

The Effectiveness of Wound Dressing with *Virana Sanjeevi Thailam* (VST) in the Management of *Madhumegha Viranam* – A Case Report

Case Report

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Abstract

Diabetic foot ulcer (DFU) is one of the most prevalent consequences for those with uncontrolled diabetes mellitus (DM). The annual incidence of DFU worldwide is between 9.1 to 26.1 million, the mortality and morbidity are the common reasons for hospitalisation of diabetes patients. The available treatment modalities are expensive and unsatisfactory in the clinical management of DFU. In Siddha system of medicine Diabetic ulcers are referred to as *Madhumegha Viranam* (MV). Various *thailam* (medicated oil) are used in the management of ulcers. *Virana Sanjeevi thailam* (VST) is one of the classical Siddha topical formulations indicated for the management of chronic ulcers. As this *thailam* is not been subjected to clinical evaluation yet, this case study is to report the effectiveness of wound dressing with VST along with adjuvant Siddha medications in 60 years old, post-menopausal, house wife who reported with complaints of ulcer in the plantar aspect of right foot for a period of 6 months, along with a past history of diabetes and systemic hypertension undergoing modern treatment for the past 10 years. The patient was diagnosed to have MV and the ulcer had features of Grade 2 in Maggit Wagner system of classification of diabetic ulcers, wound area was 12cm², with pale granulation tissues and purulent discharges. Following treatment, ulcer healed completely in a span of 86 days and Leg Ulcer Measurement Tool score improved from 41/68 to 3/68. This may encourage the use of Siddha medicines in management of DFUs.

Keywords: *Madhumegha viranam, Virana Sanjeevi Thailam, Siddha, Wound dressing, Diabetic Foot ulcer, Case Report.*

Introduction

Diabetes mellitus (DM), a chronic endocrine disorder, is characterised by persistent hyperglycaemia which resulted due to ineffective production or utilisation of insulin (1). One of the deadliest diseases in the world, it typically has a number of secondary consequences. One of the most prevalent consequences in patients with uncontrolled DM is diabetic foot ulcers (DFU). Poor foot care, peripheral vascular disease, underlying neuropathy, and poor glycaemic control are the usual causes of developing DFU. Additionally, it is a frequent contributor to lower extremity amputation and foot osteomyelitis which results in serious social and economic burden on the patients (2). An estimated 463 million persons worldwide have diabetes, with India having the second-highest number of 77 million. According to reports, a person with diabetes has a 25% lifetime risk of developing a foot ulcer, and foot ulcers account for roughly 30% of hospital admissions for diabetic individuals. The annual incidence of diabetic

foot ulcer worldwide is between 9.1 to 26.1 million. In India, the prevalence of diabetic foot patients is rising in both urban and rural areas, with foot ulcers being the cause of 85% of amputations. Furthermore, 80% of DFU are caused by neuropathic lesions and 20% by neuroischemic lesions (2,3). According to a population-based cohort research conducted in the United Kingdom, the occurrence of a DFU is linked to mortality rates of 5% in the first year and 42% in the next five years. Additionally, it was discovered that patients with DFUs had a 2.5-fold higher chance of death than diabetic patients without foot wounds (4). Oral antibiotic regimens containing dicloxacillin, cephalexin, and clindamycin are the preferred medications for the therapy of DFUs. However, continued use of such drugs may cause the microbes to develop antibiotic resistance, a serious problem at the moment. Exfoliation of the lesion, off-loading of the ulcer, control of the infected area, and revascularization treatments, if necessary, constitute the generally regarded gold standard therapy for the management of DFU. Other techniques have also been proposed as beneficial adjunct therapies, such as usage of total contact cast (TCC), negative pressure wound therapy (NPWT), hyperbaric oxygen therapy, and the use of advanced wound care products. Diabetic foot syndrome is escalating into a severe problem due to the lack of effective treatments, drug resistance, high cost, and other negative effects (5).

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Diabetes can be correlated with *Madhumega Noi* described by *Siddhar Yugimuni*, the complications of *Madhumegam* are described as *Avathaigal* (6). In the text *Agathiyar Rana Vaithiyam*, *Viranam* (Ulcers) is classified into two types *Theerum Viranam* (Healing ulcers), and *Theeratha Viranam* (Chronic non healing ulcers). *Madhumega viranam* (MV) owing to its chronicity may be correlated with *Theeratha Viranam* (Chronic non healing ulcers) (7). Furthermore, siddha system has various types of external medicines for treating ulcers such as *Thailam* (Medicated oil), *Neer* (Medicated aqueous extract), *Podi* (Medicated powders), *Pugai* (Wound Fumigation), *Seelai* (Medicated plaster) and *Kalimbu* (Ointment) (8). *Thailam* (medicated oils) is one of the feasible medications for treating wounds, though various *thailam* are available for treating chronic non healing ulcers such as *Mathan Thailam*, *Pathirasara Virana Poochi thailam*, *Thuvar ennai*, *Virana Sanjeevi thailam* etc., *Virana Sanjeevi thailam* (VST), being a potential Herbo mineral formulation in treating wounds, its clinical usage is limited and not yet subjected to scientific evaluation. Hence, this case study reports the successful management of MV with wound dressing using VST along with adjuvant siddha internal medications described as per CARE guidelines for reporting case study.

Patient Information

A 60-year married female from Chennai who is a home maker reported with complaints of ulcer in the base of Right foot, with difficulty in walking and pus discharges following trivial trauma on 28/11/2022 to *Puramaruthuvam* Out Patient Department of Ayothidoss Pandithar Hospital (APH), National Institute of Siddha (NIS). She was nonvegetarian in diet, her sleep was disturbed and her bowel habits were normal.

She was a known diabetic and hypertensive patient for the past 10 years, she was on tablet: Metformin 500mg bd – 1 tab, Glipizide 5mg – 1tab before food (morning) & Amlodipine 5 mg 1tab after food (morning). At the time of reporting her fasting blood glucose level was 162mg/dl, post prandial blood glucose level was 238mg/dl and HbA1C was 9.6%. History revealed that due to improper dietary regimen and poor drug compliance her blood sugar profile was not under control.

History revealed numbness in both the sole for past one year. She has undergone treatment in the nearby clinic with oral antibiotics and conservative wound care, despite the wound did not heal, due to the unsatisfactory result the patient visited APH, NIS for management. Positive diabetic history in first degree relatives were reported. No other surgical or past history was reported.

Clinical findings

On examination, patient was stable, conscious and oriented. The ulcer was present in the base of right foot, irregular in shape, size was 4 cms in length, 3 cms in breadth and 1 cms in depth, the floor was pale in colour with no healthy granulation tissues, edges were

punched out and with moderate purulent discharges. The X ray of the foot showed that there were no bone erosions. The ulcer had features of Grade 2 in Maggit Wagner system of classification of Diabetic ulcers.

Diagnostic assessments

Routine blood investigation and blood sugar profile are listed in Table1. X ray of right foot in antero-posterior and oblique view revealed that there was no osteomyelitis (Figure 1). The ulcer was measured by placing the gauze over the wound with measuring tape. Clinical features, Leg ulcer measurement tool (LUMT) form and measurement of wound area was used to assess the efficacy of the treatment. LUMT wound assessment tool for leg and diabetic ulcers was developed in Canada in 2004, it contains 17 items, which are sub divided into two domains namely, clinician rated domains and patient rated domains. Clinician rated domains contains 14 items such as exudate type, exudate amount, size, depth, undermining, necrotic tissue amount, granulation tissue type, granulation tissue amount, characteristics of edges, characteristics of periulcer skin, leg edema type, leg edema location, and assessment of bioburden. The patient rated domains contains 3 items such as amount of pain, frequency of pain and quality of life. LUMT has a score of range of 0-68, with zero indicating complete healing (9).

Table No:1 Routine blood Investigations and blood sugar profile (Before Intervention)

Haematology	
Hb (mg/dl)	13.5
Total WBC (cells/cu.mm)	10,900
Difference Count	
Neutrophils (%)	59
Lymphocytes (%)	38
Eosinophiles (%)	0
Monocytes (%)	3
PCV/HCT %	39.1
MCV (fl)	81.1
MCH (pg)	28.0
MCHC (g/dl)	34.5
Platelet (10 ³ /uL)	3.0
Biochemistry	
Fasting Blood Sugar(mg/dl)	162
Fasting Post prandial Sugar (mg/dl)	238
HbA1C (%)	9.6

**Therapeutic intervention
Wound dressing with VST**

VST is a classical Siddha formulation coded in the text *Theraiyar Thaila Varga Surukkam*(8) indicated for the treatment of *Sagala Viranagal* (various type of ulcers). This medicine was procured from IMPCOPS ltd (GMP certified company) and used. The composition of VST is listed in the Table No:2. Wound management was done as per the Siddha principle of wound care described in the text *Siddhar Aruvai Maruthuvam* (7). First of all, the wound was cleaned with Normal saline

followed by *Padigara Neer* which is a classical siddha formulation indicated for wound washing. The composition of *Padigara Neer* is listed in Table No:3. Following wound washing with *Padigara Neer*, the wound was covered with a gauze piece impregnated with VST, a sterile gauze pad was placed over the gauze piece and bandaged with sterile gauze roll twice a day till the wound healed.

Figure 1: Right foot X ray AP & Oblique View



Table 2: Composition of VST

Tamil Name	Scientific Name	Quantity
<i>Thalagam</i>	Purified Arsenic trisulphide	5 grams
<i>Serangkottai</i>	Purified <i>Semecarpus anacardium</i> Linn.	20 grams
<i>Nalennai</i>	<i>Sesamum indicum</i> Linn.	155 grams
	Washed rice water	q.s

Table No:3 Composition of *Padigara Neer*

Tamil Name	Scientific Name	Quantity
<i>Padigaram</i>	Potassium aluminium sulphate	35 grams
<i>Neer</i>	Distilled water	28 millilitres

Concomitant medication

The patient was treated with regular OPD medications listed in Table No: 4. Along with all the Siddha medication for the management of Diabetic ulcer, patient was also under oral antihyperglycemic and antihypertensive medications. The patient was advised to follow the dietary regimen for Diabetes.

Table 4: Concomitant medications

Days	Medication	Dosage
1-15 Days	Capsule <i>Madhumegha Chooranum</i>	2 TDS with Warm water
	<i>Seenthil Chooranum</i>	2 grams BD with Warm water
	Tablet. <i>Kukkil Parpam</i>	2 BD with warm water
15-30 Days	Capsule <i>Madhumegha Chooranum</i>	2 TDS with Warm water
	<i>Seenthil Sarkarai</i>	2 grams with warm water
	Capsule <i>Rasagandhi Mezhugu</i>	2 BD after food with Palm jaggery
30-45 Days	Capsule <i>Madhumegha Chooranum</i>	2 TDS with Warm waters
	<i>Seenthil Sarkarai</i>	2 grams with warm water
	Capsule <i>Rasagandhi Mezhugu</i>	2 BD after food with Palm jaggery
45-60 days	Capsule <i>Madhumegha Chooranum</i>	2 TDS with warm water
	Tablet. <i>Silasathu Parpam</i>	2 BD with warm water
	<i>Aavarai Kudineer Chooranum</i>	5 grams BD made into concoction
60-75 days	Capsule <i>Madhumegha Chooranum</i>	2 TDS with warm water
	Tablet. <i>Silasathu Parpam</i>	2 BD with warm water
	<i>Aavarai Kudineer Chooranum</i>	5 grams BD made into concoction
75-86 days	Capsule <i>Madhumegha Chooranum</i>	2 TDS with warm water
	Tablet. <i>Kukkil Parpam</i>	2 BD with warm water

Follow up and outcome

At initial assessment (28/11/2023) wound area was 12cm² and LUMT score was 41/68. With regular wound dressing with VST, complete wound healing was achieved in 86 days and the LUMT score improved to 3/68 after the treatment. The clinical presentation of the ulcer before and after treatment are presented in Figure No: 2 and the timeline of clinical findings are elaborated in Table No: 5 Following regular dressing, the quantity of purulent discharge reduced gradually and ceased on day 25, following which there were serous discharges which gradually decreased and ceased on Day 60. Evaluation of wounds showed that, on day 15, 10-25% of wound bed was covered with healthy granulation tissues, and the advancing border of epithelium was almost less than 25%, the wound area was 10cm² and LUMT score was 31/68. On day 30, 25-50% of wound bed were covered with healthy granulation tissues, the advancing border of epithelium was less than 50%, the wound area was 7.6 cm² and LUMT score was 24/68. On Day 45, 50-75% of wound bed were covered with healthy granulation tissues, the advancing border of epithelium was less than 50%, the wound area was 2.5 cm² and LUMT score was 13/68. On Day 60 greater than 76 % of the wound bed has healthy granulation tissues, the advancing border of epithelium was greater than 50 %, the wound area was 2 cm² and LUMT score was 6/68. The patient was

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followed up for 6 months, there were no recurrence of ulcer. No adverse reactions were noted in the treatment

and follow up period. Patient was advised to take up regular OPD medications.

Figure No: 2 Clinical presentations of ulcer on Day 1, 30, 60 and 86 of treatment

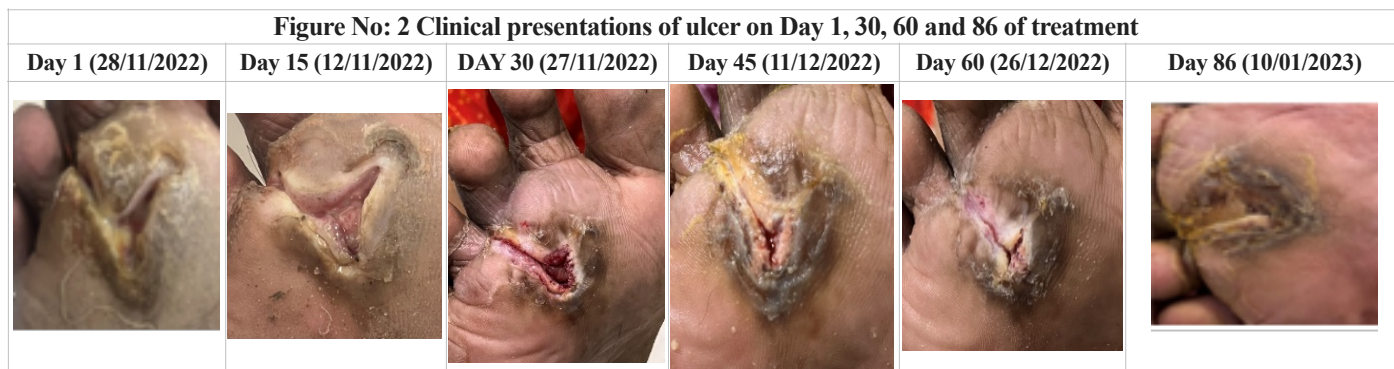


Table 4: Timeline of Clinical findings

Clinical findings	Day 1 (28/11/2022)	Day 15 (12/11/2022)	DAY 30 (27/11/2022)	Day 45 (11/12/2022)	Day 60 (26/12/2022)	Day 86 (10/01/2023)
Size	Length: 4cm Breath: 3cm Depth: 1cm	Length:4cm Breath: 2.5cm Depth: 0.8cm	Length:3.8cms Breath: 2cms Depth: 0.5cm	Length: 2.5 cm Breath: 1cm	Length: 2cm Breath: 0.8cm	Healed
Shape	Irregular	Irregular	Irregular	Elliptical	Elliptical	Healed
Granulation tissue type	Pale with slough	Pale tissues	Bright beefy red	Bright red	Bright red	Healed
Granulation Tissue amount	No healthy granulation tissues	10-25% of wound bed covered with healthy granulation tissues	25-50% of wound bed covered with healthy granulation tissues	50-75% of wound bed covered with healthy granulation tissues	76-100% of wound bed covered with healthy granulation tissues	Healed
Discharges	Moderate purulent discharges	Mild purulent discharges	moderate serous discharges	Scant serous discharges	No discharges	None
Edges	No advancing border of epithelium	Less than 25% of advancing border of epithelium	Less than 50 % advancing border of epithelium	Less than 50 % advancing border of epithelium	Greater than 50% advancing border of epithelium	Healed
Wound area in cms ²	12cm ²	10cm	7.6cm ²	2.5cm ²	2cm ²	0
LUMT Score	41/68	31/68	24/68	13/68	8/68	3/68

Discussion

Wound healing is a complex physiological process which consists of four stages namely, homeostasis, inflammatory, proliferation and remodelling. Patients with diabetes mellitus frequently develop chronic wounds due to impaired vascular, neuropathic, immune, and biochemical components. In this condition wound healing is impaired as it is characterised by the inflammatory conditions being chronic, the angiogenic process being interrupted, the loss of endothelial progenitor cells, and an imbalance in the regulation of the extracellular matrix. Furthermore, Reactive oxygen species present in wound may impair healing. The primary treatment comprises of topical dressings, an ideal dressing material should promote reepithelization, maintain moisture environment, possess antimicrobial properties, prevent further trauma and absorb exudates. As the available dressing options have limitations, none seem sufficient to ensure a successful, complete, non-recurring healing and are

often possess costly affairs (10,11,12). Traditional medicines may be used in overcoming these difficulties. Siddha system may be described as multicomponent, multitarget and multi effective. Promising results were observed in this case by treating through wound dressing with VST along with adjuvant Siddha medications. The exact mechanism of action of VST is not explored yet, but it may be due to the potent organoleptic characters, phytochemical constituents and pharmacological activity of its ingredients. The organoleptic characters of the ingredients show that Sesame oil has sweet taste, cold potency and *Semecarpus anacardium* Linn. has Bitter taste, Hot potency. As per the Siddha Materia medica, *Semecarpus anacardium* Linn. possess alternative and caustic actions, Sesame oil possess demulcent and emollient action and Arsenic trisulphide possess tonic, alternative and antitoxic actions. The medicinal properties of these ingredients described in the text *Agathiyar Gunavagadam* also supports its wound healing properties (8,13). Sesame oil is rich in biologically

active components such as linoleic acid, linolenic acids, lignans such as sesamin, sesamol, and sesaminol, natural vitamin E, and phytosterols (12,14). *Semecarpus anacardium* Linn. also possess bioactive phytoconstituents such as bhilwanols, phenolic compounds, biflavonoids, sterols and glycosides (14). Previous researches proved that *Semecarpus anacardium* Linn. and Sesame oil possess potent antioxidant, anti-inflammatory and wound healing activity (16-24). Arsenicals, both organic and inorganic, have antiviral, antiparasitic, and anticancer properties and in tumor-bearing C57BL, transdermal delivery of the realgar nanoparticles significantly decreased the tumour volumes with minimal toxicity to the mice. Furthermore, arsenic therapy was used to treat leukaemia (25-27). Dressing was done as per the traditional method using sterilized gauze piece, gauze pad and gauze roll, this helps in absorbing the exudates and protecting the wound from the external environment. The *thailam* used has sesame oil as the base, which is a plant oil, generally plant oil possess occlusive effect, and retain the moisture (11). Hence using this oil as wound dressing material, may act as occlusive moist environment with bioactive constituents along with antimicrobial, antioxidant and anti-inflammatory activity, which may be postulated to create the optimal conditions for the skin regeneration process and to prevent the failure of the healing process. Previous studies proved the effectiveness of wound dressing with topical medicines such as *Mathan Thailam*, *Padigara Parpam* and *Sagala Ranagulkum Kailmbu* in the management of MV. Though VST is a potent wound healing agent, that is easily available and cost effective, till date there are no scientific evidences documenting its efficacy, thereby this is the first study in exploring the wound healing potential of VST in the management of MV.

Conclusion

The results of this one case study have raised significant hopes for treating MV through wound dressing with VST along with concomitant medication. These results cannot be generalised but will act as evidences for carrying out further clinical trials in this field.

Patient perspectives

The patient self-reported that she was highly satisfied with the treatment. Her quality of life was improved. She was very much impressed about the treatment modalities received at APH-NIS.

Informed consent

Written informed consent was obtained from the patient. The patient has given her consent for her images and other clinical information to be reported in the scientific conferences and writings. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Source(s) of Funding: None.

Conflict of interest: None.

Acknowledgement: The authors gratefully acknowledge the staff nurses, Minor Operation Theatre, APH-NIS for their support.

References

1. <https://www.ncbi.nlm.nih.gov/books/NBK499887/> dated 17-01-2024 time 20:59 IST
2. <https://www.ncbi.nlm.nih.gov/books/NBK537328/> dated 17-01-2024 time 21:03 IST
3. Das A, Pendsey S, Abhyankar M, Malabade R. Management of diabetic foot in an indian clinical setup: An opinion survey. *Cureus*. 2020 June 15; 12(6): 1-6.
4. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. *Ann N Y Acad Sci*. 2018 Jan; 1411(1): 153-165. <https://doi.org/10.1111/nyas.13569>
5. Kumar S, Bharali A, Sarma H, Kushari S, Gam S, Hazarika I, Prasad SK, Laloo D. Traditional complementary and alternative medicine (TCAM) for diabetic foot ulcer management: A systematic review. *Journal of Ayurveda and Integrative Medicine*. 2023 July 1; 14(4): 100745. <https://doi.org/10.1016/j.jaim.2023.100745>
6. Mudhaliar DN. *Siddha Pothu Maruthuvam*. 2nd Edition. Chennai; Department of Indian Medicine and Homeopathy; 2012. 493p
7. Uthamarayan S. *Siddhar Aruvai Maruthuvam*. 6th Edition. Chennai; Department of Indian medicine and Homeopathy; 2013. 59-68p
8. Mohammed Iqbal PA. Methods of preparation of oil by *Theraiyar* (Siddhar) based on *Theraiyar Thaila Varukka Churukkam*. 1st Edition. Chennai; National Institute of Siddha; 2016. 117p
9. Jais S, Pratama K. A diabetic foot wound healing assessment tool: A scoping review. *Heliyon*. 2023 Apr 25. <https://doi.org/10.1016/j.heliyon.2023.e15736>
10. Spampinato SF, Caruso GI, De Pasquale R, Sortino MA, Merlo S. The treatment of impaired wound healing in diabetes: looking among old drugs. *Pharmaceuticals*. 2020 Apr 1; 13(4): 60-77. <https://doi.org/10.3390/ph13040060>
11. Lin TK, Zhong L, Santiago JL. Anti-inflammatory and skin barrier repair effects of topical application of some plant oils. *International journal of molecular sciences*. 2017 Dec 27; 19(1): 70. <https://doi.org/10.3390/ijms19010070>
12. Rayate AS, Nagoba BS, Mumbre SS, Mavani HB, Gavkare AM, Deshpande AS. Current scenario of traditional medicines in management of diabetic foot ulcers: A review. *World Journal of Diabetes*. 2023 Jan 1; 14(1): 1-16. <https://doi.org/10.4239%2Fwj.d.v14.i1.1>
13. Murugesu Muthaliar. *Gunapadam Mooligai Vaguppu-Siddha Materia Medica*. 6th Edition. Chennai; Department of Indian Medicine and Homeopathy; 2006. 99,365p.

14. Wei P, Zhao F, Wang Z, Wang Q, Chai X, Hou G, Meng Q. Sesame (*sesamum indicum* L.): A comprehensive review of nutritional value, phytochemical composition, health benefits, development of food, and industrial applications. *Nutrients*. 2022 Sept 30; 14(19): 4079. <https://doi.org/10.3390/nu14194079>
15. Semalty M, Semalty A, Badola A, Joshi GP, Rawat MS. *Semecarpus anacardium* Linn.: A review. *Pharmacognosy reviews*. 2010 Jan; 4(7): 88-94. <https://doi.org/10.4103%2F0973-7847.65328>
16. Barman N, Sharma A, Kumar A. Radical scavenging and antioxidant potential of nuts and leaves extracts of *Semecarpus anacardium* (L.). *American Journal of Plant Sciences*. 2013 July 30; 4(8): 1679-1683.
17. Ramprasath VR, Shanthi P, Sachdanandam P. Anti-inflammatory Effect of *Semecarpus anacardium* L Inn. Nut Extract in Acute and Chronic Inflammatory Conditions. *Biological and Pharmaceutical Bulletin*. 2004; 27(12): 2028-31. <https://doi.org/10.1248/bpb.27.2028>
18. Lingaraju GM, Krishna V, Joy Hoskeri H, Pradeepa K, Venkatesh, Babu PS. Wound healing promoting activity of stem bark extract of *Semecarpus anacardium* using rats. *Natural product research*. 2012 Dec 1; 26(24): 2344-7. <https://doi.org/10.1080/14786419.2012.656108>
19. Bagewadi ZK, Siddanagouda RS, Baligar PG. Phytochemical screening and evaluation of antimicrobial activity of *Semecarpus anacardium* nuts. *International journal of pharmacology and pharmaceutical technology*. 2012; 1(2): 68-74.
20. Sharma K, Shukla SD, Mehta P, Bhatnagar M. Fungistatic activity of *Semecarpus anacardium* Linn. f nut extract. *Indian Journal of Experimental biology*. 2002 March; 40(3): 314-318. <http://nopr.niscpr.res.in/handle/123456789/17572>
21. Sharif MR, Alizarger J, Sharif A. Evaluation of the wound healing activity of sesame oil extract in rats. *World journal of medical science*. 2013; 9(2): 74-8
22. Saleem TM. Anti-microbial activity of sesame oil. *Int J Phytochem Pharmacol*. 2011 Jan;1(1): 21-3.
23. Shahidi F, Liyana-Pathirana CM, Wall DS. Antioxidant activity of white and black sesame seeds and their hull fractions. *Food Chemistry*. 2006 Jan 1; 99(3): 478-83. <https://doi.org/10.1016/j.foodchem.2005.08.009>
24. Hsu E, Parthasarathy S. Anti-inflammatory and antioxidant effects of sesame oil on atherosclerosis: a descriptive literature review. *Cureus*. 2017 July 6; 9(7): e1438.
25. Paul NP, Galván AE, Yoshinaga-Sakurai K, Rosen BP, Yoshinaga M. Arsenic in medicine: Past, present and future. *Biometals*. 2023 Apr; 36(2): 283-301.
26. Waxman S, Anderson KC. History of the development of arsenic derivatives in cancer therapy. *The oncologist*. 2001 Apr 1;6(S2): 3-10. https://doi.org/10.1634/theoncologist.6-suppl_2-3
27. Zhao QH, Zhang Y, Liu Y, Wang HL, Shen YY, Yang WJ, Wen LP. Anticancer effect of realgar nanoparticles on mouse melanoma skin cancer in vivo via transdermal drug delivery. *Medical Oncology*. 2010 June 27;27: 203-12.
