

Epidermal wound healing potentials of methanolic extract of *Tetracapidium conophorum* leaf on the limb of West African Dwarf goat

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ABSTRACT

A wound is a disruption to the anatomic structure and the functional continuity of living tissues and wound healing is a survival mechanism and represents an attempt to maintain the normal structure and function. The aim of this study is to evaluate the healing properties of methanol extract of *Tetracapidium conophorum* leaf on epidermal wound in West African Dwarf (WAD) goat. Eight adult West African Dwarf (12 to 15 kg) goats grouped into control and experimental of four animals each were used. Epidermal wounds were created on the trunk of all the goats using a square stencil of dimension 1 cm by 1 cm after shaving. Each wound was measured (in centimetre²) daily using the length of the mid-horizontal and mid-vertical sides of the wound with the aid of a Vernier caliper. Epidermal skin biopsies were taken also on days 0, 5, 10 and 20 for histology. The study demonstrated that wound contraction was much faster in treated groups compared with the control group indicating the wound healing properties of *T. conophorum* leaf extract. The quantification of macrophages and neutrophils in the control animals (88 ± 0.4 , 172 ± 4.8) were significantly higher than in the treated animals ($40 \pm 0.7^*$, $48 \pm 2.8^*$). Lymphocytes and fibroblast were significantly higher in the control animals (68 ± 0.5 , 24 ± 0.41) than the treated animals ($36 \pm 0.7^*$, $12 \pm 1.12^*$). The histopathological examination showed observable granulation tissue on day 20 in the treated group while no granulation tissue in the control group. The quantification results revealed an increased fibroblast, neutrophil in the treated group as compared to untreated group which indicated healing. The extract of the leaf showed remarkable wound healing activity and it may be used for treating various types of wounds and injuries in animals and humans.

Keywords: *Tetracapidium conophorum*, wound, WAD, epidermal.

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INTRODUCTION

A wound is a disruption to the anatomic structure and the functional continuity of living tissues (Robson et al., 2001) or a breakdown in the protective function of the skin; loss of continuity of epithelium, with or without loss of underlying connective tissue - muscle, bone, nerves following injury to the skin or underlying tissues/ organs caused by surgery, a blow, a cut, chemicals, heat/cold, friction/shear force, pressure or as a result of disease, such as leg ulcers or carcinomas (Velnar et al., 2009). It may be described by aetiology, anatomical location,

whether acute or chronic, method of closure, presenting symptoms or the appearance of the predominant tissue types in the wound bed (White, 2015). All definitions serve a critical purpose in the assessment and appropriate management of the wound through to symptom resolution or, if viable, healing.

The skin provides a life-protective barrier between the body and the external environment against physical damage, pathogens and has physiological functions that contribute to body homeostasis maintenance (Canedo-

Dorantes and Canedo-Ayala, 2019). Wound healing is a survival mechanism and represents an attempt to maintain the normal structure and function (Olaifa, 2017). The capacity of a wound to heal depends partly on its depth, overall health and nutritional status of the individual (Atiyeh et al., 2005). To heal a wound, the body undertakes a series of actions collectively known as the wound healing process. Wound healing is a dynamic and complex process having a series of coordinated events. These include bleeding, coagulation, acute inflammatory response, regeneration, migration and proliferation of connective tissue and parenchyma cells; synthesis of extracellular matrix proteins, remodeling of new parenchyma, connective tissue and collagen deposition (Gonzalez et al., 2016). Wound healing progression is comprised of a systematic process of events starting from the moment of injury, that is, the inflammatory phase (the establishment of homeostasis and inflammation), the proliferation phase (granulation, contraction, and epithelialization), and finally, the remodeling phase, which determines the strength and appearance of the healed tissue (Kondo, 2007; Wasman et al., 2010). The mechanisms involved in wound healing include: inflammation; epithelialization, fibroplasias, angiogenesis, wound contraction; and remodeling. These mechanisms are initiated at the time of physical injury and proceed continuously throughout the repair process (Broughton et al., 2005; Velnar et al., 2009).

Indigenous and traditional medicines make extensive use of natural products and derivatives and provide a large portion of all medicine consumed today throughout the world (Shedoeva et al., 2019). The plant *Tetracarpidium conophorum* (Mull.Arg) Hutch & Dalziel Syn. commonly called African Walnut belongs to the family Euphorbiaceae. It is a climber found in the wet part of Southern Nigeria and West Africa in general. Its habitat is usually large trees; the fruits are greenish with four round seeds in each fruit. The seed testa is hard, and the cotyledons are white in colour (Ehiagbanare and Onyibe, 2007). The fruits are edible; the plant is medicinal and used for various purposes (Burkill, 1984). The leaves, bark, and fruit of *T. conophorum* are used medicinally, and their uses include masticatory, giddiness, thrush, antihelminthic, toothache, syphilis, dysentery, and as an antidote to snakebite (Odugbemi and Akinsulire, 2008). In the Southern Nigeria ethnomedicine, African walnut is used as a male fertility agent and in the treatment of dysentery (Ajaiyeoba and Fadare, 2006). The methanol and ethylacetate extracts of *T. conophorum* leaves have been shown to possess good antibacterial activities especially against Gram +ve organisms (Ajaiyeoba and Fadare, 2006).

Wound is a common threat to the life of ruminants and other animals at large which can reduce their effectiveness, productivity and economic important. Injuries to the limb usually has a slow healing rate due to poor circulation to the limb; constant and regular joint movement; minimal soft tissue between the skin and the

bone of the limb; greater risk of limb contamination as it is closer to the ground (Olaifa et al., 2017). Therefore, proper wound care and management needs to be ensured for wound complications not to set in which could be life threatening.

Over the years, there have always been problems with antibiotics resistance, affordability of choice of drug needed with regards to wound healing (Li and Webster, 2018) which make researchers to be exploring the composition of several herbs for answers. In developing countries, about 80% of the population depends upon medicinal plants for treating different diseases (Sharif et al., 2018). Therefore, medicinal plant derived drugs is under great demand due to a common belief that they are safe, reliable, clinically effective, low cost, globally competitive and better tolerated by patients (Balekar et al., 2012). Since ancient times, human beings have been using many plant resources based on empirical observations without any scientific knowledge for the treatment of wounds, cuts, and burns (Wang et al., 2011). The woods, roots, barks, seed, shells and kernels of *T. conophorum* have been explored for nutritional and therapeutic functions. The plant has been used in fish wound healing (Bello et al., 2013). However, there is dearth of information on the wound healing activity of this plant in ruminants. Therefore, the need to investigate its healing and morphometric activity in wound using methanolic extraction.

MATERIALS AND METHODS

Experimental animals

Eight adult West African Dwarf goats grouped into control and experimental of four animals each were put in stalls. The animals were housed in individual pens three weeks for stabilization before commencement of the experiment. Well-balanced diet consisting of concentrate, grass and cassava peels were fed to the animals and water provided *ad libitum*. The animals were dewormed with levamisole (10%) I/M at the dose rate of 10 mg/kg body weight and also given penicillin-streptomycin preemptively to take care of possible bacterial infections.

Plant extraction

Air-dried leaves of the plant were ground into powder. The powdered leaves were then soaked in methanol (analar grade) for 72 hours. The extracts were filtered respectively first through a piece of satin cloth, then Whatman filter paper no. 42 (125 mm). The filtrate was completely removed by rotary evaporator and further removal of water was carried out by freeze drying. The dry extracts were weighed, respectively, stored in clean sample bottles and kept at 4°C (Akomolafe et al., 2017).

Wound creation

Using a square stencil of dimension 1cm by 1cm, the portion of the epidermis to be surgically removed which is the right lateral side of the animal just ventral to the vertebrae column was marked using an ink marker. Three mg/kg of 2% lignocaine was used in caudal

epidural block and local infiltration (inverted L-Block) to desensitize the skin in order to ensure complete desensitization of nerves that might escape epidural block and provide the required anaesthesia. Each marked portion was blocked individually before surgery was done. Epidermal wounds were created on the trunk of all the goats. A sharp sterilized scalpel was used with particular care taken that wound edges were sharply defined and bleeding reduced by the use of pressure gauze and shortening of surgery duration. The full thickness of the skin within the incision was then carefully stripped away by sharp dissection from its underlying muscle (Olaifa and Fadason, 2016).

Wound contraction measurement

Each wound was measured (in centimetre²) daily using the length of the mid-horizontal and mid-vertical sides of the wound with the aid of a Vernier caliper. Error due to parallax was reduced by ensuring that wounds were measured under adequate illumination using the same blind observer all through the experiment. The length (L) and breadth (B) were then used to calculate the wound area in cm² (Olaifa and Fadason, 2016).

Epidermal skin histology (H & E staining)

Skin tissue of 1 cm area was harvested from the leg as wounds were created in these parts of the body on day 0. Skin biopsies were taken also on days 5 and 9 respectively. Tissues were preserved/fixated using formalin (10%) before arrival at the laboratory for histology. The staining method involves application of hematoxylin, which is a complex formed from aluminum ions and

oxidized hematoxylin. This colors nucleus of cells (and a few other objects, such as keratohyalin granules) blue. The nuclear staining is followed by counterstaining with eosin, which colors eosinophilic other structures in various shades of red and pink (Avwioro, 2010).

Data analysis

Data obtained during the experiment were subjected to student T-test. All data processing, charts and analysis were carried out using SPSS version 15 and Microsoft Office Excel 2010 (Microsoft Corporation).

RESULTS

From Figure 1, the wound in the experimental animal showed a higher level contraction compared (80%) with the control (90%). This pattern continued up until the 25th day when the experiment was terminated with the control animal showing consistently slower wound contraction rates than the *Tetracapidium conophorum* treated animals (Figure 1).

As shown in Table 1, the quantification of macrophages and neutrophils in the control animals were significantly higher than in the treated animals. Lymphocytes and fibroblast were significantly higher in the control animals than the treated animals on day 5, 15 and 20.

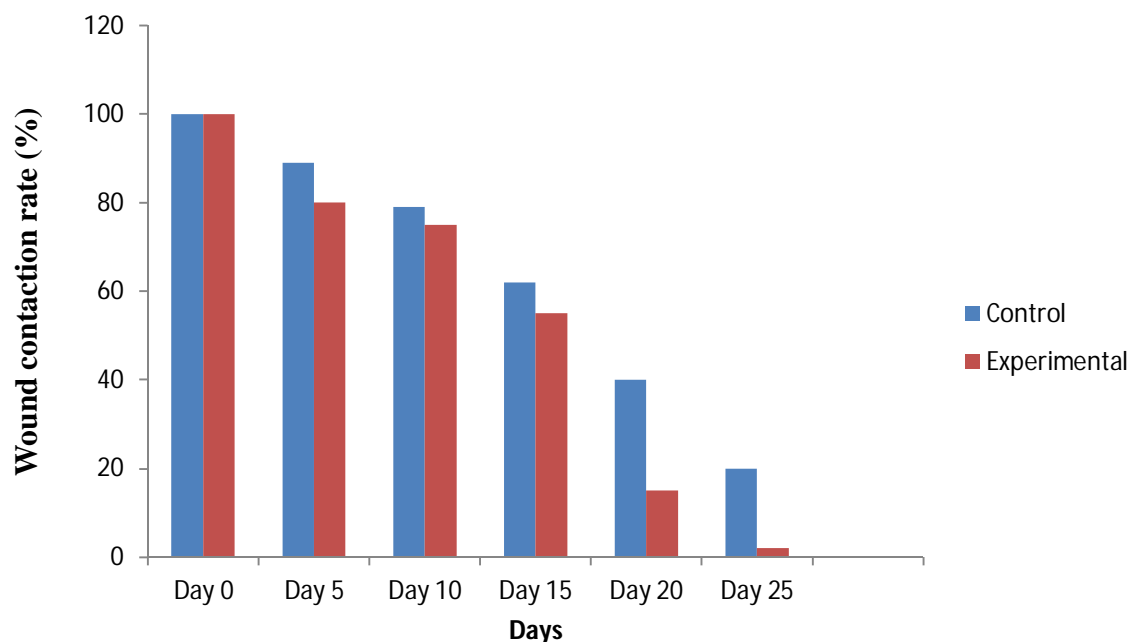


Figure 1. Wound contraction rate in control and methanolic extract *Tetracapidium conophorum* treated groups.

Histology

Histopathological studies of the wound healing process

are normally used for evaluating the efficacy of pharmacological products which promote and accelerate dermal skin substitutes (Figure 2 and 3). The

Table 1. Quantification of leucocytes, collagen fibre arrangement, degree of angiogenesis and epithelialization (Mean ± SEM).

	Code	MQ	LC	FIBRO	NEUT	EOS	MC	PLAT	C	A	E
Methanolic extract											
	DAY 0	28	28	4	0	0	2	0	1p	1	1
DAY 5	C	88 ± 0.4	68 ± 0.5	24 ± 0.41	172 ± 4.8	0	0	0	2p	1	1
	E	40 ± 0.7*	36 ± 0.7*	12 ± 1.12*	48 ± 2.8*	0	1	6	3p	2	1
DAY 10	C	44 ± 0.8	8 ± 1.2	48 ± 0.8	104 ± 2.8	0	2	5	3h	2	1
	E	32 ± 0.8*	44 ± 1.6*	60 ± 2.2	88 ± 1.0*	0	2	12	3h	2	2
DAY 15	C	32 ± 0.8	28 ± 0.8	72 ± 2.9	44 ± 0.9	0	0	0	3h	2	2
	EX	12 ± 1.0	8 ± 0.5*	48 ± 0.9*	8 ± 0.3*	6	1	4	1p	1	1
DAY 20	C	8 ± 1.2	8 ± 1.2	12 ± 1.5	4	0	1	1	2p	2	3
	EX	4 ± 0.8*	4 ± 0.8*	8 ± 1.2*	0	0	0	5	3h	2	3

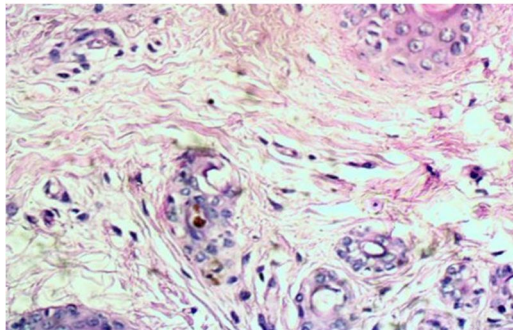
Quantitative (relative, %) {multiply by 400} *P < 0.05

MQ - macrophages, LC - Lymphocytes, Fibro- fibroblast, Neut- neutrophils, Eosin- eosinophils, MC- mast cells, Plat- platelets

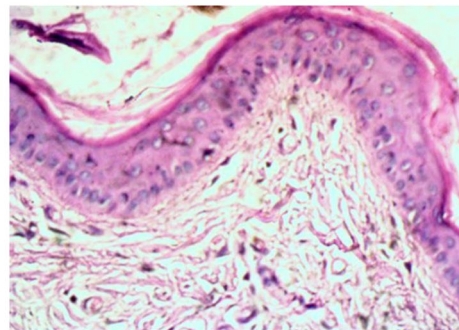
Qualitative: C - collagen fibre arrangement, A - degree of angiogenesis, E - degree of epithelialization.

1-mild, 2-moderate, 3- severe, h- haphazard, p - parallel arrangement.

Day 0

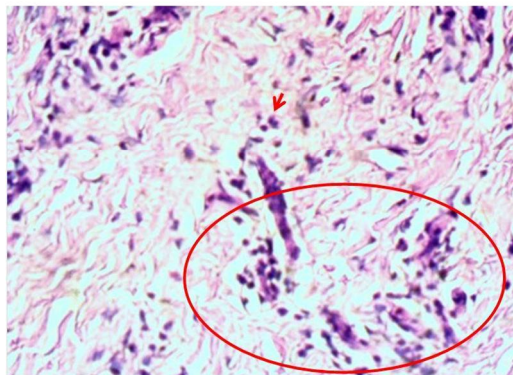


Control



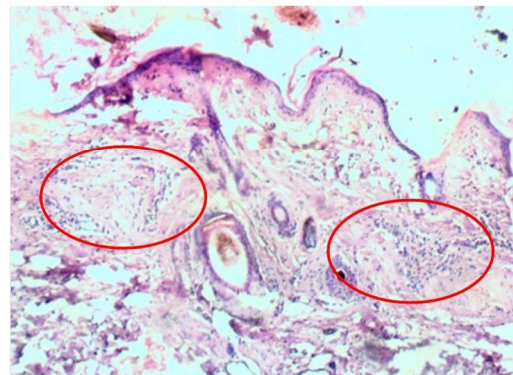
Treated

Day 5



Early inflammatory phase.

Dermis contain a few inflammatory cells (red arrows) within collagen fibres. HE x400

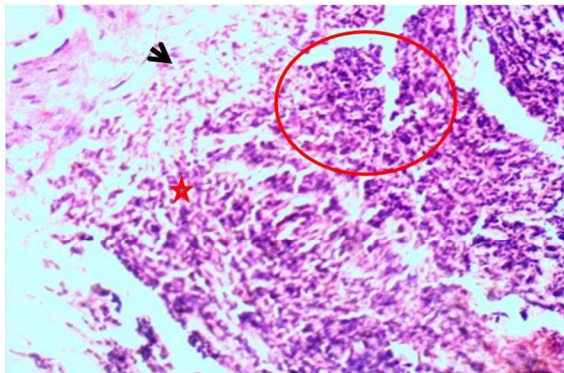


Treated

Early inflammatory phase. HE x100

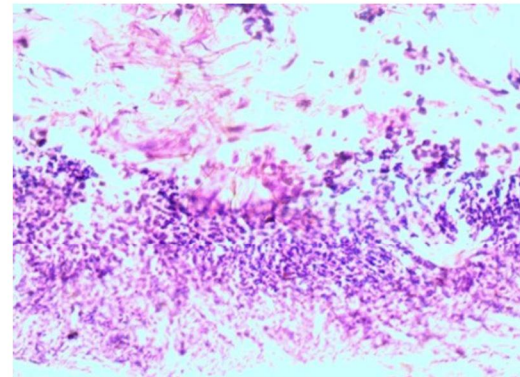
Figure 2. Epidermal skin histology.

Day 10



Control

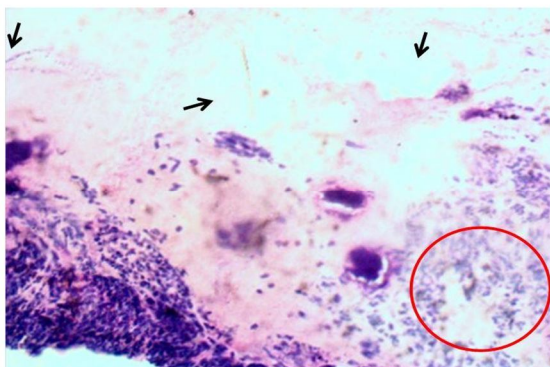
Granulation tissue and inflammatory cells. Note granulation tissue (asterisk) containing numerous fibroblasts on the skin. Necrotic zone (black arrow) separates granulation tissue and skin surface
HE x100, 400



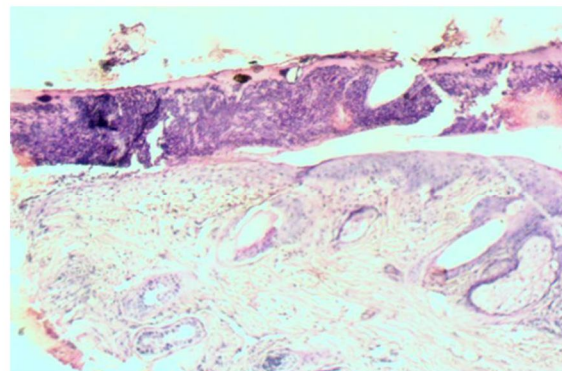
Treated

Layers of Inflammatory cells and scab (asterisk)
HE x100, 400

Day 20



Wound with blood clot/scab and acute inflammatory response
Oedema (black arrows) and some inflammatory cells
HE x100, 400



Granulation tissue (asterisk) separated from underlying epidermis

Figure 3. Epidermal skin histology.

histopathological examination provided additional evidence for the experimental wound healing studies which was based on the contraction value of wound area. The histopathological examination showed observable granulation tissue on day 20 in the treated group while no granulation tissue in the control group. Granulation tissue primarily contains fibroblasts, collagen fibers, with less oedema and newly generated blood vessels which were observed in leaf extract treated animals. Layers of inflammatory cells were also seen in the untreated groups.

DISCUSSION

This study demonstrated that wound contraction was

much faster in treated groups compared with the control group indicating the wound healing properties of *T. conophorum* leaf extract. This is in agreement with previous studies in rats (Ezealisiji et al., 2014) and fish (Bello et al., 2013). Phytochemical screening of the leaf of *T. conophorum* showed the presence of tannins, alkaloids, saponins, steroids, tannins and flavonoids. The presence of several secondary metabolites in the plant could possibly account for the reasons why the leaf has numerous therapeutic indications including wound healing studies have shown that phytochemical constituents like flavonoids (Tsuchiya et al., 1996) and triterpenoids (Scortichini and Pia, 1991) are known to promote the wound healing process mainly due to their astringent and antimicrobial properties which appear to be responsible for the wound healing and increased rate

of epithelialization (Tsuchiya et al., 1996). Tannins have been reported to possess wound healing action by improving the regeneration and organization of the new tissue (Leite et al., 2002). Alkaloids, a major constituent of the extract could also be responsible for the enhanced healing. The wound healing activity of the total alkaloid extract could be attributed to the fact that extract caused an increased rate of formation of epithelial cells thus speeding up the re-epithelialization process which is critical in wound healing. There is also the possibility that angiogenesis which is the formation of new blood vessels was accelerated. This will in turn increase blood supply to the newly formed epithelial cells and thus in effect cause an overall increase in the rate of wound contraction. Zahra et al. (2011) showed that wounds treated with some plant extracts contain more collagen deposition and fewer inflammatory cells and angiogenesis. An increase in the rate of healing activity has been attributed to angiogenesis and collagen deposition in granulation tissue (Paladini et al., 1996). Acceleration of wound-healing potential of the total alkaloid extract may therefore be due to the deposition of more collagen fibers with angiogenesis and less inflammatory cells in granulation tissue of wound area. This could be achieved by the inhibition of the production of cytokines following a cutaneous injury. Inflammation results in trauma and in the presence of trauma wound healing is delayed (Hess, 2011). On the other hand, the anti-inflammatory effect of the extract may give rise to a quickening of the wound healing process. Research conducted by Priya et al. (2004) also revealed that alcoholic extract of *Celosia argentea* (Amaranthaceae), which contains several alkaloids, has a good wound healing activity.

The quantification results revealed an increased fibroblast, neutrophil in the treated group as compared to untreated group which indicated enhanced healing. Severe parallel arrangement of collagen and degree of epithelialization were also observed in the treated group as opposed to moderate arrangement of collagen and mild degree of epithelialization in untreated group. Fibroblasts produce collagen in skin, which plays an important role in preserving the anatomic integrity of wound healing. Collagen deposition increases the strength of the wound; before it is laid down, the only thing holding the wound closed is the fibrin-fibronectin clot, which does not provide much resistance to traumatic injury (Singh et al., 2018). During the inflammation phase of healing, neutrophils and macrophages are attracted into the injured tissue by various chemo tactic factors (Hernandez et al., 2001; Singh et al., 2014). They locate, identify, phagocytize, kill and digest the microbes and thus eliminate wound debris through their characteristic 'respiratory burst' activity and phagocytosis. This was seen in the quantification in day 0 and day 5 by increased number of macrophages and lymphocyte in the control group. However, suppression of inflammatory cells (macrophages, lymphocyte) in treated groups in days 10, 15, 20 could be responsible for the accelerated wound

healing in the treated animals. The presence of flavonoids, alkaloids, cardenolides, saponins along with other secondary metabolites in the leaves of *T. conophorum* with analgesic and anti-inflammatory properties has been established (Amaeze et al., 2011; Onasanwo et al., 2016).

Conclusion

The present study clearly demonstrated that the methanolic extract of *T. conophorum* promoted wound healing activities in goats. The extract of the leaf showed remarkable wound healing activity and it may be suggested for treating various types of wounds and injuries in animals. The enhanced wound healing activity of *T. conophorum* could possibly be made use of clinically in the healing of open wounds, most especially on the distal aspect of the limbs where wound healing is slow due to poor vascularization and high tendencies of infection. Also, the equine species have a high tendency for the formation of excessive granulation tissue termed 'Proud flesh' and the application of this plant could offer a permanent solution to this problem.

REFERENCES

- Ajaiyeoba EO, Fadare DA, 2006.** Antimicrobial potential of extracts and fractions of the African walnut—*Tetracarpidium conophorum*. *Afr J Biotechnol*, 5(22): 2322-2325.
- Akomolafe SF, Oboh G, Oyeleye SI, Olasehinde TA, 2017.** Toxicological effects of aqueous extract from African walnut (*Tetracarpidium conophorum*) leaves in rats. *J Evid Based Complementary Altern Med*, 22(4): 919–925.
- Amaeze OU, Ayoola GA, Sofidiya MO, Adepoju-Bello AA, Adegoke AO, Coker HAB, 2011.** Evaluation of antioxidant activity of *Tetracarpidium conophorum* (mull. Arg) Hutch and Dalziel leaves. *Oxidat Med Longevity*, 976701.
- Atiyeh BS, Hayek SN, Gunn SW, 2005.** New technologies for burn wound closure healing - Review of the literature. *Burns*, 31: 944-956.
- Avwioro OG, 2010.** Textbook of histochemistry and tissue pathology, principle and techniques. 2nd edition. Claverianum Press, Nigeria.
- Balekar N, Katkam NG, Nakpheng T, Jehtae K, Srichana T, 2012.** Evaluation of the wound healing potential of *Wedelia trilobata* (L.) leaves. *J Ethnopharmacol*, 141(3): 817-824.
- Bello OS, Emikpe BO, Olaifa AK, Olaifa FE, 2013.** Investigation into the healing properties of walnut (*Tetracarpidium conophorum*) leaf and onion (*Allium cepa*) bulb residues in *Clarias gariepinus*. *Arch Med Vet*, 45: 291-297.
- Broughton SJ, Piper MD, Ikeya T, Bass TM, Jacobson J, Driege Y, Martinez P, Hafen E, Withers DJ, Leever SJ, Patridge L, 2005.** Longer lifespan, altered metabolism, and stress resistance in *Drosophila* from ablation of cells making insulin-like ligands. *Proc Natl Acad Sci*, 102(8): 3105-3110.
- Burkill HM, 1984.** The useful plants of West Tropical Africa, Families E-I. Royal Bot Garden Kew, 2: 127–128.
- Canedo-Dorantes L, Canedo-Ayala M, 2019.** Skin acute wound healing: A comprehensive review. *Int J Inflammat*; Article ID 3706315: 1-15
- Ehiagbanare JE, Onyibe HI, 2007.** Effect of pre-sowing treatments on seed germination and seedling growth of *Tetracarpidium conophorum* Mull. *Afr J Biotechnol*, 6(6): 697–698.
- Ezealisiji KM, Omotosho AE, Udoh R, Agbo MO, 2014.** Wound healing activity of n-hexane and methanol extracts of *Tetracarpidium conophorum* (Mull. Arg.) Hutch (African walnut) in Wistar rats. *Malay*

- J Pharmaceut Sci, 12(1): 79–88.
- Gonzalez AC, Costa TF, Alves AR, Medrado P, 2016.** Wound healing – A literature review. *An Bras Dermatol*, 91(5): 614-620.
- Hernandez V, Recio MDC, Manez S, Prieto JM, Giner RM, Rios JL, 2001.** A mechanistic approach to the *in vivo* anti-inflammatory activity of sesquiterpenoid compounds isolated from *Inula viscosa*. *Planta Med*, 67: 726-731.
- Hess CT, 2011.** Checklist for factors affecting wound healing. Lippincott Williams & Wilkins; 24: 192.
- Kondo T, 2007.** Timing of skin wounds. *Legal Med*, 9(2): 109–114.
- Leite SN, Palhano G, Almeida S, Blavattii MW, 2002.** Wound healing activity and systemic effects of *Vernonia scorpioides* gel in guinea pig. *Fitoterapia*, 73: 496–500.
- Li B, Webster TJ, 2018.** Bacteria antibiotics resistance: New challenges and opportunities for implant-associated orthopaedic infections. *J Orthop Res*, 36(1): 22-32.
- Odugbemi O, Akinsulire O, 2008.** Medicinal plants by species names. In *Outlines and Pictures of Medicinal Plants from Nigeria*, T. Odugbemi, Ed., University of Lagos Press, Lagos, Nigeria p. 112.
- Olaifa AK, 2017.** Epidermal wound contraction rates on different parts of the body of West African Dwarf goats. *J Vet Med Surg*, 1(7): 1-4.
- Olaifa AK, Fadason ST, 2016.** Studies on zinc and copper ion in relation to wound healing in male and female West African dwarf goat. *Niger J Physiol Sci*, 31: 171-176.
- Onasanwo SA, Babatunde LD, Faborode OS, 2016.** Anti-nociceptive and anti-inflammatory potentials of fractions from the leaf extract of *Tetracarpidium conophorum* in rats and mice. *Afr J Biomed Res*, 19: 45-54.
- Paladini RD, Takahashi K, Bravo NS, Coulombe PA, 1996.** Onset of re-epithelialization after skin injury correlates with a reorganization of keratin filaments in wound edge keratinocytes: defining a potential role for keratin. *J Cell Biol*, 132(3): 381-397.
- Priya KS, Arumugam G, Rathinam B, Wells A, Babu M, 2004.** *Celosia argentea* Linn leaf extract improves wound healing in a rat burn wound model. *Wound Repair Regenerat*, 12(6): 618-625.
- Robson MC, Steed DL, Franz MG, 2001.** Wound healing: biologic features and approaches to maximize healing trajectories. *Curr Prob Surg*, 38: 72–140.
- Scortichini M, Pia RM, 1991.** Preliminary *in vitro* evaluation of the antimicrobial activity of terpenes and terpenoids towards *Erwinia amylovora* (Burrill). *J Appl Bacteriol*, 71: 109-112.
- Sharif AA, Asif H, Younis W, Riaz H, Bukhari IA, Assiri AM, 2018.** Indigenous medicinal plants of Pakistan used to treat skin disease: A review. *Chin Med*, 13: 52.
- Shedoeva A, Leavesley D, Upton Z, Fan C, 2019.** Wound healing and the use of medicinal plants. *Evid Based Complement Alternat Med*, 2684108.
- Singh AV, Batuwangala M, Mundra R, Mehta K, Patke S, Falletta E, Patil R, Gade WN, 2014.** Biomaterialized anisotropic gold microplate-macrophage interactions reveal frustrated phagocytosis-like phenomenon: A novel paclitaxel drug delivery vehicle. *ACS Appl Mater Interfaces*, 6(16): 14679-14689.
- Singh AV, Gemmati D, Kanase A, Pandey I, Misra V, Kishore Vimal, Jahnke T, Bill J, 2018.** Nanobiomaterials for vascular biology and wound management: A review. *Vein Lymphat*, 7: 7196.
- Tsuchiya H, Sato M, Miyazaki T, Fujiwara S, Tanigaki S, Ohyama M, 1996.** Comparative study on the antibacterial activity of phytochemical flavanones against methicillin-resistant *Staphylococcus aureus*. *J Ethnopharmacol*, 50: 27-34.
- Velnar T, Bailey T, Smrkolj V, 2009.** The wound healing process: An overview of the cellular and molecular mechanisms. *J Int Med Res*, 37: 1528–1542.
- Wang JP, Ruan JI, Cai YI, Luo Q, Xu HX, Wu YX, 2011.** *In vitro* and *in vivo* evaluation of the wound healing properties of *Siegesbeckia pubescens*. *J Ethnopharmacol*, 134(3): 1033-1038.
- Wasman SQ, Mahmood AA, Salehuddin H, Zahra AA, Salmah I, 2010.** Cytoprotective activities of *Polygonum minusaqueous* leaf extract on ethanol-induced gastric ulcer in rats. *J Med Plant Res*, 4(24): 2658–2665.
- White P, 2015.** Wound Essentials: Phases of Wound Healing. Accessed on 30th June, 2017. Clinimed.co.uk
- Zahra AA, Kadir FA, Mahmood AA, Al hadi AA, Suzy SM, Sabri SZ, Latif II, Ketuly KA, 2011.** Acute toxicity study and wound healing potential of *Gynura procumbens* leaf extract in rats. *J Med Plant Res*, 5(12): 2551–2558.

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