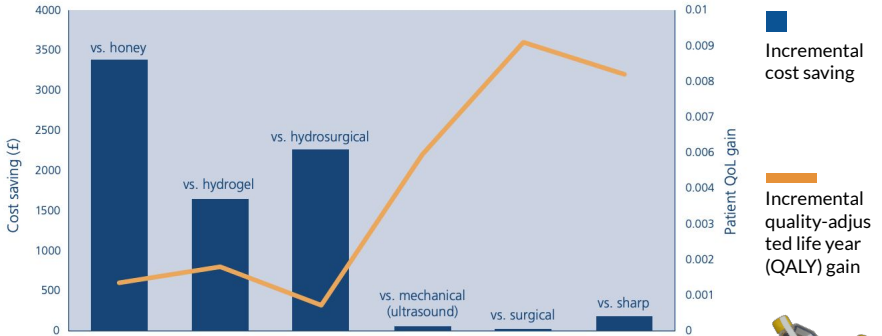
The study has demonstrated that based on the available evidence MDT is shown to be less costly and more effective than the other debridement methods tested. [2]

Costs	Maggot therapy cost (Thai Baht), (n = 80)	Conventional therapy cost (Thai Baht), (n = 70)
Main therapeutic cost		
- Median cost	3,000	8,400
- Range (Min. – Max.)	6,750 (2,250 – 9,000)	14,400 (3,000 – 17,400)
- Interquartile range	3,000 – 6,000	4,200 – 12,000
Related cost		
- Median cost	2,960	8,400
- Range (Min. – Max.)	15,330 (210 – 15,540)	17,400 (0 – 17,400)
- Interquartile range	210 – 8,140	4,100 – 11,100
Total cost		
- Median cost	6,700	16,800
- Range (Min. – Max.)	16,080 (2,460 – 18,540)	30,300 (4,500 – 34,800)
- Interquartile range	3,210 – 14,140	8,400 – 22,200

Table 1. Cost comparison between maggot therapy and conventional therapy

Curing duration	Maggot therapy (Days), (n = 80)	Conventional therapy (Days), (n = 70)
- Median curing duration	6.5	14
- Range (Min. – Max.)	18(3-21)	40(5-45)
- Interquatile range	3-11	7-20

Table 2: Comparison of curing duration in maggot therapy and conventional therapy



Source: [1] Eamkong, Suwannee & Pongpanich, Sathirakorn & Rojanaworarit, Chanapong. (2010). COMPARISON OF CURING COSTS BETWEEN MAGGOT AND CONVENTIONAL THERAPIES FOR CHRONIC WOUND CARE. Journal of Health Research.
[2] Bennett H. et al 2013. Cost-Effectiveness of Interventions for Chronic Wound Debridement; an Evaluation in Search of Data. London: Wounds UK 2013; 9(4) Suppl.

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Efficacy

- Targeted Debridement
- Promote Growth of Granulation Tissue
- Antimicrobial Effect
- Reduce Amputation Rate
- Effective for Complex and Hard-to-reach Wounds

Safety

- Minimal Side Effects
- Low Pain Levels
- Widely Used in the World
- Approved by Health Sciences Authority (HSA) Singapore

Price

- Cost-effective
- Shorten Length of Hospital Stay

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Our MDT Products

Free Range

- Applied for maximum of 72-hrs
- Allows natural mechanical benefit of maggots' movement
- Extensive coverage

Baggots

- Applied for maximum of 96-hrs
- Reduces pain
- Removes 'Yuck' factor
- Time management – quick application and removal

MDT Application

Step 1

Primary Dressing

Frame the wound with Hydrocolloid dressing

Step 2

Primary Dressing

Place live maggots onto gauze and invert onto the wound

Step 3

Primary Dressing

Encage using gas/air permeable tape e.g. Tegaderm

Step 4

Secondary Dressing

Place gauze slightly above the Bio Dressing

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Case Study (1/3)

- 68 years old female patient.
- Post surgical infection.
- Methicillin-resistant Staphylococcus aureus, MRSA.
- Recommended forefoot amputation.

Day 1: Initial presentation chronic MRSA wound

Day 3: Post 1st application of MDT. Necrotic edges are reduced and evidence of granulation present

Day 5: Post 2nd application of MDT. Granulation tissue clearly evident

Day 7: Post 3rd application of MDT. No further vials needed due to nicely granulating base

Day 14: Wound after MDT before discharging

Case Study (2/3)

- 80-year-old diabetic male complicated with nephropathy and neuropathy.
- Clinical history of peripheral arterial disease with mild chronic venous insufficiency.
- Presented with a chronic non-healing ulcer on the left malleolus.
- Sloughy, erythematous, and tender wound.
- Treated with four cycles of Baggot MDT with no adverse effects.

Pre-MDT:
NVT: 100%

1st Removal Change:
NVT: 70%

2nd Removal Change:
NVT: 55%

3rd Removal Change:
NVT: 10%

Post-MDT (Completion)

NVT: Non-Viable Tissue

Case Study (3/3)

- A 59-year-old male presented with worsening gangrene of left posterior heel despite previous revascularization and DAPT (Aspirin + Clopidogrel).
- Methicillin-resistant Staphylococcus aureus, MRSA.
- Wound care management: Alternating treatment involving 1-week MDT, 1- week NWPT and back to 1-week of MDT.

Pre-MDT

3rd Cycle of MDT
&
Start Negative Pressure Wound Therapy (NPWT)

5 Days of NPWT
&
Restart MDT

6th Cycle of MDT
&
Restart NPWT

3-Weeks of NPWT

Completion

Frequently Asked Questions (FAQs)

- **Can the maggots turn into flies in my wound?**

  No. The next stage of the natural life cycle of a maggot is to form into a pupa before becoming a fly. The maggots can only pupate in dry conditions- not a moist wound.

- **Is it painful?**

  Most of the patients on MDT mentioned that they feel no pain or just a very slight pain from the treatment.

- **Are there any side effects?**

  No. There are no side effects of MDT.

- **What do care providers for the patient need to do?**

  Leave the primary dressing alone until the removal of the maggots. Only change the secondary dressings once every 3-4 hours or whenever the secondary dressing is soaked by the exudate. This prevents the maggots from drowning.

- **How long does the maggot debridement therapy take and how long to leave it for?**

  The application of MDT takes 20-25 mins by the nurses or podiatrist. The maggots are left in the wound for 48 hours for the free range and 72 hours for the Baggots(Maggots in a bag).

Attained Regulatory Standards

National Environment Agency **(NEA)**

Attained Singapore's NEA License to collect, keep, breed and sell the Lucilia Cuprina Blowfly

International Organization for Standardization **(ISO 13485)**

Quality Management Systems and Manufacturing Processes and Controls have attained ISO 13485 standards

Health Science Authority **(HSA)**

Attained Class C Medical Device Classification under the Health Sciences Authority Singapore

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Pamela Youde Nethersole Eastern Hospital

Clinical Papers & Media


Case reports

Reintroduction of maggot debridement therapy in the treatment of diabetic foot ulcers in Singapore: a single institution's initial experience

Key words:
- Diabetic foot
- Foot ulcer
- Maggot debridement therapy
- Peripheral vascular disease
- Wound healing

Background: Diabetes mellitus is often associated with peripheral vascular disease and limb ulcers. Among diabetics, the lifetime risk of developing a foot ulcer is approximately 15%. Maggot debridement therapy (MDT) uses sterile, medical-grade maggots for non-surgical treatment of necrotic or sloughy wounds. **Aim:** This study aims to ascertain the safety and efficacy of MDT using locally produced, sterile maggots of *Lucilia cuprina* as a means of biological debridement in diabetic foot ulcers (DFU). **Methods:** We prospectively recruited patients with DFUs to undergo MDT. Baseline and interim wound characteristics, change in slough or necrotic tissue were studied. **Results:** Our results were promising with minimal side effects besides discomfort and mean visual analogue pain score was 3.3. All wounds showed reduction in slough, with an average reduction of 15% after one application and 45% after two applications (p<0.001). **Conclusion:** MDT has proven to be a safe and effective method of debridement, with the pain resulting from MDT easy to manage.

Diabetes mellitus is a condition often associated with peripheral vascular disease and limb ulcers. Diabetic foot ulcers (DFU) are one of the most prevalent complications in patients who have suboptimal control of their diabetes. It is also a common cause for amputation of lower extremities (Ohlrer and Murtaugh, 2020). There are 1 in 3 people aged 65 and above with diabetes and by the year 2050, up to 1 million Singaporeans are predicted to be affected by diabetes (National Health Survey, 2018) [AQ1: missing from the reference list]. Among patients with diabetes, 2–3% will develop a DFU each year, while the lifetime risk of developing a DFU is approximately 15%. There has been a rising trend in lower extremity amputation rates in Singapore, related to complications arising from diabetes. The amputation rates increased from 28 per 100 000 residents in 2001 to 47 per 100 000 residents in 2007 and 55 per 100 000 residents in 2014. These high rates of lower extremity amputations in Singapore, compared with other Organization for Economic Co-operation and Development (OECD) countries [AQ2: ref], not only have subsequent implications on patients' quality of life, but also have indirect costs on society, as a significant number of amputees are unable to return to work and require a long-term carer.

Maggot debridement therapy (MDT), using sterilised medical-grade maggots, was described in 1933 for chronic wounds that have moist slough, where surgical debridement is not required [AQ3a: ref]. There has also been emerging evidence for its use in wounds infected with multiple drug-resistant organisms (Naik and Harding, 2017). The technique has had a resurgence in recent times due to improved ways to deliver maggots to the wound bed (Paul, 2006). MDT in Singapore since has recently been reintroduced in the local healthcare system. It has been shown to be associated with faster growth of granulation

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Maggot debridement therapy in the tropics – Preliminary outcomes from a tertiary hospital

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Nursing

ABSTRACT

This paper aimed to describe the clinical outcomes and patients' acceptance of Maggot debridement therapy (MDT) at a tertiary hospital in Singapore. Patients with non-viable tissue (NVT) covering at least 25% of wound bed on lower limbs and/or unable to tolerate sharp debridement at the bedside were recruited between January and August 2021. Sterile medical-grade maggots of *Lucilia Cuprina* were used. Wound specialist nurses assessed the size and wound to determine the type of MDT, either Baggots or free-range larvae (FRL), and the number of maggots required prior to commencement of therapy. Wound sites were measured and photographed at multiple time points: before the start of MDT therapy, during the wound review at 48 or 72 h after each cycle of MDT and completion of therapy. Three patients received Baggot therapy, while the remaining 11 received FRL therapy. The mean age for patients receiving Baggot and FRL were 78.3 (SD = 13.6) and 63.8 (11.4), respectively. Each patient received three cycles of MDT treatment on average. The most common type of wound was ray amputated toe wounds (n = 8), while the most common wound aetiology was arterial ulcerations (n = 12). A reduction of NVT was observed in 11 out of 14 patients, and ten of these 11 patients achieved successful debridement (at least 25% reduction in NVT). Five out of 14 patients had to undergo amputation within the same admission due to poor wound healing, and 80% of those five patients failed to achieve successful debridement. MDT was quite well-accepted by the patients, and they felt some improvement in their wounds. MDT can facilitate wound healing through successful debridement and potentially reduce the need for amputation. Further research needs to be done regarding the type of MDT that is optimal to use in tropical countries with high humidity.

1. Introduction

Wound healing is an intricate and regulated process that is crucial in maintaining the protective function of the skin [1]. The restoration of this protective barrier is sometimes impeded by comorbidities [2], resulting in the formation of a chronic wound. Features of chronic wounds include persistent infection, prolonged inflammation, formation of drug-resistant microbial biofilms, and lack of response to reparative stimuli [3].

Chronic wounds exert a significant burden on healthcare costs, resources, and the patients. The Singapore General Hospital (SGH), an academic tertiary hospital, receives approximately 20% of local patients requiring wound care. The overall cost of chronic wounds management in SGH is approximately SGD 5.45 million per annum [4]. Patients can experience significant pain, financial constraints, physical and emotional distress due to the prolonged nature of the chronic wounds [5, 6]. Chronic wounds on the lower limb that cannot be managed by existing interventions may also lead to eventual amputations, thus affecting their quality of life [7].

Debridement is one of the standard treatment approaches in both acute and chronic wound management. Wound debridement removes devitalised or necrotic tissue, reduces pathogen load, and allows topical medications to be directly applied onto the wound bed for better absorption and efficacy of wound products [8, 9]. There are several methods of wound debridement, including autolytic, larval, mechanical, sharp, surgical and hydrosurgery [3]. The method of choice depends on

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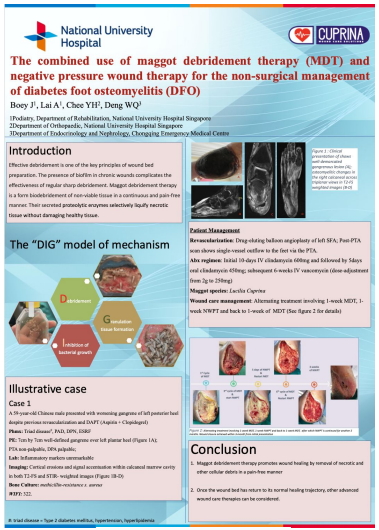
National University Hospital

CUPRINA

The combined use of maggot debridement therapy (MDT) and negative pressure wound therapy for the non-surgical management of diabetes foot osteomyelitis (DFO)

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3Department of Endocrinology and Nephrology, Chongqing Emergency Medical Centre

Introduction

The "DIG" model of mechanism

Illustrative case

Case 1

Conclusion

NUH National University Hospital

More Papers to Read:

- Sherman, R. "Indications, Contraindications, Interactions, and Side-effects of Maggot Therapy." A Complete Guide to Maggot Therapy: Clinical Practice, Therapeutic Principles, Production, Distribution, and Ethics (2022): 63-78.
- Stadler, F. "The maggot therapy supply chain: a review of the literature and practice." Medical and veterinary entomology 34.1 (2020): 1-9.
- Sherman, Ronald A. "Maggot therapy takes us back to the future of wound care: new and improved maggot therapy for the 21st century." Journal of diabetes science and technology 3.2 (2009): 336-344.

MEDIA

- CNA - Maggots eating rotting flesh: The unusual hospital treatment that's helping save limbs
- TODAY - Unlikely helpers: 'Fresh' maggots that are hungry to feed on patients' wounds as healing therapy
- 8 Worlds (8視界新聞網) - 晨光|善方保健: 慢性伤口护理疗法 蛆虫治疗免除截肢

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