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Review article

Medicinal plants used for cutaneous wound healing in Uganda; ethnomedicinal reports and pharmacological evidences

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ABSTRACT

Background: Wounds have become a major health challenge worldwide, presenting marked humanistic and economic burdens such as disabilities and death. Annually, approximately 14 million people suffer from wounds worldwide and 80 % of these occur in developing countries like Uganda. In Uganda, besides many cases of daily wound occurrences, approximately 10 % of surgical procedures become septic wounds and consequently lead to increased morbidity and mortality. Accordingly, several ethnomedicinal studies have identified plants used for wound treatment in different parts of Uganda and the wound healing activities of some plants have been reported. However, at present, these information remain largely separated without an all-inclusive repository containing ethnomedicinal and pharmacological information of the plants used for wound healing in Uganda, thus retarding appropriate evaluation. Therefore, this review focused on extensively exploring the plants used for treating cutaneous wounds in Uganda, along with associated ethnomedicinal information and their globally reported pharmacological potential.
Methods: Electronic data bases including Google Scholar, PubMed, and Science Direct were searched using key terms for required information contained in English peer reviewed articles, books, and dissertations. Additionally, correlations between selected parameters were determined with coefficient of determination (r^2).
Results: The literature survey revealed that 165 species belonging to 62 families are traditionally used to treat wounds in Uganda. Most of the species belonged to families of Asteraceae (14 %), Fabaceae (10 %), and Euphorbiaceae (7 %). The commonest plant parts used for wound treatment include leaf (48 %), root (22 %), stembark (11 %), and stem (7 %), which are prepared majorly by poultice (34 %), decoction (13 %), as well as powdering (25 %). Fifty-four (33 %) of the plant species have been investigated for their wound healing activities whereas, one hundred eleven (67 %) have not been scientifically investigated for their wound healing effects. Pearson correlation coefficient between the number of wound healing plant families per part used and percent of each plant part used was 0.97, and between the number of wound healing plant families per method of preparation and percent of each method of preparation was 0.95, showing in both strong positively marked relationships.

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Conclusion: The preliminarily investigated plants with positive wound healing properties require further evaluation to possible final phases, with comprehensive identification of constituent bioactive agents. Additionally, the wound healing potential of the scientifically uninvestigated plants with claimed healing effects needs examination. Subsequently, information regarding efficacy, safety, bioactive principles, and mechanism of action could prove valuable in future development of wound healing therapies.

1. Introduction

Wounds are physical injuries resulting in an opening/breaking of the skin that cause disturbance in the normal skin anatomy and function [1]. There are different classification methods of wounds; based on underlying cause of wound creation, wounds are classified as open and closed, while classification on the basis of physiology of wound healing categorize wounds into acute and chronic [2]. Acute wounds are caused by environmental factors and they heal in an ordered manner within a short period due to balanced production and degradation of cells [3]. Acute wounds are further grouped into two general categories of traumatic wounds and surgical wounds [3]. Chronic wounds are caused by metabolic disorders and take long to heal due to lack of balance in the production and degradation of cells [3]. Chronic wounds are further grouped into four categories namely venous/vascular ulcers, pressure ulcers, diabetic ulcers, and ischemic wounds [3]. Wounds have become a major health challenge worldwide [4] with marked economic and humanistic burdens at both individual and societal levels such as reduced mobility as well as high treatment cost, respectively [5]. Chronic wounds could lead to disabilities when all available treatment options have been exhausted and amputation is recommended and it is reported that there is an amputation every 30 s as a result of diabetic ulcer worldwide [6]. Consequently, chronic wounds especially diabetic ulcers cause 85 % of all amputations [7]. The five-year mortality rate after development of diabetic ulcer and amputation are estimated to be 40 % and 40%–70 %, respectively [6,7]. Additionally, at least 10,000 in 1 million patients with wounds die from microbial infection as antimicrobial resistance has been escalating [8]. Annually, approximately 14 million people suffer from wounds worldwide and 80 % of this occur in developing countries like Uganda [9]. Chronic wound prevalence rate is approximately 1 %–2 % of the general population in developed countries and higher in developing countries [10]. Moreover, every wound has the potential to turn chronic [7]. Currently, there are no wounds prevalence estimates in developing countries including Uganda although wound problem remains serious [11]. In Uganda, approximately 10 % of surgical procedures turn out to be septic wounds and consequently lead to an increased morbidity and mortality [12].

Generally, human beings have natural abilities to undergo wound healing that involves an interaction of a complex cascade of cellular and bio chemical actions, these result into the restoration of anatomical and functional integrity of injured tissues [13]. The wound healing process are generally divided in to: inflammatory phase, proliferative phase, and remodeling phase [14]. Delay in wound healing processes are attributed to many factors such as, age, bacterial infection, necrotic tissue, and chronic diseases like diabetes mellitus among others [15]. In order to treat wounds, several conventional wound management approaches such as topical antibiotics and compression bandages have been applied [13]. However, in addition to high treatment costs, the clinical outcome of the conventional therapy has continued to be unsatisfactory with 50 % and above of chronic wounds being refractory to available therapies [13]. Studies in Uganda show that wound pathogens are highly resistant to several drugs used for wound treatment namely, ampicillin, amoxicillin, chloramphenicol, and oxacillin thereby giving a huge challenge in wound treatment since many healthcare centers have only a narrow class of drugs [12]. The multidrug resistance in Uganda is at 78 % among the bacterial isolates of surgical site infection [12]. These challenges in wound care management warrant continued efforts to explore alternatives to improve outcomes. For many years, herbal medicine has been used for human health care [16]. World Health Organization reported that about 80 % of people worldwide use herbal medicine for their health care needs like wounds, infectious, and non-communicable diseases [17]. In sub-Saharan Africa, 80%–90 % of the population use traditional medicine for primary health care [18,19]. Indeed, more than 80 % of the population in Uganda depend on herbal medicine for treatment of diseases including wounds [20]. The high prevalence of traditional medicine use for health care in Uganda is majorly attributed to accessibility, affordability, perceived safety, cultural preferences, effectiveness, and abundance [21]. It is to be noted that the government of Uganda has currently embarked on upscaling the use of herbal medicine and are on course of integrating it into the mainstream health care system [22]. In line with this, many ethnomedicinal studies have identified plants used for wound treatment in different parts of Uganda [23–44]. Notably, the wound healing activities and mechanism of action of some plants have been reported [45–62]. However, at present, these information remain largely separated without an all-inclusive repository containing ethnomedicinal and pharmacological information of the plants used for wound healing in Uganda, thus retarding appropriate evaluation. Therefore, this review focused on extensively exploring the plants used for treating cutaneous wounds in Uganda, along with associated ethnomedicinal information and their globally reported pharmacological potential, upon which further evaluation could be performed for possible development of future wound therapeutic medicine.

2. Methodology

In order to obtain information about different plants used for wound treatment in Uganda, electronic data bases namely, PubMed, Web of Science, Google Scholar, and Science Direct were searched for required information contained in peer reviewed articles, books, thesis, and dissertations. The information search was performed between August 13th, 2022 and January 06th, 2023, based on the

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (Fig. 1) [63,64]. Key search terms used included: “Wound,” “Wound healing plants,” “wound healing herbs,” “traditional medicine,” “ethnomedicine,” “phytomedicine,” “alternative medicine,” “pharmacology,” “ethno-pharmacology,” “phytochemicals,'' “mechanism of action,” “Safety,” “Toxicity,” and “Uganda.” Full text published works until January 2023 written in English on ethnomedicine of wound healing plants in Uganda were considered. Publications with results not relevant to the study, original articles not in English, reviews, and unpublished work were excluded (Fig. 1). Plant names were verified and presented in Latin as per the World Flora Online at http://www.worldfloraonline.org/ and Royal Botanic Garden Kew at www.theplantlist.org (Accessed on: February 10, 2023). The pertinent ethnomedicinal data obtained consisted of plant species, local name, families, plant parts used, and mode of preparation as well as administration. Regarding pharmacological reports, wound healing activities, dosage, mechanisms of action, type of study, active phytochemicals, toxicity, and safety information were recorded. Subsequently, summarization, analysis, and deductions were made from the data attained.

Additionally, correlations between selected parameters were determined with coefficient of determination (r^2) via Pearson correlation test using GraphPad Prism v 10.1.1 as per the method of Vijayakumar et al. [65]. The determined correlations included between (1) number of wound healing plant families and both percent of each plant part used and percent of each method of preparation. (2) Average annual temperature (as a parameter of climate) of some ethnomedicinal study sites in Uganda and each of the following; number of wound healing plant families, number of plant parts used, and number of methods of preparation.

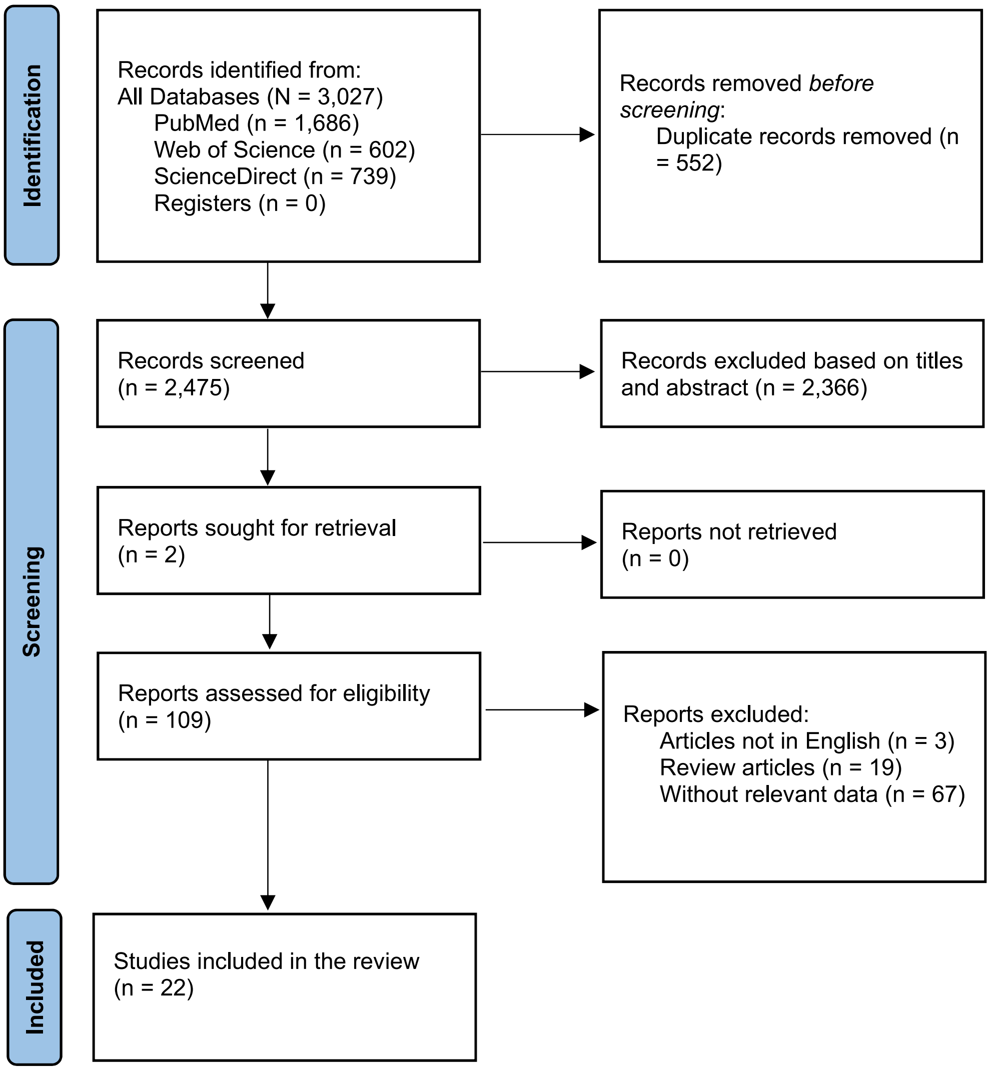

Fig. 1. PRISMA flow diagram showing the retrieval and exclusion steps of the review adapted from Ref. [64].

3. Results and discussion

3.1. Traditional concept of wounds in Uganda

Generally, the Ugandan population have good knowledge of wounds and commonly classify wounds as opening on skin, discharge, eruption, and injury [29]. Treatment and management of wounds using medicinal plants is a common practice across various communities in Uganda [23,29]. Knowledge about medicinal plants have been passed from elders to young people for generations [21]. This finding about knowledge transfer corroborates the reports of workers from other countries such as Wodah and Asase [66] in Ghana.

3.2. Wound healing plants used in local communities of Uganda

In this study, 165 species belonging to 62 families traditionally used for wound treatment in Uganda were retrieved (Table 1 supplementary). The most cited families included Asteraceae (14 %), Fabaceae (10 %), and Euphorbiaceae (7 %) (Fig. 2). The least cited families with only one species each were categorized as others (38 %) (Fig. 2). The common use of plant species from Asteraceae and Fabaceae for treatment may be due to high number of both their bioactive compounds and population that in turn render them superior with respect to efficacy and availability [44,67]. The observed widespread use of medicinal plants to treat wounds could be attributed to availability, low cost, cultural acceptability, minimal side effects, and effectiveness [22]. This indicates that medicinal plants are important alternative or supplement to conventional wound therapies. Previously, Muwanguzi [29] also reported highest number of plant species from Asteraceae, Euphorbiaceae, and Fabaceae utilization for wound treatment in Uganda. Similarly, many researches from other countries recorded predominant use of plant species from Asteraceae and Fabaceae for treating wounds and other diseases [68–70]. Additionally, some of the plant species documented in this study are being used as wound healing plants in various countries. For example, *Ageratum conyzoides* L. has been recorded for wound treatment in Kenya [70]. *Aspilia africana* (Pers.) C. D.Adams and *Moringa oleifera* Lam have been utilized for treating wounds in Nigeria [69]. *Aloe Vera* (L.) Burm.f is used in India as a wound healing plant [71]. *Galinsoga parviflora* Cav. is reported to be traditionally utilized for wound healing in Brazil [72]. Prescription of *Centella asiatica* (L.) Urb. for wound healing was registered in China as well as other countries in South East Asia [73]. Importantly, the most cited species (three times each) in this study were *Bidens pilosa* L., *Oxalis corniculata* L., *Hoslundia opposita* Vahl, and *Jatropha curcas* L., suggesting their widespread use. Common usage could potentially be an indicator that these plants are good candidates for further biochemical evaluation.

3.3. Parts used, preparation, and mode of administration

The common plant parts used are leaf (48 %), root (22 %), stembark (11 %), and stem (7 %) (Fig. 3 and Supplementary Table 1). The observed high level of leaf usage traditionally is reflective of *materia medica* characteristic in Uganda [74]. This may be because leaves are highly potent, easy to harvest, and possess strong ability to regenerate [42]. Additionally, leaves are the major photosynthetic organ and function as storage site of photosynthates, of which some are bioactive [75]. Many workers around the world also reported high use of leaves for treatment of wound and other diseases compared to other plant parts [69,76,77].

The major methods of preparation recorded include poultice (34 %), powdered material (drying and pounding-25 %), decoction (13 %), and sap extraction from fleshy parts by cutting (9 %) (Fig. 4). Plants such as *Bidens pilosa* L., *Crassocephalum montuosum* (S. Moore) Milne-Redh., and *Cynanchum nigricans* Vahl ex Decne. are all prepared through poultice (Supplementary Table 1). Accordingly, many methods of preparation could be applied to same medicinal plant for wound care based on the plant parts. For instance, the stem bark of *Cassine buchananii* Loes. is prepared by decoction while the leaf is dried and powdered. The popularity of preparing wound healing plants by poultice is due to the fact that it is the easiest way of medicine application to the wounded organ or body part [78].

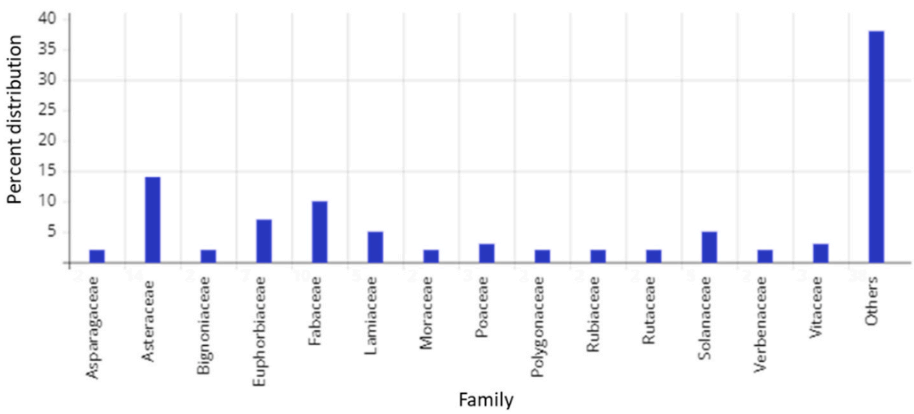

Fig. 2. Distribution of medicinal plant families used for treating wounds in Uganda.

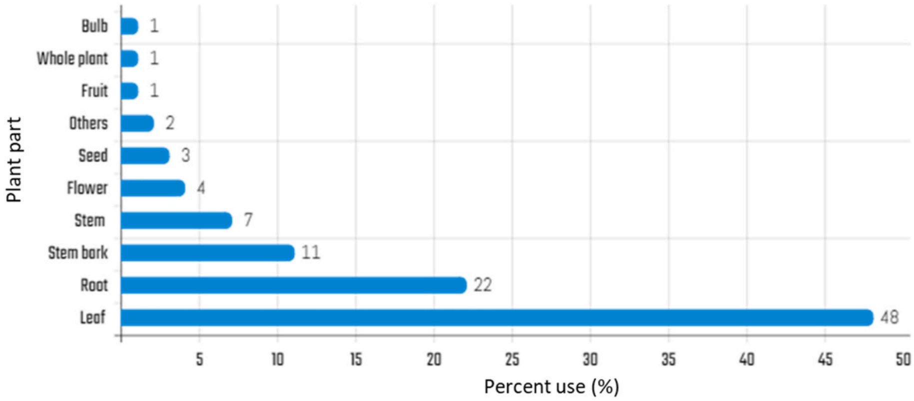

Fig. 3. Plant parts percentage use for treatment of wounds in Uganda.

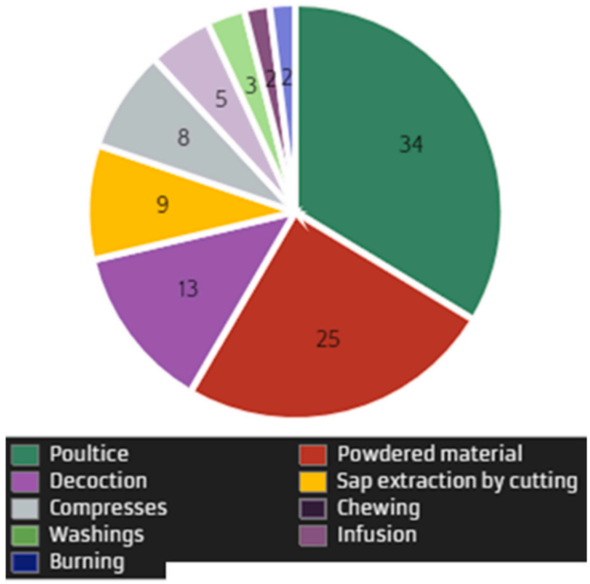

Fig. 4. Preparation methods of plants used for treatment of wounds in Uganda.

This finding is concordant with the report of Ong and Milo [79] who also registered poultice as the commonest preparation technique. The preparations are mainly topically applied in wound management and care (Supplementary Table 1).

Regarding formulations, herbal preparations to treat wounds in Uganda are mostly made of a single plant (Supplementary Table 1). In some cases, the preparations consist of a combination of more than one herbal plant, for instance, leaf powder of *Hoslundia opposita* Vahl and *Aspilia* sp are mixed and applied on wound surface [25]. Notably, no study from Uganda has reported precise doses or potions of the plant therapies for wounds, except some reports such as that of Tugume et al. [43] containing attempted description of the recommended doses (Supplementary Table 1). As an example of unstandardized dose, Tugume et al. [43] reported that one handful of *Kalanchoe pinnata* L. leaves and one teaspoon of sugar were mixed and heated until the content became brown, then used to dress wound. Absence of precise dosage and formulations could possibly be attributed to the fact that herbal healers depend on their personal judgement [29]. This poses a challenge in sharing good practice for desired outcome on patients. Similarly, studies from countries neighboring Uganda reported descriptions of preparations for wound healing without specific doses or potions and these included Tanzania [80,81], Democratic Republic of the Congo [82], and Kenya [83,84]. On the other hand, some studies in Uganda [9, 85] and beyond [86–88] prepared standard formulations from these medicinal plants for wound care and reported positive results (Supplementary Table 2).

Accordingly, plant part, method of preparation, and dosage are among the major factors that affect bioactivity of medicinal plants, yet several ethnobotanical reports retrieved from Uganda have not included these information. Crucially, active compounds are distributed differently in various plant parts and this consequently lead to variation in bioactivities [89]. Therefore, information on plant part used can guide evaluation and enables identification of most effective parts. Method of medicinal plant preparation influences their phytochemical composition, which directly affect efficacy [90]. Thus, knowledge of appropriate preparation method (for example, decoction), which facilitates exhaustive extraction of bioactive compounds without degradation, is vital for effectiveness of end product. Additionally, dosage is critical as over- or under-dosing can potentially be dangerous. Going forward, assessment of these aspects (plant part, method of preparation, and dosage) in relation to the identified medicinal plants and wound healing have to be conducted, this will aid the development of rational botanical preparations and identification of new lead compounds.

The number of wound healing plant families per part used and percent of each plant part used was highly positively correlated ($r^2 = 0.97, p < 0.0001$) (Fig. 5A). This means that the use of each plant part increased with increasing number of families. The number of wound healing plant families per method of preparation and percent of each method of preparation was strongly positively correlated ($r^2 = 0.95, p < 0.0001$) (Fig. 5B). This implies that use of each method of preparation increased with increasing number of families. These results suggest that level of plant diversity could strongly influence frequency of plant part use and method of preparation.

However, no significant correlation was observed between average annual temperature of study sites and number of wound healing plant families ($r^2 = 0.09, p = 0.3633$) (Fig. 6A). This means that number of wound healing plant families did not increase with increasing temperature. Although temperature has been reported to influence number of plant families at larger scales such as globally and regionally [91], the observed non-association could possibly be because temperature variation across selected study sites was small (20–23 °C) and the entire Uganda is within tropics [92]. Similarly, no significant correlation was recorded between average annual temperature of study sites and number of plant parts used ($r^2 = 0.19, p = 0.1854$) (Fig. 6B), implying that number of plant parts used did not increase with increasing temperature. There was also no significant correlation between average annual temperature of study sites and number of methods of preparation ($r^2 = 0.04, p = 0.5817$) (Fig. C). This means that number of methods of preparation was not increased with increasing temperature. These results indicate that average annual temperature of study sites probably does not influence number of plant parts used and methods of preparation.

3.4. *Wound healing activities of plants and pharmacological evidence as per global reports*

3.4.1. *In vitro and in vivo studies*

The goals of wound care comprise reduction of risk factors associated with inhibiting wound healing, enhancement of the process of wound healing, and reduction of infection incidence [93]. As per the objectives of WHO Traditional Medicine Strategy, experimental validation using specified doses is the sole way to properly understand the safety and efficacy of herbal medicines, although they have been used traditionally over a long period [18]. Various pharmacological studies have shown that plant bioactive compounds possess marked wound healing properties [93]. During the assessment of wound healing activities of medicinal plants, many models have been employed; broadly categorized into *in vivo* and *in vitro* methods [2]. *In vivo* models consist of artificial models such as subcutaneous tubes and tissue models, which include dead space, incision wounds, burn wounds, excision wounds, as well as superficial wounds [2]. The *in vivo* models are always used to evaluate degree of collagenation, re-epithelialisation, tensile or breaking strength, and neo-vascularization of wounds [94,95]. *In vitro* models are critical in studying of cell-cell and cell-matrix interaction for mimicking cell migration during wound healing as well as antimicrobial properties [2].

Fifty-four (33 %) of the plants recapitulated in this study have been investigated for their wound healing activities in both *in vivo* and *in vitro* tests worldwide (Supplementary Table 2). Reported mechanisms of action through which these medicinal plants exerted their wound healing activities comprise anti-oxidative activities [96–99], anti-inflammatory and immunomodulatory effects [100–103], antimicrobial effects [104–107], collagen synthesis [95,101,108], cell proliferation [109–111], DNA synthess [112,113], and angiogenesis [101,114,115] (Fig. 7). Notably, some medicinal plants in this study acted through more than one mechanism and have shown healing activities at different stages of the wound healing process. The wound healing activities of these medicinal plants have been attributed to constituent bioactive compounds in the classes of terpenoids, phenolics, alkaloids, tannins, flavonoids, essential oils, and saponins (Supplementary Tables 1 and 2) [1,9,116]. Regarding the anti-oxidative mechanism, antioxidants promote the process of wound healing and protect tissues against oxidative damage through scavenging reactive oxygen species (ROS), inhibition of lipid peroxidation, as well as enhancing the intracellular activities of antioxidant enzymes like superoxide dismutase (SOD)

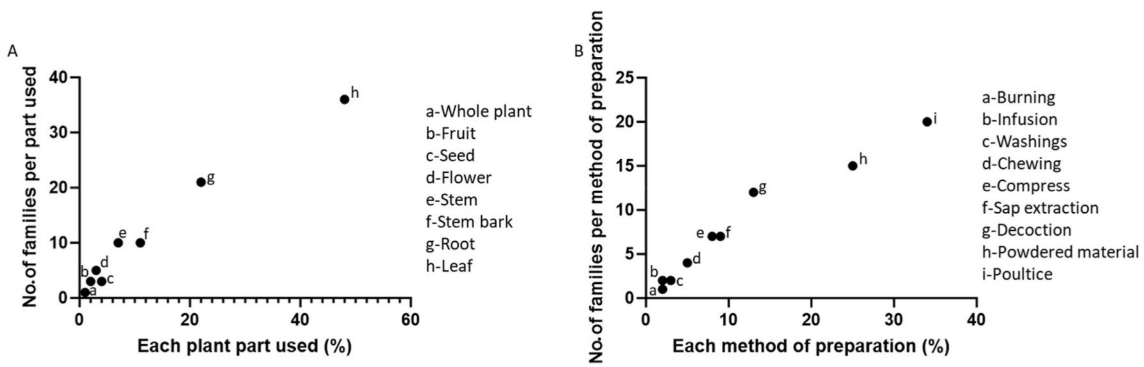

Fig. 5. The correlation between number of wound healing plant families and percent of each plant part used and percent of each method of preparation. (A) Correlation between number of wound healing plant families per part used and percent of each plant part used. (B) Correlation between number of wound healing plant families per method of preparation and percent of each method of preparation.

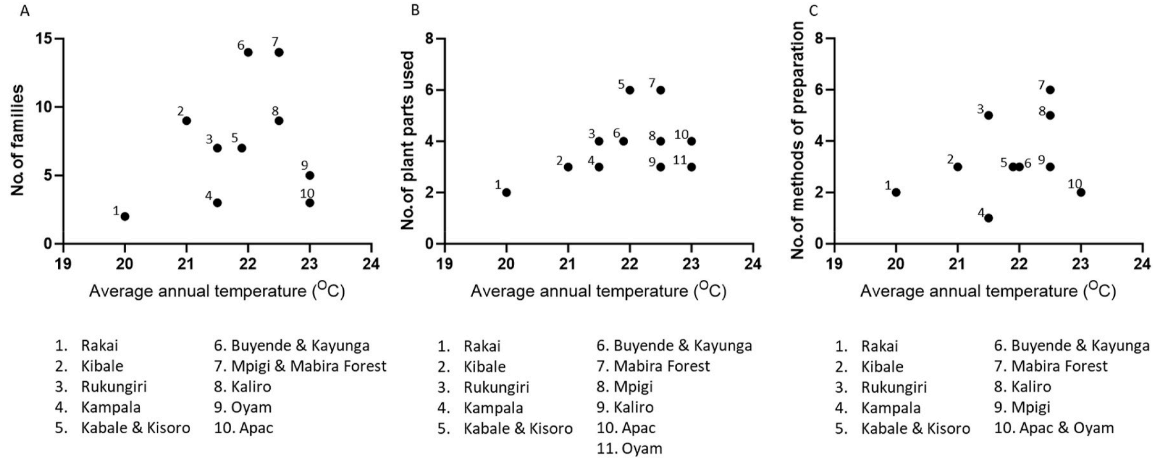

Fig. 6. The correlation between average annual temperature of some selected ethnomedicinal study sites in Uganda and number of wound healing plant families, number of plant parts used, and number of methods of preparation. (A) Correlation between average annual temperature of study sites and number of wound healing plant families. (B) Correlation between average annual temperature of study sites and number of plant parts used. (C) Correlation between average annual temperature of study sites and number of methods of preparation.

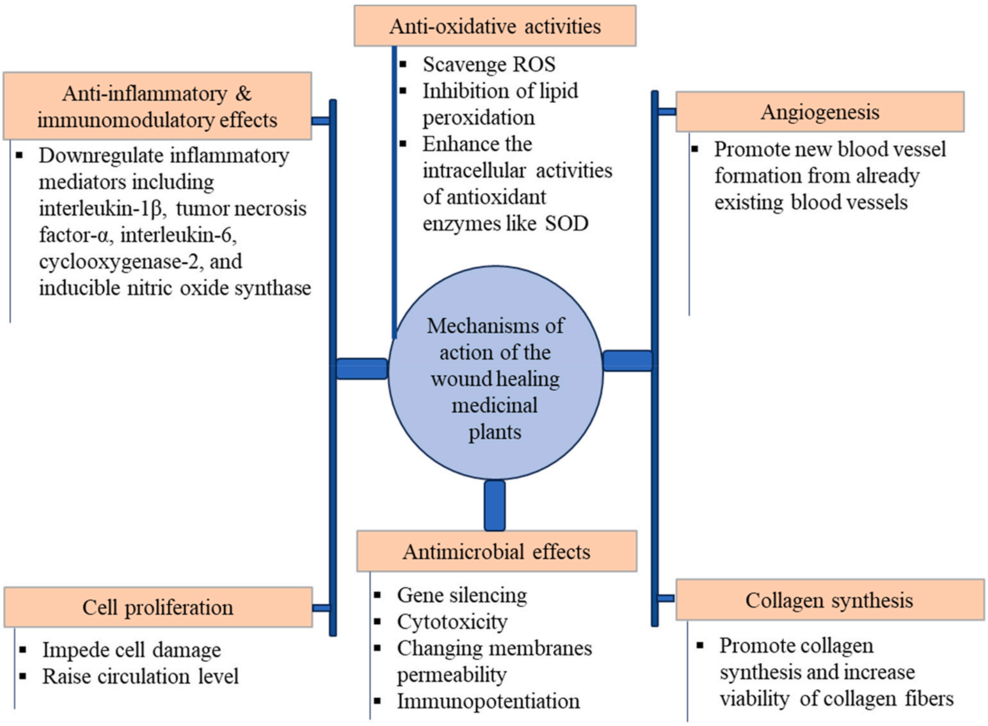

Fig. 7. Mechanisms of action of the wound healing plants based on global pharmacological reports.

[117]. Accordingly, drugs or bioactive compounds that produce inhibitory effect against lipid peroxidation tend to increase viability of collagen fibers through enhancing their strength, impeding cell damage, raising circulation level, and promoting synthesis of DNA [93]. Major phytochemical classes known to improve wound healing via antioxidant effects include tannins, flavonoids, terpenoids, sterols, and polyphenols [117,118]. For example, madecassoside (a triterpenoid) a major phytochemical of *Centella asiatica* L.Urb. has been reported to accelerate wound healing via anti-oxidation [99]. Similarly, methanol extract of *Balanites aegyptiaca* (L) Delile improved wound healing through oxidative activities [119]. In line with anti-inflammatory and immunomodulatory effect, medicinal plant extracts or bioactive compounds exert these effects by downregulating inflammatory mediators including interleukin-1β, tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), cyclooxygenase-2, and inducible nitric oxide synthase (iNOS) [100,118]. For instance, *Moringa oleifera* Lam aqueous leaf fraction containing Vicenin-2 as a major bioactive compound promoted wound healing through

anti-inflammatory effects by inhibiting the expression of inflammatory mediators such as tumor necrosis factor-α (TNF-α) [120]. The anti-inflammatory and immunomodulatory effect are critical for the reason that prolonged elevated levels of proinflammatory cytokines impair wound healing and could consequently turn wounds chronic [7,121]. As per antimicrobial effects, phytochemicals act via gene silencing, cytotoxicity, changing membranes permeability, and immunopotentiation against microbes thus controlling wound microbial infection, allowing accelerated and more effective healing [122–124]. Tannins, terpenoids, and saponins are among major phytochemicals with antimicrobial properties [93]. A case in point is when different whole plant extract fractions of *Sigesbeckia orientalis* L. exhibited antimicrobial properties against various microbes including methicillin-resistant *Staphylococcus aureus* [96]. Phytochemicals like 16β-hydro-*ent*- kauran-17,19-dioic acid (**1**) and 16α,17-dihydroxy-*ent*-kauran-19-oic acid (**2**) were implicated for the antimicrobial activities of *Sigesbeckia orientalis* L. extracts [96]. In another study, *Aspilia africana* (Pers.) C.D.Adams leaf methanol extract as well as fractions of hexane and methanol (100 μg/ml) caused varying degrees of growth inhibition of microbe clinical isolates from wounds namely *Pseudomonas fluorescens*, *Staphylococcus aureus*, strains of *Ps. Aeruginosa*, and *Staph. aureus* with MIC ranging between 0.063 and 0.5 mg/ml [125]. Increased angiogenesis is another mechanism of action through which phytochemicals of medicinal plants improve wound healing [126]. Angiogenesis involves new blood vessel formation from already existing blood vessels and this is critical in several physiological processes such as wound healing and repair of tissues [127]. Bioactive constituents of medicinal plants improve angiogenesis via upregulating mediators such as vascular endothelial growth factor (VEGF) and/or activating mitogen-activated protein kinases pathway which contribute remarkably to reducing wound contraction time [128]. Proangiogenic activity have been mainly associated with phytochemicals like polyphenols, sterols, and saponins [126]. As an example, increases in angiogenesis was shown by ethanolic leaf extract of *Bidens pilosa* L. which resulted into significantly ($p < 0.05$) faster rates of wound contraction on days 3, 6, and 9 than negative control in Wistar albino rats [129]. Epithelialisation and total healing time in *Bidens pilosa* L. treatment was comparable to that of neomycin sulfate/standard ($p > 0.05$) [129]. Indeed, the major constituents of the ethanolic leaf extract of *Bidens pilosa* L. included flavonoids. Generally, the observed bioactive compounds and associated mechanisms of action of the wound healing medicinal plants indicate potential therapeutic benefits of these plants and therefore, may be useful in the development of wound healing agents. Consistent with our findings, investigated medicinal plants used for wound healing in other countries including *Combretum mucronatum* Schum. & Thonn., *Prunus africana* (Hook.f.) Kalkman, *Mallotus oppositifolius* (Geiseler) Müll. Arg., and *Plantago major* L. have shown similar mechanisms of action [2,93,130].

It is noteworthy that pharmacological wound healing activities of one hundred eleven (67 %) of the medicinal plants used for traditional wound treatment recorded in this review have not been validated scientifically despite their continued folkloric use. These scientifically uninvestigated medicinal plants might potentially posses effective wound healing agents therefore, assessment of their pharmacological wound healing activities could prove beneficial.

3.5. Clinical studies and toxicity of the reported wound healing plants

At present, no clinical trial with standardized extracts of wound healing medicinal plants in Uganda has been reported. Globally, three clinical trials with two wound healing medicinal plants in this review have been conducted namely *Centella asiatica* L.Urb. and *Aloe Vera* (L.) Burm.f [131–133]. Both plant products showed positive results regarding wound healing [131–133] (Supplementary Table 2). The lack of clinical studies in Uganda with traditional wound healing plants can be due to paucity of preclinical study data, high cost, and stringent regulatory requirements for clinical studies [74]. This implies that the clinical efficacy and safety of plants traditionally used for wound healing in Uganda remain to be ascertained.

Much as medicinal plants exert pharmacological activities possibly useful for therapy, their phytochemicals could interact with body receptors and become toxic [134]. Due to the fact that all substances show toxicity, it is necessary to establish relative toxicity of possible therapeutic products through toxicity studies. Most plants in this review did not show acute dermal, cell, oral toxicity (Table 2 supplementary). For instance, *in vitro*, hydroethanolic leaf extract of *Leonotis nepetifolia* (L.) R. Br did not show cytotoxicity on CHO–K1 cells with $IC_{50} > 200$ μg/mL [58]. Additionally, formulation of *Jatropha curcas* L latex exerted no toxicity to human fibroblast cells, promoted production of collagen, and healed injury of cell within 24 h [135]. Similarly, ethanol stem extract of *Nicotiana tabacum* L was not toxic against L929 cell line [136]. *In vivo*, topical treatment with ointment containing ethanolic extract of *Bidens pilosa* L leaf (300 mg/kg) showed no cutaneous reactions (erythema, swelling, and vesicular eruptions) after 24 h in rats, suggesting its safety for topical use [9]. Furthermore, up to 8000 mg/kg (p.o) aqueous extract of *Asparagus racemosus* Willd root exhibited no toxic symptoms on general behavior, cardiovascular system, central nervous system, and gastrointestinal tract in Albino rats [55].

However, some plants exhibited signs of toxicity. For example, *Hoslundia opposita* Vahl extracts of dosages above 50 mg/mL had toxic effects on fibroblast cells [119]. In another study, compounds quercetin and ursolic acid from *Sigesbeckia orientalis* L exhibited cytotoxic activities [96]. Accordingly, several factors have been reported to influence toxicity of plants including concentration of potentially toxic secondary metabolites, quantity taken, dosage, body chemistry of patients, environmental factors, and age of plant [137]. This means that care should be taken when using plants with potential toxicity. Important to note is that toxicity of most recapitulated plants in this review have not been studied and majority of the reported evaluations are acute in nature. Therefore, this calls for extensive acute and chronic toxicity assessments of these medicinal plants as a requirement for ensuring safety.

3.6. Advantages and disadvantages associated with traditional medicine in Uganda

Generally, traditional medicine (TM) is deemed relatively cheaper than conventional medicine since in some cases TM are made from simple home remedies [21]. Additionally, TM has been recorded to be more accessible by the people in different communities compared to modern medicine, an important criterion for an effective primary health care service as per Alma Ata declaration [29].

This is supported by the fact that more than 80 % of the population in Uganda rely on TM for treating various diseases [20]. The heavy reliance on TM by Ugandans may be attributed to shortage of health facilities, modern medicine, and personnel [29,138]. Also, TM has a wide acceptability among the population due to its availability and cultural preference [21]. Another advantage is that TM remedies are largely perceived to be less harmful because they are derived from natural products [139]. Moreover, it is claimed that TM potions treat many diseases simultaneously as they consist of various components and patients prefer these potions to taking many different tablets as is the case in modern medicine [29].

However, there are many disadvantages associated with TM reported among people in Uganda and these include; First, a number of TM therapies lack scientific proof for their efficacy and consequently, morbidities and mortalities have been recorded due to treatment failure and toxicities [29]. Additionally, TM potions are in most cases not standardized [29] and indeed, no report retrieved in this review provided precise dosage for wound healing remedies in Uganda. Another disadvantage is that in most cases, diagnosis in TM is not precise and seeking treatment from traditional healers before being diagnosed from modern health facilities may lead to delay in treatment and further complications [140]. Furthermore, simultaneously receiving TM and orthodox medicine may lead to drug interaction, resulting in to adverse events [29]. A classic example beyond Uganda is, combination of tricyclic antidepressant-yohimbe (*Pausinystalia yohimbe*) induced high blood pressure [141]. Also, TM poses a threat to nature for example, most medicinal plants used for wound healing in Uganda are obtained from the wild and this practice could cause extinction of endangered species [29]. On this basis, efficacy and safety claims of TM needs to be ascertained [142] and concerted efforts towards addressing other TM associated challenges such as non-standardization are required.

4. Conclusions

Ethnomedicinal studies have revealed several medicinal plant species used for treating cutaneous wounds in Uganda. The present review retrieved and compiled ethnomedicinal and ethnopharmacological information of these wound healing plants (165 species). Of the 165 species, only fifty-four (33 %) of the plants have been experimentally validated for their wound healing activities in different pharmacological, phytochemical, and toxicological studies, including [143–376] (Supplementary Table 2). The findings confirmed that some plants possess substantial potential for wound treatment. Subsequently, the preliminarily investigated plants with positive wound healing properties require further evaluation for possible development and use as complementary or alternative wound therapies. Additionally, wound healing properties of the scientifically uninvestigated plants needs examination in a bid to discover and develop wound healing therapies. The ethnomedicinal and ethnopharmacological information contained in this review provides reference for future studies, relevant to development of wound therapeutic products.

Ethics statement

Review and/or approval by an ethics committee was not needed for this study because it reviewed primary data electronically.

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Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Roggers Gang: Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft. **Denis Okello:** Visualization, Writing – review & editing. **Youngmin Kang:** Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e29717.

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