RESEARCH PAPER

The Moringa Oleifera Extract Topical Preparations And Pycnogenol Gel As Adjuvant Synergic Treatment For Skin Recovery Structure Of Diagnosed (Baghdad Boil) Cutaneous Leishmanial (CL) Face Ulcer .

Huda. S. Hosni[1], Muhi. N. Salman[2]

[1]M.SC, Pharmacognosy, Department of Pharmaceutical Chemistry & Pharmacognosy, Baghdad college of medical sciences, Baghdad, IRAQ.
[2]M.SC, TOXICOLOGY, Department of Pharmacology & Toxicology, Baghdad college of medical sciences, Baghdad, IRAQ.

***Corresponding Author:** Muhi. N. Salman
Email ID: muhee.nimma.salman@bcms.edu.iq

Abstract:
Opinion statement: The objectives of this study were #to evaluate the topical skin as adjuvant treatment of cutaneous leishmanial (CL) face ulcer by 3 topical dosages form (lotion, cream, gel) applications of Moringa oleifera and pycnogenol gel and to improve the skin healing process with reduction in intensity of hyperpigmented scar formation caused by promastigotes of Leishmaniasis. Method: 24 patients diagnosed with (Baghdad boil) cutaneous leishmanial (CL) ulcerative face lesions were distributed among three groups (8 cases per group). (Gel's group) ; treated with M. oleifera extract in gel and 5% Pycnogenol skin gel, (Lotion's group); treated with M. oleifera extract in lotion and 5% Pycnogenol skin gel,(Cream's group); treated with M. oleifera extract in cream and 5% Pycnogenol skin gel. Application design: The 3 dosages form of skin Moringa. Oleifera extract topical preparations were applied to the margin of the ulcer, while 5% Pycnogenol skin gel was applied into the centre of crater cutaneous leishmanial (CL) face ulcer alternatively every 12 hours for 1,2,4,5,6,7,8 weeks. All patients were currently treated with the standard drug of choice dose of stibogluconate. Clinical healing signs of skin structure of cutaneous leishmanial ulcers were evaluated through (i) a clinical crater ulcer score, (ii) degree of inflammatory signs, (iii) physiological parameters such as roughness, and oedema of infected skin area,(Iv) incidence of secondary bacterial infection(v) types of discharges from ulcer. Results; were reported depending on the Capillaroscopic Skin Ulcer Risk Index (CSURI) calculation, The ulcers areas of gel's group treated were smallest starting from week 4, becoming grade 1 instead grade 2 , while ulcers of lotion's group showed no change in width in week4 (grade 2)and ulcers aera of cream's group treated reported a reduction in weeks starting from week4(grade 2).. After week 8-follow-up persisting grade 1to2 ulcers were observed in the Lotion group. Conclusion: The good sensitivity, specificity and positive predictive value of CSURI were confirmed in all patients and presented in this study, indicating that extracts of M. oleifera may be developed in topical skin applications in combination with pycnogenol gel as an adjuvant therapy for the treatment of leishmaniasis. No adverse or serious skin reactions were observed.

Key words: Leishmaniasis, Moringa oleifera, Promastigotes, pycnogenol.
Abbreviations: cutaneous leishmanial (CL), Capillaroscopic Skin Ulcer Risk Index (CSURI)

How to cite this article: Hosni HS, Salman MN. The Moringa Oleifera Extract Topical Preparations And Pycnogenol Gel As Adjuvant Synergic Treatment For Skin Recovery Structure Of Diagnosed (Baghdad Boil) Cutaneous Leishmanial (CL) Face Ulcer. Int J Drug Deliv Technol. 2026;16(50s): 1330-1337. DOI: 10.25258/ijddt.16.50s.139

1. Introduction:

Pycnogenol is a compound of natural chemicals. It comes from the bark of a European pine tree. Pycnogenol is thought to be an antioxidant that helps protect cells from damage. Pycnogenol is the registered trademark name for a French formula with published dermatological clinical investigation (1-3), Pycnogenol was shown to provide numerous health benefits to the skin. These benefits include decreased pigmentation, reduced dark spots, melasma, limited photo-ageing and achievement of an even skin tone (3-9), as well as increased skin hydration (7, 10) and greater skin elasticity (10-12). Pycnogenol® was also shown to have anti-inflammatory effects (11, 13, 14), to be effective against acne (15), and to improve skin microcirculation and better blood perfusion (16-19).A "face ulcer" is cutaneous leishmaniasis, also known as the "Baghdad boil", a disease endemic to Iraq and transmitted by sandflies that can leave disfiguring scars on the skin and, in rare cases, the face. Cutaneous Leishmaniasis (Baghdad Boil), caused by a parasitic protozoan called Leishmania, transmitted to humans through the bites of infected sandflies.The classic symptom is a sharply demarcated, ulcerated lesion that develops from the sandfly bite and can leave lasting scars. In cutaneous leishmaniasis, the sandfly bite develops into a sharply demarcated, ulcerated lesion about 2 cm in diameter. Depending on the immune

*Author for Correspondence: muhee.nimma.salman@bcms.edu.iq

status of the host and the specific type of leishmaniasis, the disease may progress to mucocutaneous leishmaniasis. Most of the cases of leishmaniasis in Iraq are caused by *Leishmania major;* in immunocompetent patients, the lesions heal spontaneously and leave an indented scar. For the past 50 years, the only effective drug for cutaneous leishmaniasis has been the pentavalent antimonial compound sodium stibogluconate.Leishmaniasis is one of the most neglected tropical protozoal diseases. It has three main manifestations: cutaneous (CL), muco-cutaneous (MCL), and visceral (VL) leishmaniasis, with different spectra of symptoms ranging from skin and muco-cutaneous ulceration to systemic infection. Almost all parts of the tree are used for a variety of beneficial medicinal properties such as anti-inflammatory, antiulcerogenic, rubefacient, antirheumatic, and antihypertensive. All such uses of M. oleifera have been reviewed (20,21). However, so far, this highly useful tree has not been evaluated for its antileishmanial potential. Almost all parts of the tree are used for a variety of beneficial medicinal properties, such as anti-inflammatory. Debnath and Guha (22) reported that an M. oleifera aqueous leaf extract reduced the mean ulcer index in addition to increasing 5- HT concentration and enterochromaffin cell concentration. The ethyl acetate fraction of M. oleifera leaves obtained from a hydroethanolic extract of the plant increased normal human dermal fibroblast migration and cell proliferation (23). It was reported that a leaf extract of M. oleifera proliferated tissue cells, hence reducing the wound size of diabetic foot ulcers(24). An aqueous fraction of M. oleifera leaves reduced scar areas and increased the closure rates of wounds in addition to increasing the granuloma and skin breaking strength, granuloma dry weight, and hydroxyproline content of albino rats (25). M. oleifera protease activity from leaf and root aqueous extracts exhibited proteolytic, fibrinolytic, and fibrinogenolytic activity on blood clotting (26).

2. Materials and Methods:

2.1 Materials: The topical dosage skin applications ;
(Gel's group) ; treated with M.oleifera extract in gel and 5% Pycnogenol skin gel.,
(Lotion's group));treated with M.oleifera extract in lotion and 5% Pycnogenol skin gel,.
(Cream's group); treated with M.oleifera extract in cream and 5% Pycnogenol skin gel .
Pycnogenol 5% gel was ready formulated provided by the Horphag Research Ltd. (Route de Belis, France).

Table 1. Formula of Cream Containing Moringa oleifera Seed Oil.

Composition	%w/w
Stearyl alcohol	4.00
Cetyl alcohol	5.00
Stearic acid	3,00
M. oleifera seed oil	25.00
Sorbitan ester 80	0.60
Propylene glycol	5.00
Polysorbate 80	4.40
Concentrated parabens	1.02
Triethanolamine 0.	0.01
Purified water	51.88

Chemical Constituents Cosmetics 2021, 8, 2. https://doi.org/ 10.3390/cosmetics8010002 (27)

Sirivan Athikomkulchai , Prakairat Tunit , Sarin Tadtong , Pensak Jantrawut , Sarana Rose S; Moringa oleifera Seed Oil Formulation Physical Stability and

Table 2. The formulation of M.oleifera leaf extract in gel.

Composition	Weight (g)
Carbopol	1
Ethanolamine	0.05
Glycerine	2
propylene glycol	1
Methyl paraben	0.03
Extract of Moringa	5%
Aquadest	100

and Gel as Sunscreen. DOI: 10.5220/0008241001540158 In Proceedings of the 1st

Sugihartini, N., Fajri, M. and Rahmawati, D. Formulation of Moringa oleifera Leaf Extract in Lotion

pages 154-158 ISBN: 978-989-758-349-0. (28)

Muhammadiyah International Conference on Health and Pharmaceutical Development (MICH-PhD 2018),

Table 3. The formulation of M.oleifera leaf extract in lotion.

Composition	Weight (g)
Stearic acid	4
Cetyl alcohol	4
Triethanolamine	2
Glycerine	2
Methyl paraben	0.2
Propyl paraben	0.03
Extract of moringa	5%
Aquadest	Add 100

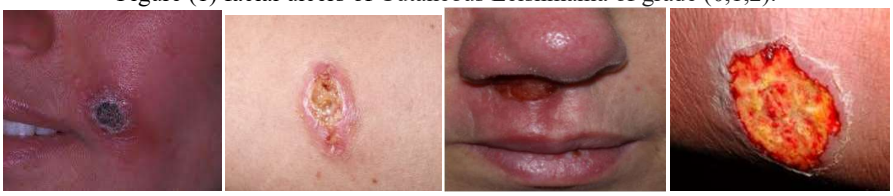
enlarges to a nodule, very slowly, the central part necrotizes and when the crust falls off, it leaves an ulcer with an indurate edge . This well-defined, firmly infiltrated border is very typical for CL and is helpful in the differential diagnosis. The whole process takes several weeks (1–6 weeks) to reach its final size, usually in the range of 0.5–10 cm in diameter. The bacterial superinfection of ulcers leads to suppuration or erythematous painful borders (Figure 1).

Vongsak, B., Sithisarn, P., Mangmool, S., Thongpraditchote, S., Wongkrajang, Y., Gritsanapan, W. 2013.Maximizing total phenolics, total flavonoids contents and antioxidant activity of Moringa oleifera leaf extract by the appropriate extraction method. Industrial Crops and Products, 44: 566-571.(29).

2.2 Methods:

2.2.1 The recorded medical history: the treated Skin ulcer of Cutaneous Leishmania usually starts at the place of the insect bite as a papule that gradually

Figure (1) facial ulcers of Cutaneous Leishmania of grade (0,1,2).



to predict ulcer development , was based on parameters observed during nailfold videocapillaroscopy (NVC): N: The total number of capillaries in the distal row.

- D: The maximum diameter of megacapillaries (abnormally enlarged capillaries).
- M: The number of megacapillaries.

The formula for the CSURI is: $D \times M / N^2$.

End point treatment: Ulcer area contracture (reduction) including collagen deposition and lower the intensity of scar formation.

3-Results ; The receiver operating characteristic curve analysis for CSURI showed an area under curve of 0.705 for the image width of 1.33 mm(gel group), 0.786 for the image of 1.70 mm (cream group), and 0.888 for the image width of 1.57 mm (lotion group) .The healing process of ulcers were observed in weeks1, 2,4, 5,6, 7 and 8 post- dual application of the M.olifera skin (gel,lotion,cream and pycnogenol gel each group of patients individually to observe infiltrating inflammatory cells, ulcer contracture including collagen deposition and intensity of scar formation. The ulcers areas of gel group treated were

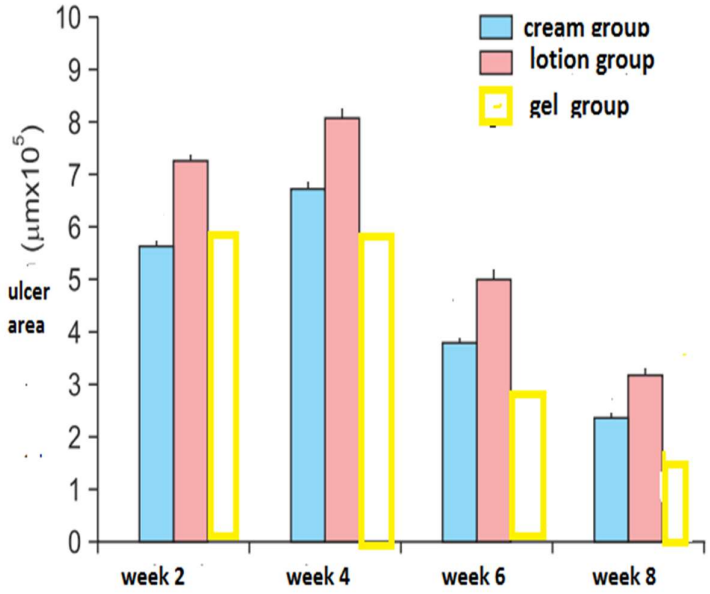
2.2.2 Topical design and treatment ;24 patients of diagnosed of (Baghdad boil) cetaceous leishmanial (CL) face ulcers , were distributed among three groups (8 patients per each group) .According to the Wagner system classify by their severity, in a Grade 0 ulcer means that the skin is intact, Grade 1 signifies a superficial ulcer on the outer layers of skin and Grade 2 is a deep ulcer(30) .Lotion's group ; treated with M.oleifera extract in lotio and 5% Pycnogenol skin gel ,Gel's group;treated with M.oleifera extract in gel and 5% Pycnogenol skin gel,Cream's group; treated with M.oleifera extract in cream and 5% Pycnogenol skin gel .

Application design: The 3 dosages form of skin Moringa .Oleifera extract topical preparations (gel, lotion,cream) were applied to the margin while 5% Pycnogenol skin gel was applied into center of crater cutaneous leishmanial (CL) face ulcer , alternatively every 12 hours for1,2,4 ,5,6,7,8 weeks. The reduction of ulcer size were observed and reported by using the (CSURI)(31) , quantifies capillary damage, including the number of capillaries, the presence and size of megacapillaries, and uses this data in a specific formula

Inflammatory cells in the (gel.,cream groups)treated ulcers were decreased at week 4 compared to ulcers in(lotion group). Though the degree of contraction in the cream's group and lotion's group treated lower than that of gel's group from week 4 , but appeared significantly higher on week 8. From this result, it may support the possibility that gel's group would be useful agent for early inflammatory response and matrix remodeling phase of the skin wound (figure 2).

smallest starting from week 4 , becoming grade 1 instead grade 2 , while ulcers of lotion group showed non change in width in week4 (grade 2)and ulcers area of cream group treated reported a reduction in weeks starting from week4(grade 2).. After week 8-follow-up persisting grade 1to2 ulcers were observed in Lotion's group. the types of discharges from ulcers were serous , usually seen in healing ulcer ,while purulent, seen in infected ulcer lotion group with yellow creamy discharge is observed due to bacterial infection.

Figure2 ; The reduction in ulcer area along the weeks 2 to 8 of topical treatment groups(cream,lotion,gel)



healing, with moderate inflammation, edema , hyperkeratosis and no parakeratosis on week 8(figure 3).while Cream's group treated was atrophic scarring (sunken scarring), which also has an over expression of collagen blocking regeneration ,meanwhile ,gel's group treated ulcer tissues showed the movement of epithelial cells was confirmed at week 4and most dermal residues grow up starting from week4 , slight flat scar starts to appear on week 5 and Scab was early disappear . The ulcer measurements showed that reduction scale of the gel's group treated markedly on week 6 compared to others two group (Figure 2). The ulcer area decreased significantly. In the gel's group treated , the improvement of skin healing parameters started clearly from week 4. Difference in collagen accumulation (blue color) in the healing area of the ulcer gel's treated group (Fig .3).The 5% gel's group treated was found to accelerate the healing process of ulcer by 1.5week as compared to cream's group treated. Furthermore, The 5% gel's group treated in term of scar size was found to accelerate the healing ulcer process by 2,5 week compared to lotion's group treated .The

3-1. Histological and Morphometric Analysis of the Skin ulcer Healing following Treatment ;

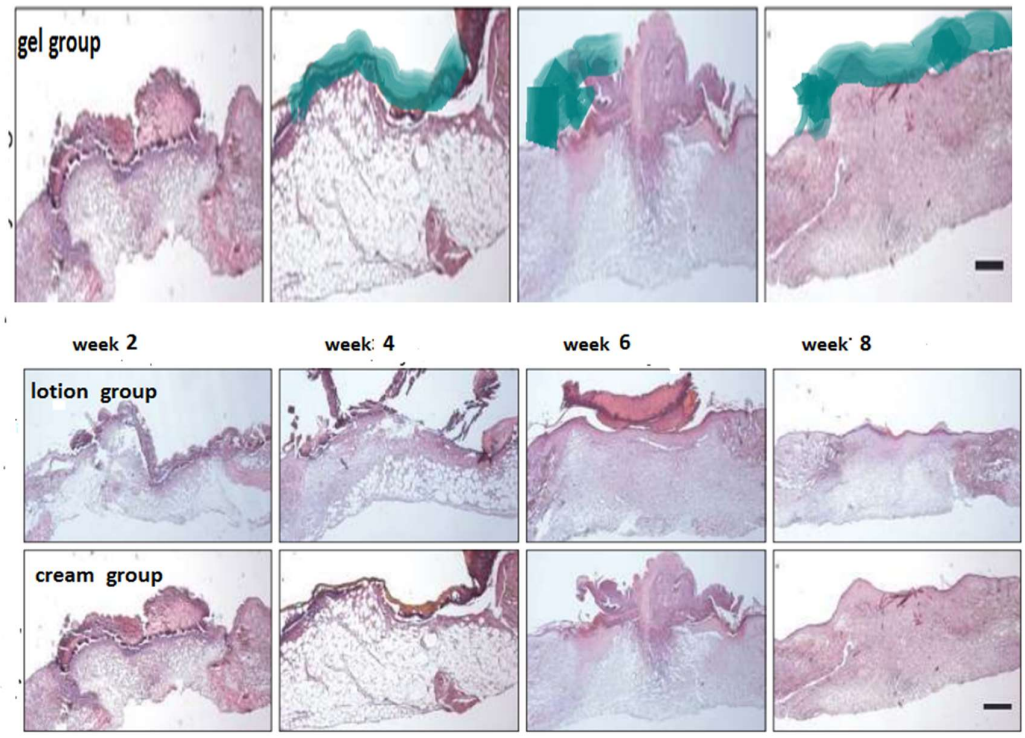
Healing prognosis per dosages form treated groups;

Differences In the term of ulcer area of the 3 skin topical dosages form ,were no differences the groups until week 4. However, healing parameters of skin tissues were observed in the gel's group -treated on week5 . Lotion's group treated ;was appeared to be collapsed and lost on week 2, and scabs caused by blood clots and fibrous tissues were observed and it was the most common ulcer end overextending the tissue, blocking off regeneration of tissues and Ulcer area of the lotion's group -treated was larger than other two groups on week 8, based upon morphometric analysis of the ulcer area from 3 treated groups. In contrast, treated topically of gel's group, exhibited complete healing (ulceration) throughout the skin's thickness on week 8 , while lotion's treated group showed signs of inflammation, edema, and hyperkeratosiswith Significant parakeratosis was also observed on week 8 . Finally, in cream's group treated , the histological picture showed partial thickness

scars that remain confined to the original site of injury . keloids Scars that grow beyond the boundaries of the initial wound and can be painful or itchy.

resultant of scar crater cutaneous leishmanial (CL) face ulcer healing as the tissue integrity is restored without excessive collagen. Thick, hypertrophic scars raised

Figure 3: Histological assessment results among the 3 topical skin applications (cream, lotion, gel groups) from week 2 to 8.



4- Discussion ; A drug's therapeutic result is greatly influenced by the mode of delivery. The primary route of topical drug delivery systems is through the skin, one of the human body's most accessible organs for topical administration. The application of a herbal containing formulation to the skin to treat the cutaneous symptoms of a general disease (like cutaneous leishmania) directly with the goal of containing the drug's pharmacological or other effect to the skin's surface. In this article, we presented the dual evaluation of efficiency of Moringa oleifera extract in topical pharmaceutical forms and Pycnogeol skin preparations as synergic action for their coetaneous antileishmanial activity . The used extract Morenga .Oleifera roots and the methanolic extract of leaves showed a moderate inhibitory of Antileishmanial activity with previous reported (32).Therefore, in order to find new therapy for the treatment of leishmaniasis, researchers have directed their attention to the use of natural products (33), particularly, those from plants may be future treatment options for leishmaniasis. However, treatment with the latter is expensive and remains unaffordable for the poor population, so far this highly useful trees have not been evaluated for its antileishmanial potential.The pH values of prepared formulation incorporated with m.oliefera extract was found to be 6.2 (almost neutral) which are considered acceptable to avoid the risk of irritation upon application to the skin because adult skin pH is 5.5. Face cutaneous Leishmanial ulcers treatment is basically with minimum permanent scar formation as accepted outcome for infected patient . Treatment involves timely diagnosis via a direct smear test and appropriate medical intervention to prevent worsening or spread to other forms of leishmaniasis. It is well established that skin wound healing is a complex ,the dermis remodeling phase of skin wound healing involves the full growth of the wound accompanied by collagenous scarring (34).Pycnogenol , which is one of the polyphenol compounds, is a pine bark extract and has been used as a medicine for wound recovery and inflammatory diseases since the ancient times(35) but as an agent to improve vascular integrity and endothelial function and to stimulate anti-inflammatory responses (36). Pycnogenol was demonstrated to promote wound recovery time in mice with treatment with 5% Pycnogenol after induction of burn wounds , and the measurement of the scar tissue was also 2.6 times less involved (37). Our project dhowed that , From week 2 to 4, there were more inflammatory cells in all treated groups of ulcerated lesions . On week 5 of treatment , higher tendency appears to inhibit inflammatory responses in the early period of ulcer healing. However, both the degree of contraction of ulcers and the collagen deposit time were higher in gel's and cream;s treated groups than lotion's treated group on week 6 and also stimulates the formation of collagen in ulcerated area of the skin recovery period (38). Pharmacology Anti-inflammation study reported that an ethanolic extract of the M. concanensis flower

and fruit inhibited inflammation by 78.4 atopic dermatitis mice and human keratinocytes (38,39,40) and to avoid secondary bacterial infection [41,42).

5. CONCLUSION:

The herbal remedy of (M. oleifera extract gel and Pycnogenol 5% gel presented a good extrudability, spreadability and other physical qualities, which show that M.oleifera and Pycnogenol can be an excellent companion for standard pharmacotherapy of diagnosed (Baghdad boil) cutaneous leishmanial (CL) face ulcer. The wide use of Moringa as a vegetable is evidence for its safety and non-toxicity. Therefore, Moringa-based herbal preparations may be used in the future as an adjuvant therapy for the treatment of leishmaniasis. We suggested that the early onset of treatment with M. oleifera extract in gel and 5% Pycnogenol skin gel will inhibit the initial inflammatory response, promote collagen deposition and matrix remodelling, and lower scar formation.

References:

1. Sofen B, Prado G, Emer J. Melasma and Post Inflammatory Hyperpigmentation: Management Update and Expert Opinion. Skin Therapy Lett. 2016;21(1):1-7.
2. Elbuluk N, Grimes P, Chien A, Hamzavi I, Alexis A, Taylor S, et al. The Pathogenesis and Management of Acne-Induced Post-inflammatory Hyperpigmentation. Am J Clin Dermatol. 2021;22(6):829-36.
3. Kim YJ, Kang KS, Yokozawa T. The anti-melanogenic effect of pycnogenol by its anti-oxidative actions. Food Chem Toxicol. 2008;46(7):2466-71
4. *Ayres EL, Silva JDS, Eberlin S, Facchini G, Vasconcellos C, Costa A. In-vitro effect of pine bark extract on melanin synthesis, tyrosinase activity, production of endothelin-1 and PPAR in cultured melanocytes exposed to Ultraviolet, Infrared, and Visible light radiation. J Cosmet Dermatol. 2021.*
5. *Grether-Beck S, Marini A, Jaenicke T, Krutmann J. French Maritime Pine Bark Extract (Pycnogenol(R)) Effects on Human Skin: Clinical and Molecular Evidence. Skin Pharmacol Physiol. 2016;29(1):13-7.*
6. *Pinto CAS, Delfes MFZ, Reis LMd, Garbers LE, Passos PCVdR, Torre DSd. The use of pycnogenol in the treatment of melasma. Surgical & Cosmetic Dermatology. 2015;7(3).*
7. *Zhao H, Wu J, Wang N, Grether-Beck S, Krutmann J, Wei L. Oral Pycnogenol(R) Intake Benefits the Skin in Urban Chinese Outdoor Workers: A Randomized, Placebo-Controlled, Double-Blind, and Crossover Intervention Study. Skin Pharmacol Physiol. 2021:1-11.*
8. *Ni Z, Mu Y, Gulati O. Treatment of melasma with Pycnogenol. Phytother Res. 2002;16(6):567-71.*
9. *Saliou C, Rimbach G, Moini H, McLaughlin L, Hosseini S, Lee J, et al. Solar ultraviolet-induced erythema in human skin and nuclear factor-kappa-B-dependent gene expression in keratinocytes are modulated by a French maritime pine bark extract. Free Radic Biol Med. 2001;30(2):154-60.*
10. *Marini A, Grether-Beck S, Jaenicke T, Weber M, Burki C, Formann P, et al. Pycnogenol(R) effects on skin elasticity and hydration coincide with increased gene expressions of collagen type I and hyaluronic acid synthase in women. Skin Pharmacol Physiol. 2012;25(2):86-92.*
11. *Grimm T, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, et al. Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol). J Inflamm (Lond). 2006;3:1.*
12. *Grimm T, Schäfer A, Högger P. Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (pycnogenol). Free Radic Biol Med. 2004;36(6):811-22.*
13. *Canali R, Comitato R, Schonlau F, Virgili F. The anti-inflammatory pharmacology of Pycnogenol in humans involves COX-2 and 5-LOX mRNA expression in leukocytes. Int Immunopharmacol. 2009;9(10):1145-9.*
14. *Schäfer A, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, et al. Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol). Biomed Pharmacother. 2005;60(1):5-9.*
15. *Kim K-Y. The effect pycnogenol has on the acne skin of Koreans in their 10s and 20s. Journal of Digital Convergence. 2022;20(3):487–95.*
16. *Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S, et al. Diabetic ulcers: microcirculatory improvement and faster healing with pycnogenol. Clin Appl Thromb Hemost. 2006;12(3):318-23.*
17. *Liu X, Wei J, Tan F, Zhou S, Wurthwein G, Rohdewald P. Pycnogenol, French maritime pine bark extract, improves endothelial function of hypertensive patients. Life Sci. 2004;74(7):855-62.*
18. *Zibadi S, Rohdewald PJ, Park D, Watson RR. Reduction of cardiovascular risk factors in subjects with type 2 diabetes by Pycnogenol supplementation. Nutr Res. 2008;28(5):315-20.*
19. *Enseleit F, Sudano I, Periat D, Winnik S, Wolfrum M, Flammer AJ, et al. Effects of Pycnogenol on endothelial function in patients with stable coronary artery disease: a double-blind, randomized, placebo-controlled, cross-over study. Eur Heart J. 2012;33(13):1589-97.*
20. Anwar F., Latif S., Ashraf M., and Gilani A. (2007), Moringa oleifera: a food plant with multiple medicinal uses. Phytother. Res. 21, 17 – 25.

21. Debnath, S., and Guha, D. (2007). Role of Moringa oleifera on enterochromaffin cell count and serotonin content of experimental ulcer model. Indian J Exp Biol. 45, 726–731
22. Gothai, S., Arulselvan, P., Tan, W. S., and Fakurazi, S. (2016). Wound healing properties of ethyl acetate fraction of Moringa oleifera in normal human dermal fibroblasts. J. Int. Ethnopharmacol. 5, 1–6. doi: 10.5455/jice.20160201055629
23. Muhammad, A. A., Arulselvan, P., Cheah, P. S., Abas, F., and Fakurazi, S. (2016). Evaluation of wound healing properties of bioactive aqueous fraction from Moringa oleifera Lam on experimentally induced diabetic animal model. Drug Des. Devel. Ther. 10, 1715–1730. doi: 10.2147/DDDT.S96968.
24. Rathi, B. S., Bodhankar, S. L., and Baheti, A. M. (2006). Evaluation of aqueous leaves extract of Moringa oleifera Linn for wound healing in albino rats. Indian J. Exp. Biol. 44, 898–90
25. Satish, A., Sairam, S., Ahmed, F., and Urooj, A. (2012). Moringa oleifera Lam.: protease activity against blood coagulation cascade. Pharmacognosy Res. 4, 44–49. doi: 10.4103/0974-8490.91034
26. ocha L. G., Almeida J. R. G. S., Macedo R. O., and Barbosa-Filho J. M. (2005), A review of natural products with antileishmanial activity. Phytomedicine 12, 514 – 5
27. Sirivan Athikomkulchai , Prakairat Tunit , Sarin Tadtong , Pensak Jantrawut , Sarana Rose S; Moringa oleifera Seed Oil Formulation Physical Stability and Chemical Constituents , Cosmetics 2021, 8, 2. https://doi.org/10.3390/cosmetics8010002.
28. Sugihartini, N., Fajri, M. and Rahmawati, D. Formulation of Moringa oleifera Leaf Extract in Lotion and Gel as Sunscreen. DOI: 10.5220/0008241001540158 In Proceedings of the 1st Muhammadiyah International Conference on Health and Pharmaceutical Development (MICH-PhD 2018), pages 154-158 ISBN: 978-989-758-349-0.
29. Vongsak, B., Sithisarn, P., Mangmool, S., Thongpraditchote, S., Wongkrajang, Y., Gritsanapan, W. 2013.Maximizing total phenolics, total flavonoids contents and antioxidant activity of Moringa oleifera leaf extract by the appropriate extraction method. Industrial Crops and Products, 44: 566-571.
30. Evaluation and management of diabetic foot according to Wagner's classification. Waghmare S, Meshram H, Mahey R, Shetty T, Singh A. Int J Surg. 2019;3:197–201. [Google Scholar]
31. Marco Sebastiani .Andreina Manfredi, Andrea Lo Monaco, Capillaroscopic Skin Ulcers Risk Index (CSURI) calculated with different videocapillaroscopy devices: how its predictive values change.Clin Exp Rheumatol. 2013 Mar-Apr;31(2 Suppl 76):115-7.
32. Chan-Bacab M. J. and Pena-Rodriguez L. M. (2001), Plant natural products with leishmanicidal activity. Nat. Prod. Rep. 18, 674 – 688.
33. Hinz B (2007) Formation and function of the myofibroblast during tissue re.pair. J. Invest. Dermatol. 127, 526-537.
34. Devaraj, V. C., Krishna, B. G., and Viswanatha, G. L. (2011). Simultaneous determination of quercetin, rutin and kaempferol in the leaf extracts of Moringa oleifera Lam. and Raphinus sativus Linn. by liquid chromatographytandem mass spectrometry. J. Chin. Integrat. Med. 9, 1022–1030. doi: 10.3736/jcim20110914
35. Blazsó G et al. Pycnogenol® accelerates wound healing and reduces scar formation. Phytother Res 18: 579-581, 2004.
36. G.; Gábor, M.; Schönlau, F.; Rohdewald, P. Pycnogenol accelerates wound healing and reduces scar formation. Phytother. Res. 2004, 18, 579–581. [CrossRef] [PubMed]
37. Richa Srivastava*, Utkarsh Rai, Bushara Khatoon ; Formulation and Evaluation of Novel Topical Gel Incorporating Moringa and Curcumin Extracts for Skin Disorders Int. J. Pharm. Sci. Rev. Res., ISSN: 0976 – 044X, 84(6) – June 2024; Article No. 04, Pages: 15-19 DOI: 10.47583/ijpsrr.2024.v84i06.004
38. Rao, C. V., Hussain, T., Verma, A. R., Kumar, N., Vijaykumar, M., and Reddy, G. D. (2008). Evaluation of the analgesic and anti-inflammatory activity of Moringa concanensis tender
39. Jayabharathi, M., and Chitra, M. (2011). Evaluation of anti-inflammatory, analgesic and antipyretic activity of Moringa concanensis Nimmo. J. Chem. Pharm. Res. 3, 802–806
40. ayabharathi, M., and Chitra, M. (2011). Evaluation of anti-inflammatory, analgesic and antipyretic activity of Moringa concanensis Nimmo. J. Chem. Pharm. Res. 3, 802–80
41. Choi, E. J., Debnath, T., Tang, Y., Ryu, Y. B., Moon, S. H., and Kim, E. K. (2016). Topical application of Moringa oleifera leaf extract ameliorates experimentally induced atopic dermatitis by the regulation of Th1/Th2/Th17 balance. Biomed. Pharmacother. 84, 870–877. doi: 10.1016/j.biopha.2016.09.085.
42. Sarikaki V et al. In vitro percutaneous absorption of pine bark extract Pycnogenol® in human skin. J Cutan Ocul Toxicol 23(3): 149-158, 2004.
43. Torras MA et al. Antimicrobial activity of Pycnogenol®. Phytother Res 19: 647-648, 2005.