International Organization for Chemical Sciences in Development

Working Group on Plant Chemistry

CHEMISTRY, BIOLOGICAL AND PHARMACOLOGICAL PROPERTIES OF AFRICAN MEDICINAL PLANTS

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African traditional healer and *Harpagophytum procumbens* (Pedaliaceae)
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Contents

5. Wound healing with plants: the African perspective

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Introduction

A vast range of aspects have been covered already on wounds. These include: definitions (Ellis and Calne 1977), types, extent (Macfarlane and Thomas 1972), the socio-economic implication and the comfort, well being, ambulation as well as restoration of the function of wound sites. There is similarly a good coverage in the scientific press on wound healing including the historical (Fish and Owen Dawson 1967), medical and clinical aspects, the complications of wounds (Macfarlane and Thomas 1972), chemical substances responsible for and factors influencing wound healing (Macfarlane and Thomas 1972; Fish and Owen Dawson 1967; Elliot 1994; Schilling 1968; Douglas 1963).

A brief discussion of the aspects already covered is presented here with a view to familiarizing the reader with the subject matter. Emphasis will be placed on wound healing agents (WHAs) some of which are either natural, synthetic or derived products which can be sourced from plants or plant products. A list of such plants used for wound healing in Africa including the families, active morphological parts, their specific roles (modes/mechanism of their action), isolated active chemical components responsible for wound healing activity as well as their structure-activity relationships (SAR) where known will be discussed.

Wounds

Wound is a collective term for conditions in which there is interruption or damage to the structural integrity of the skin or the underlying tissues (Ellis and Calne 1977). It includes abrasions, abscesses, bites, burns, blisters, boils, bruises (contusions), clean cuts (incisions), fractures, gunshot, injuries, punctures, skin lesions, sores, scalds, sprains, tears (lacerations) and ulcers.

Wounds resulting from injuries, bruises, scalds, cuts, abrasions from road traffic accidents etc., and burns constitute the majority of cases reported at the "Casuality" or "Accidents and Emergency" Units of most hospitals. Patients with intentional or

planned wounds *i.e.* surgical wounds *e.g.* excision, orthopedic and plastic surgery, as well as wounds resulting from other already existing medical problems *e.g.* abscesses, boils, ulcers, sores, blisters also constitute a large number of the complaints of in-patients of many hospitals. The occurrence or infliction of wounds is usually of great concern. Chronic wounds, particularly in the elderly (Frantz and Gardner 1994; Lau *et al.* 1994) represent a worldwide problem. The failure of chronic wounds to heal remains a major medical problem (Bhora *et al.* 1995).

The covering of wounds has of necessity always been practiced by man. It was, for a long time, the only branch of the healing arts (Fish and Dawson 1967). As a matter of must, wounds have to be treated, and in good time, to avoid any grave complications such as hemorrhage, infection, development of contracture with subsequent deformity, limitation of joint use, scar formation, scar breakdown and adhesions to underlying tendon or bone (Macfarlane and Thomas 1972). Delayed healing or failure to heal due to poor skin integrity or a patient's multisystemic disorder (Patel and Mach 1994) can also result in keloid formation.

Treatment/management of wounds

The proper way to manage wounds is summarized as follows:

(1) The injured part should be handled gently (First Aid).

(2) The bleeding must be controlled.

(3) The pain must be relieved.

(4) Any shock must be prevented or controlled.

(5) Prophylactic measures against superimposed infections including tetanus and gangrene need to be instituted.

(6) A sterile, protective dressing should be applied immediately.

(7) The wound area or site must be cleaned and shaved. The cleaning can be done under local or general anesthetics, and irrigated with normal saline to remove all foreign bodies (debridement), damaged fat, fascia and muscle; but all essential structures such as blood vessels and nerves should be carefully preserved.

(8) All the edges of the wound must be brought together (Macfarlane and Thomas).

Wound care should generally provide support for the natural healing process and progress (Rakel 1993) and reduce cost. It must considerably decrease the patient's discomfort, morbidity and prevent prolonged hospitalization (Goldenheim 1993).

Cost containment as well as the provision of effective care are the principal goals of wound management (Ratliff and Rodeheaver 1995). Wounds must be attended to very early because the cost of managing chronic wounds in terms of staff time and dressing materials is phenomenal (Benbow 1995). The type of wound, its subsequent treatment and the defense mounted by the injured individual, all affect or

mediate microbial infection of wounds. The pathogenicity of the microbes is also of great importance. Wounds can be protected from exogenous microfloral contamination with dressing *e.g.* hydrocolloid dressing with the right moisture content (Mertz and Ovington 1993).

The nutritional status, presence of underlying diseases or co-administration of drugs *e.g.* antineoplastics, anticoagulants and high-doses of steroids, all affect wound repair (Telfer and Moy 1993). Prevention of fibrosis and scar formation are also important clinical considerations in wound healing.

Wound repair

Wound repair is a part of the wound healing process and the stages involved are integrated. In spite of continued research concerning wound repair, it is still not clear precisely what begins the wound healing process and what ultimately stops it (Esterhai (Jr.) and Queenan 1991). It is, however, well known that certain chemicals appear only at the onset of wound, some persist throughout, while others are found only at the end of the wound healing process. Some aspects of the cellular basis and the involvement of intermolecular macromolecules in wound repair have been reviewed (Schilling 1968). After cell injury and following several other occurrences, in parallel or in series, concentric lamellar configurations occur. Some lamellar arrangements and proliferations also occur in the cell and cell contents. Certain chemical substances *e.g.* acid hydrolases are released, though this may be restricted to the wound site (Schilling 1968).

The basic science and clinical aspects of wound repair and healing consist of the following three phases:

(1) The inflammatory phase is marked by platelet accumulation, coagulation and leukocyte migration.

(2) The proliferative phase is characterized by re-epithelialization, mitosis, angiogenesis, synthesis, fibroplasia and wound contraction.

(3) Finally, the remodeling of the extracellular matrix phase takes place over a period of months during which the dermis responds to injury with the production of collagen and matrix proteins and then returns to its preinjury phenotype.

Wound healing

Wound healing is the art of restoring the structural integrity of a disrupted skin or underlying tissues of a deep cut. It comprises:

(1) contraction (gradual approximation of the wound edges),
(2) restoration of the patient to health and
(3) return of body function to normal (Elliot 1994).

Although the wound healing processes are not yet fully understood, they are known to be chemically mediated (Douglas 1963). This is corroborated by the fact that pouring, smearing or impregnating active medicinal compounds (such as gums and other cellulose materials, capsicum, white lead, nettle seed, saline ammoniac and mustard) on the surface of wounds and binding up such in wound protectant materials (like silk or linen) aids the healing of wounds. Antimony litharge, oil, water and wines were also amongst items used as dressings for wounds. Lion grass and oil of roses, honey, starch, aromatic herbs and substances such as borax, salt, spiders webs and boiled snails have also been used. Frankincense, aloes, white of egg and hare's fur were used as styptic for some wounds (Elliot 1994).

The healing of wounds is by the deposition of connective tissue - which is the primary unit of repair. It is a form of a universal cement which appears whenever tissues are wounded (Peacock and van Winkle 1976). It is a fluid, distributed throughout the body, which keeps the various tissues in good health and repairs them when they are injured (Elliot 1994). The connective tissue is concerned with supporting the framework of the body (Peacock and van Winkle 1976). It is found in virtually every part of the organism. Wound healing could also be effected by preventing the alteration of this fluid as well as by maintaining its balance (Elliot 1994).

Wound healing research has produced some startling discoveries during the past decades. For instance, cutaneous wounds created *in utero* are histologically indistinguishable from intact, unwounded tissue (Broker and Reiter 1994). Topical application of hyaluronic acid to wounds in adult diabetic rats leads to enhanced epithelial migration, whilst the addition of cytokine transforming growth factor (TGF-B) to fetal wounds causes an adult like healing reponse with fibrosis and inflammation. When neutralizing antibody to TGF-B was used in adult wounds, it caused an enhanced healing with a more normal dermal architecture with few macrophages, few blood vessels and less collagen (Bleacher *et al.* 1993).

In addition to the local response to injury, there are also sequences of clinical, metabolic and hormonal events of a general nature, called 'recovery or convalescence' which are designed for an ultimate return to full health (Macfarlane and Thomas 1972).

Wound healing does not take a single course of event, but rather a synopsis of events and changes that occur at the cellular and subcellular levels involving purely chemical, biochemical, physical, immunological and other processes, either one after the other or simultaneously. The networks are integrated and sequential, as well as tightly controlled (Clark 1993).

Factors influencing wound healing

Wound Healing is influenced by many factors (Macfarlane and Thomas 1972) including local and general (systemic) factors.

Local factors - These modify the healing process, prevent rapid and effective healing which requires prompt and complete healing or they interfere with the process of repair. They include:

- Inaccurate skin apposition, large tissue defects (creation of gaps).
- Foreign bodies - dead or damaged tissues, blood clots, etc.
- Impaired blood supply- slows healing and inhibits fibroplasia which can cause death of tissues and inadequate defense against infection. The impairment may be due to damage to an artery.
- Venous and lymphatic stasis may cause edema and as such lead to deficient tissue perfusion.
- Local infection - this must be prevented, as subsequent treatment with antibiotics/ antiseptics may interfere with wound healing.
- Complete immobilization of the wounded area may accelerate repair by avoiding damage to the delicate capillaries and regenerating cells. For instance, this value is apparent in dealing with fractures. It may not even be of value in dealing with soft tissues injury, and it may not even be achievable in wounds of heart, lung and arteries.
- Hemorrhage.
- Suture materials.
- Irradiation.

General (systemic) factors - These may be grouped as follows:

(A) Nutritional disturbance which includes:

- Protein deficiency - this is due to lack of collagen in the wound and dehiscence is common in the malnourished, the essential amino acids- cysteine and methionine, being of particular importance.
- Lack of Vitamin C - this leads to defective formation and maintenance of collagen

(B) Others, which include:

- Lathyrism
- Methionine
- Hormones (hypophysis, adrenals, thyroid and gonads). It has not been proved that cortisone or other adrenal steroids will, even in high therapeutic dosage, impair wound healing.
- Anemia - there is little evidence that anemia alone interferes with wound healing, but problems caused can be associated with hypo-proteinemia.
- Age - the young heal better than the elderly but the factors involved are not obvious. This may, however, be due to the fact that the young is still growing,

and certainly more rapidly when compared with the elderly. Therefore, growth in wound healing may be more enhanced in the young.

- Other diseases - systemic disorders, such as diabetes, uremia, jaundice, Cushing's disease and disseminated neoplasia, but no other specific causes are obvious other than hypoproteinemia and lack of vitamin C.

Precautions for appropriate wound healing

Wounds should not be allowed to: get infected, as infected wounds scar more severely (Ward and Saffle 1995), heal more slowly, and re-epithelialization is more prolonged. There is also the risk of systemic infection and eventually death through an infected open wound (Schilling 1968). In addition, wounds should not dry out, as desiccation kills healthy cells. Wound healing is mainly a prerogative of the body, the conditions for adequate healing, However, must be provided by the patient (Rakel 1993).

Chemical wound healing agents (WHAs)

There is a host of agents that are employed in wound healing, namely, chemical, electrical, surgical, thermal agents etc. However, chemical agents, mainly as dressings, out number other agents used in wound healing.

Dressings are materials applied to protect a wound and favor its healing (Fish and Dawson 1967). Much thought has been given to ways of increasing the efficiency of dressings as wound healing agents and means of facilitating their quicker and neater application (Fish and Dawson 1967). Fibrous dressings are known to be fibrous on the macroscale, the microscale and at the molecular level, being composed of flexible, linear macromolecules (polymers) with regular repetition of chain building units (Fish and Dawson 1967). These are of great advantage in the process of sealing up wounds. Some dressings interact with hemoglobin to form a coagulum. This is attributable to the presence of polyanhydro-glucuronic acid *e.g.* in oxidizable cellulose. For this reason, uronic acids and their derivatives are preferred to oxidizable cellulose (Fish and Dawson 1967).

The benefits and advantages of dressings over other well known WHAs, including antibiotics, are:

(1) If wound infection is adequately prevented, there will be no need for wound healing agents (WHA) such as antibiotics, antiseptics, vaccination, surgery etc., since normal wound healing is primarily by deposition of connective tissue (meshwork of fibrils etc.) - the micellar seals up the wounds in plants too (Ikan 1969). However, sutures may be inevitable in cases of deep/wide wounds, the edges of which have to be appropriated.

(2) If such complications as arise from the use of these groups of WHAs is prevented, probably through the use of appropriate dressings, a lot of

improvements would be achieved in wound healing and there will be no need for many of the procedures observed in the management of wounds. The physical aspects of WH, such as aesthetics, lack of deformity and eventual handicap (Elliot 1994) also would be preserved. Extended time of healing, a great disadvantage, would be minimized.

The need to close or cover up wounds to prevent infection cannot be over emphasized, though the presence of some infection may not necessarily prevent the healing of the wound *i.e.* open wounds do not need to be sterile to heal (Clark and Sherman 1993). Wound closure is the ultimate goal of burn care (Smith (Jr.) *et al.* 1994) and the art of closing up wounds has been practiced for long (Fish and Dawson 1967).

Even in clinical practice of wound management, moist occlusive dressings with or without medication, are preferred to many other forms of wound management, since occlusion enhances wound healing primarily by preventing wound desiccation. As a result, epidermal necrosis or eschar formation do not occur thus enabling the wound to re-epithelialize more quickly (Kannon and Garrett 1995). Occlusive dressings have been found to reduce inflammation and subsequent scarring (Hulten 1994).

Moist wound healing agents are associated with hydrocolloid dressings which may provide an alternative treatment modality for certain "partial - unclean" injuries. These dressings produce good functional and cosmetic results, rapid re-epithelialization, and improve patient comfort (Smith (Jr.) *et al.* 1994). Hydrocolloid dressings facilitate the healing of wounds via granulation tissue formation, they keep wound moist and solve many of the practical problems associated with the traditional method of keeping the metal plates, exposed bone and tissues moist (Sochen 1994).

Initial results of a pilot study based on the application of newer dressing materials to animal wounds was reported to support their recommendation for use in human wounds (Cockbill and Turner 1995). Use of collagenous matrices in wounds, made of native bovine collagen I fibres, hyaluronic acid, fibronectin or elastin was added and covered with a protective semi-permeable urethane membrane (De vries *et al.* 1995). Calcium alginate dressing significantly reduced the pain severity and it is easy to use for the nursing personnel (Bettinger *et al.* 1995).

"Chemical component impregnated dressings" *e.g.* saline solution - impregnated dressing followed by hydrocolloid dressing is also advocated (Morris *et al.* 1994). The use of dressing of conventional gauze in wound care and management has such disadvantages as increased frequency of change: harm and associated pain while changing; it also affects the function, freedom and hygiene of the patient (Wijetunge 1994).

Intrasite gel is a hydrogel designed for the debridement of necrotic tissue and effective desloughing, clearing the way for effective wound healing. It is also designed for wounds that are granulating and epithelializing (Williams 1994).

Duoderm - Is an hydrocolloid dressing (Hulten 1994) which lyses fibrin more effectively than others. Pain is significantly reduced when wounds are covered with occlusive dressings (Field and Kerstein 1994).

Hydrocolloid polypeptide biomaterials, *e.g.* Procuren - (William and Da Camara 1993) and synthetic polymers including Polyvinylpyrollidone Iodine (PVP-I) *e.g.* Betadine preparations have also been used (Rakel 1993; Goldenheim 1993).

Some chemicals involved in wound healing

The connective tissue is composed of fibrils, cells, amorphous element or ground substance. The fibrils in turn contain chemical compounds such as collagen (albuminous), reticulin, elastin, proteoglycans and glycosaminoglycans (Lorenz and Adzick 1993; Meyer 1958). These substances intended to heal the wounds are usually applied (Elliot 1994) either to:

- make the wound cicatrize,
- make the flesh grow,
- make the growing flesh firm,
- arrest hemorrhages, or
- remove foreign bodies.

The profiles of fetal proteoglycans, collagens and growth factors are different from those in adult wounds. High level of hyaluronic acid and its stimulation is more rapid and there is highly organized collagen deposition (Bleacher *et al.* 1993; Broker and Reiter 1994). Growth factors are characteristically less prominent in fetal wounds. Topical application of wound healing promoting agents *e.g.* regulated amounts of growth factor to wounds may soon be possible.

All these three compounds viz;- proteoglycans, collagens and growth factors characterize fetal wound which heals without scar formation. These findings are of advantage in the clinical application in the modulation of adult fibrocytic disease and of abnormal scar forming conditions.

Biomaterials *e.g.* biodegradable biopolymers such as some acids and peptides have been reported to enhance dermal and corneal wound healing. This acceleration improves the quality of regenerated tissue, restricts the extent of fibrosis and reduces the risk of microbial infection (Sochen 1994).

Topical therapeutic agents have also been shown to be quite effective in the management of open skin wounds (Ward and Saffle 1995) as or in addition to moist dressings and protectants (Leitch 1995). Growth factors (Falanga 1993), moist bio-occlusive dressings with or without medication *e.g.* alginates etc. (Piacquadio and Nelson 1992) are also used in wound treatment as they provide moist wound healing environment. Pretreatment of skin with all-*trans* retinoic acid (tretinoin) has been shown to enhance wound healing dramatically in photodamaged skin (Popp *et al.* 1995). Acidic firoblast growth factor (aFGF) has been shown to be a potent

mitogenic and chemotactic agent for the principal cellular constituents of the skin. It increases wound closure in a dose-dependent manner. It increased granulation tissue formation and re-epithelialization throughout healing. It has potential therapeutic applications for promoting healing of dermal ulcers, especially in healing-impaired individuals (Gerstein *et al.* 1993).

Some wound healing chemical compounds are enzyme inhibitors or antienzymes *e.g.* Echinacin (antihyaluronidase) from *Echinacea* species, lysyl oxidase in *Tridax* spp., and Aloe carboxypeptidase from *Aloe* sp., as well as kauranoic acid which inhibits Bovine serum albumin coagulation. Others are hormones *e.g.* traumatic acid, a straight chain dicarboxylic acid. It is a specific wound hormone which is very active in inducing meristematic activity.

These wound healing chemical compounds have been classified as wound healing accelerators. Their biological activities vary (just as do their structures) and include: anti-inflammatory, antipyretic, analgesic, antimicrobial (antibacterial, antifungal and antiviral) detoxicant, deobstruent, hemostatic, anti-enzyme, antiseptic, anesthetic, nutrient, immunosupressive, peripheral stimulant, astringent and cicatrizant.

Acidic firoblast growth factor (aFGF) has also been found to be one of the most effective wound healing components of the human system. It has potential therapeutic applications for promoting the healing of dermal ulcers, especially in healing-impaired individuals (Popp *et al.* 1995) and has been recommended for that use.

Mucopolysaccharides, which are the major components of the connective tissue and the ground substance are also acidic in nature, examples include: hyaluronic acid, chondroitin, keratan, dermatan and heparin sulfate (Peacock and van Winkle 1976). Some of these compounds have been applied directly as dressings to wounds and hyaluronic acid, chondroitin sulfate (De vries *et al.* 1995; Pruden 1964) have shown good results. They contain at least one uronic acid moiety. Generally, polyuronides are the chief constituents of most mucilages (Trease and Evans 1989) which have also been used in wound healing. In plants, mucilages and gums are well known to bathe cells and keep them healthy as well as repair them when wounded. Alginic acid is a related compound which is also in use (as alginate) for wound healing (Bettinger *et al.* 1995).

Wound healing situation in plants

In plants, gums and related compounds effect wound healing, by acting as protective agents that cover accidental wounds (Ross and Brain 1977). The cellulose fibrils are arranged in a multidimensional net in the primary cell wall whilst the middle lamella contains a plastic cementing layer that holds the adjacent cells together. The cellulose fibrils are arranged with specific orientations such that adjacent layers re-inforce one another (Ross and Brain 1977). This deposition pattern seals wounded cells (Ikan 1969) and could be likened to mucopolysaccharides (glycosaminoglycans) which are biological polymers acting as the flexible

connecting matrix between the tough protein filaments in cartilage to form a polymeric system similar to re-inforced rubber (Meyer 1958).

When a plant is wounded, the P-protein, a cell wall material called calose, produces plugs that seem to block the sieve platter. Normal cells do not develop such plugs. The major function of the P-protein is to seal off the sieve cell by blocking the sieve plates thereby eliminating leakage of the assimilates when the plant is wounded (Devlin and Witham 1986). The slime layer is a secretion of complex polymers around the outside cell wall. It may be diffuse or thick. Usually, these polymers are polysaccharides but polypeptides are found in some species (The Pharmaceutical Handbook, 19th edn. 1980).

Plants possess the groups of chemical compounds implicated in the primary repair of tissues which basically include: polysaccharides and specifically, glycosaminoglycans, polyuronides (Ikan 1969), some of which are found as main constituents of mucilages and gums (Ross and Brain 1977; MacGregor and Greenwood 1980). Some of these compounds which also possess antibiotic and/or antimicrobial property would be of double advantage in wound treatment.

A group of chemical compounds which are released by plants after and in response to injury is referred to as phytoalexins. They combat infections and have been tested on zoological pathogens, some of which may be implicated in wounds (Adesanya and Pais 1995).

If latex, waxes, resins, balsams, mucilages and gums are produced, they function for the purpose of wound repair in some plants. They may well function similarly in some animals and humans, especially since some of their current uses have extended to those related to, or primarily intended to achieve wound healing, such as in the cases of cellulose and its derivatives (Fish and Dawson 1967; Ikan 1969; Burkill 1985).

Propolis, a resinous substance found in beehives collected by bees from buds, contains caffeic acid and cinnamyl alcohol. It has been used in the treatment of wounds (Magro-Filho and de Carvalho 1994) just as honey is used (Komolafe 1996). In fact, in some parts of western Nigeria, it is believed that any wound that does not heal with the application of honey may never heal (Komolafe 1996). The future use of plant extracts externally in the management of wounds, is bright because there is a growing interest in the clinical practice of wound management with the use of chemical component - impregnated dressings (Morris *et al.* 1994).

Criteria for selecting prospective wound healing agents

There is a pointer in the scientific literature to the fact that with respect to prospective wound healing agents, emphasis should be on ways of increasing the efficiency of dressings as wound healing agents since they can be applied quickly and neatly (Fish and Dawson 1967). This is a result of the fact that the regeneration of tissues, in the last analysis must be a matter of the synthesis of new chemical substances in the wound, since the processes involved in wound healing are

emical in nature. It is in this area that most advances are to be hoped for in the ture (Douglas 1963).

The utilization of medicinal and aromatic plants and plant constituents in the celeration or promotion of wound healing seems to be the ultimate, and is actively vocated, especially because wound healing has been very successful with the use natural products (Elliot 1994).

Plants used in wound healing in Africa

Some of the clinical practices of wound management can be likened to the procedures in African traditional medicine and Chinese traditional medicine *e.g.* in bone setting, fracture management, uvulectomy, abdominal surgery, trephination and circumcision (Sofowora 1982, Sofowora 1996).

The African traditional medical practitioners have, over the years, also been treating various wounds with herbal remedies. A compilation of such plants which have been or are in use for the treatment of different types of wounds in Africa is presented in Table 5.1. The plants are used as first aids, in cleansing, washing of wounds, in the extraction of pus, as well as for infected and festering wounds. Other uses include the treatment of boils, abscesses, cuts, skin lesions, wounds, snakes and dog bites, insect stings, bruises, pains, soothing of burns, ulcers, fractures, trauma, sprains, aches, suppurations, inflammations, wounds, scabies, rabies and to dress wounds.

Many of these plants are reported to be effective for diverse activities but all directly or indirectly culminate in the cure or healing of wounds. This implies that their mechanism or mode of action varies. Some act as cicatrizants, antiseptic, antifungal, antiviral, antibacterial, antipyretic, anesthetic, analgesic, hemostatic, antimicrobial, anti-inflammatory, growth promotor, collagen synthesis/fibroblast formation enhancer; whilst others enhance the closing up of wounds with or without scar formation. Yet others are glycosaminoglycan synthesis stimulators.

Most medicinal plants used in the healing of wounds, specifically accelerate the process of wound healing. A majority of these plants have been in use for the purpose of wound healing for a long time now, and a number of them are within reasonable reach of and can be identified with relative ease by the villagers. Some of the plants are reputed to be quite effective and to yield instant results. Most of the plants are used fresh either as juice or sap or latex, while a few are used as extracts against the various types of wounds mentioned above. The plant part(s) are usually rubbed in between the palms and the juice squeezed onto the wound surface with or without tying or binding up with protective bandage.

Mucilages are used as a soothing application to the mucous membranes (Ellis and Calne 1977). The mucilage of Slippery elm *Ulmus rubra* bark is used for its soothing effect on inflamed tissues either in the crude state or in the form of lozenges.

Table 5.1. African plants used in wound healing

Family/Plant Name	Part used	Wound Type/Uses	Ref.
Acanthaceae			
Brillantaisia lamium	juice	sores	Dalziel (1956, p. 450)
Elytraria marginata	leaves	fresh wounds	Dalziel (1956, p. 11)
Graptophyllum pictum	leaves	ulcers, abscesses, cuts, broken bones	Holdsworth and Rali (1989), Ozaki *et al.* (1989)
Hypoestes verticillaris	plant sap	sores	Dalziel (1956, p. 15)
Justicia shimperi	leaves	fresh wounds	Dalziel (1956, p. 18)
Phaulopsis falcisepala		wound dressing, sores	Adesomoju and Okogun (1985)
Phaulopsis falcisepala	whole plant, juice, root	fresh wounds, sores	Dalziel (1956, pp. 23, 24. 452)
Thomandersia hensii	plant sap, leaves	external ulcers, sores	Dalziel (1956, p. 28)
Amaranthaceae			
Amaranthus caudatus	seed	sores, antifungal	Watt and Breyer-Brandwijk (1962, p. 14), Kubas (1972).
Amaranthus paniculatus	whole plant	sores	Watt and Breyer-Brandwijk (1962, p. 16)
Boophone disticha	fresh/dry leaves	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 23)
Cyathula postrata	leaves, twigs	fresh wounds, burns, sores	Dalziel (1956, p. 58)
Cyathula spathulifolia	stem fruit, seed	sores	Watt and Breyer-Brandwijk (1962, p. 18)
Grinum kirkii	whole plant	sores	Kokwaro (1993, p. 248)
Haemanthus coccineus	fresh leaves	ulcers	Watt and Breyer-Brandwijk (1962, p. 33)
Hypoxis rooperi	root juice	anti-burn	Watt and Breyer-Brandwijk (1962, p. 41)
Anacardiaceae			
Lannea barteri	bark	sores, ulcers	Dalziel (1956, p. 76)
Lannea velutina	bark	fresh wounds, ulcers	Dalziel (1956, p. 80)
Schinus molle	bark, leaves	sores	Dalziel (1956, p. 87)
	oleoresin	used as a cicatrizant	Martinez (1984)
Sorindeia longifolia	bark, leaves	sores, ulcers	Dalziel (1956, p. 341)
Trichoscypha longifolia	bark, leaves	fresh wounds, sores, ulcers	Dalziel (1956, p. 96)
Annonaceae			
*Annona senegalensis***	bark, root, leaves	used as dressing, sores	Burkill (1985); Adesakin . personal communication
Enantia chlorantha	bark, leaves	fresh wounds, ulcers, sores	Dalziel (1956, pp. 4, 111, 112)
Hexalobus crispiflorus	bark	fresh wounds	Dalziel (1956, p. 114)
Uvaria chamae	leaves juice	fresh wounds, sores, swelling	Hedberg *et al.* (1983a), Arnold and Gulumian (1984)
Xylopia aethiopica	bark	sores	Dalziel (1956, p. 8)
		used to dress umbilicus after cord stump has dropped off	Ayensu (1978).
Apocynaceae			
Alafia lucida	leaves	sores	Dalziel (1956, p. 137)
Alafia multiflora	latex	fresh wounds	Dalziel (1956, p. 137)
Alstonia bonnei	juice	fresh wounds	Adesakin, personal communication
Conopharyngia usambarensis	latex	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 81)
Diplorhynchus condylocarpon	bark	fresh wounds, snake bites, sore eyes	Watt and Breyer-Brandwijk (1962, p.83), Chhabra and Uiso (1991)
Funtumia africana	leaves	anti-burn	Dalziel (1956, p. 150)
Isonema smeathmanni	latex	sores	Dalziel (1956, p. 157)
Strophanthus preussi	sap	fresh wounds, sores	Dalziel (1956, p. 183)
Araceae			
*Colocasia esculenta***	rasping	applied to maturate boils	Burkill (1985)
Araliaceae			
Polyscias fulva	leaves	external ulcers	Adjanohoun *et al.* (1993, p. 45, 321)
Asclepiadaceae			
*Calotropis procera***	juice	used as dressing	Burkill (1985)
Kanalua laniflora	latex	sores	Dalziel (1956, p. 229)
Tylophora conspicua	leaves	fresh wounds, ulcers	Dalziel (1956, p. 390-391)
Asteraceae			
Ageratum conyzoides	latex	fresh wounds, antimicrobial	Watt and Breyer-Brandwijk (1962, p. 197), Kokwaro (1993, p. 69)
Anisopappus africanus	leaves	sores	Kokwaro (1993, p. 69)
Artemisia tridentata	leaf oil	wounds	Northway (1975)
Bidens bipinnata	juice	fresh wounds	Dalziel (1956, p. 416)
Bidens pilosa	leaves	external ulcers, antiseptic, skin lesions, anti-inflammatory, wounds, cuts	Adjanohoun *et al.* (1993, p. 61, 321), Gonzalez *et al.* (1993)
Blumea aurita	leaves	ulcers	Dalziel (1956, p. 452-3)
Calendula officinalis[a]	flowers, tincture	gunshot wounds	Reynolds (1886), Livezey (1868), Rao *et al.* (1991).
Crassocephalum picridifolium	leaves	fresh wound	Dalziel (1956, p. 462); Kokwaro (1993, p. 74)
Echinacea angustifolia[b,c]	aq. extract (echinacin)	leukocytes stimulation, activation of the reticulo-endothelial system	Nikol'skaya (1954), Tunnerhoff and Schwabe (1955a,b, 1956, 1965), Zoutewelle and van Wijk (1990),
Echinacea pallida	extract	antibody formation	Kabelik (1965)
Echinacea purpurea[c]	extract	antibody and fibroblast formation	Kabelik (1965)

Table 5.1. Cont'd

Family/Plant Name	Part used	Wound Type/Uses	Ref.
Asteraceae cont'd			
Gutenbegia fischeri	leaves	sores	Kokwaro (1993, p. 76)
Gynura cernua	fresh juice	sores	Dalziel (1956, p. 418)
Helichrysum appendiculatum	leaves	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 237)
Helichrysum foetidum	leaves	sores	Dalziel (1956, p. 477)
Helichrysum pedunculare	leaves	sores	Watt and Breyer-Brandwijk (1962, p. 239)
Notonia spp.	leaves	fresh wounds	Kokwaro (1993, p. 79)
Senecio fuchsia	extract	wounds	Nikol'skaya (1954)
Tridax procumbens	fresh leaves	fills wounds dead space	Diwan *et al.* (1982), Sarma *et al.* (1990), Udupa *et al.* (1991),
Vernonia aemulans	whole plant	fresh wounds	Kokwaro (1993, p. 83)
Vernonia cinerea	whole plant	fresh wounds, boils, blisters	Kloos (1977), Abebe, (1986), Desta (1993)
Vernonia homilantha	leaves	sores	Kokwaro (1993, p. 85)
Wedelia chinensis	leaves	sutured wounds	Hedge *et al.* (1994)
Basellaceae			
*Basella alba***	stem, leaves	poultices	Burkill (1985)
Bignonaceae			
Kigellia africana	inner bark	wounds, abscesses, anti-inflammatory	Dalziel (1956, p. 256), Khan *et al.* (1978)
Newbouldia laevis	bark	inflamed sores, ulcers, antibacterial	Dalziel (1956, p. 444), Le Grand (1989)
Stereospermum kunthianum	bark	ulcers, skin lesions	Dalziel (1956, p. 265-266), Desta (1993)
Bombacaceae			
*Adansonia digitata***	bark, dry leaves	cleaning sores, 'laali' in West Africa	Burkill (1985)
*Bombax buonopozense***	bark ointment	skin-diseases, ringworm	Burkill (1985)
*Ceiba pentandra***	bark decoction	as topic on swelling and to wash sores	Burkill (1985)
*Rhodognaphalon brevicuspe***	bark and leaves liquor	sores and as poultices on 'blue boil'	Burkill (1985)
Boraginaceae			
Alkanna tinctoria[1]	root	leg ulcers	Papageorgiou (1978a,b)
*Cordia myxa***	extract	emollient plaster to maturate abscesses	Burkill (1985)
Heliotropium indicum[2]	whole plant	ulcers, wound healing acceleration	Dalziel (1956, p. 426), Schoental (1968)
Pulmonaria officianalis	leaves	wounds	Nikol'skaya (1954)
Symphytum officinale	leaves	wounds	Goldman *et al.* (1985)
Capparidaceae			
Gyandropsis gynandra		fresh wounds	Adjanohoun *et al.* (1993, p. 113)
Chrysobalanaceae			
Parinari excelsa	bark	fresh wounds	Dalziel (1956, p. 383-385)
Cochlospermaceae			
*Cochlospermum tinctorium***	leaves pulp	wet dressing to maturate abscesses	Burkill (1985)
Combretaceae			
Combretum cinereopetalum	whole plant	external ulcers	Adjanohoun *et al.* (1993, p. 123, 321)
Combretum gueinzii	leaves	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 193)
Commelinaceae			
Aneilema lanceolatum	juice	sores	Dalziel (1956, p. 465)
Aneilema pomeridianum	whole plant	sores	Dalziel (1956, p. 428)
*Commelina benghalensis***	extract, sap	as poultice for sore feet, burns	Burkill (1985)
Commelina diffusa	whole plant	fresh wounds, ulcers, bruises, sores	Caceres *et al.* (1987), Adjanohoun *et al.* (1993, pp. 127, 345)
Connaraceae			
Roureopsis obliquifoliolata	leaves	fresh wounds	Dalziel (1956, p. 524)
Convolvulaceae			
Bonamia mossambicensis	leaves, root	fresh wounds, antifungal	Sawhney *et al.* (1978), Khan *et al.* (1978), Kokwaro (1993, p. 88)
Ipomea involucrata	leaves	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 337)
Ipomea pes-caprae[3]	leaves	decreases tissue destruction in jelly fish sting	Pongprayoon *et al.* (1987)
Crassulaceae			
Kalanchoe spathulata[1]	fresh leaves	wounds, prevention of scar formation	Yadav and Yadav (1985)
Cucurbitaceae			
Luffa acutangula	leaves juice	sores	Dalziel (1956, p. 61)
Cyperaceae			
Cyperus dilatatus	stem	fresh wounds	Dalziel (1956, p. 613)
Ebenaceae			
Diosyros mespiliformis	leaves, twigs	fresh wounds, burns	Watt and Breyer-Brandwijk (1962, p. 389)

Table 5.1. Cont'd

Family/Plant Name	Part used	Wound Type/Uses	Ref.
Elaeginaceae			
Hippophae rhamoides	fruits.	wound healing acceleration	Neamtu and Cociu (1982), Mironov *et al.* (1983)
Euphorbiaceae			
	(contains corillagin)		
Aleurites fordii	oil from the plant	ulcers, burns	Watt and Breyer-Brandwijk (1962, p. 395-6), Nonaka *et al.* (1990)
Croton lechleri[c]	juice	wound healing acceleration	Vaisberg *et al.* (1989), Pieters *et al.* (1992)
Croton macrostachyus	leaves juice	fresh wounds	Kokwaro (1993, p. 101)
Euphorbia balsamifera[**]	juice, root	dressing for yaws in horse, sores	Burkill (1985)
Euphorbia grantii	sap	fresh wounds	Kokwaro (1993, p. 103)
Euphorbia hirta	leaves	wound healing acceleration	Santhanam and Nagarajan (1990)
Euphorbia maequilatera	whole plant	fresh wounds	Kokwaro (1993, p. 104)
Jatropha curcas	leaves juice	fresh wounds, sprains, sores, abscesses, mouth/throat sores infected wounds, hemostatic and anti-inflammatory	Watt and Breyer-Brandwijk (1962, p. 420), Dhawan *et al.* 1977), Arnold and Gulumian (1984), John (1984), Martinez (1984), Weniger *et al.* (1986), Kone-Bamba *et al.* (1987), Le Grand and Wondergem (1987), Le Grand (1989), Madulid *et al.* (1989), Muanza *et al.* (1994)
Jatropha multifida		fresh wounds, first aid antiseptic	Adjanohoun *et al.* (1993, p. 153 & 345), Kosasi *et al.* (1987)
Jatropha zeyheri	sap	sores and burns	Watt and Breyer-Brandwijk (1962, p. 422)
Mallotus oppositifolius		fresh wounds	Adesakin, personal communication
Phyllanthus aspreicaulis	leaves	fresh wounds	Kokwaro (1993, p. 107)
Ricinus communis	bark	fresh wounds, sores, sprains, trauma, aches, inflammation, ulcers, strong bactericide, antifungal	Watt and Breyer-Brandwijk (1962, p. 428), Khan *et al.* (1978), Holdsworth (1983), Martinez (1984), Ramirez (1988), Chhabra and Uiso (1991), Anesini and Perez (1993), Desta (1993), Muanza (1994)
	seed oil	burns	Tanaka *et al.* (1980), Adesina (1982), Boukef *et al.* (1982), Sebastian and Bhandari (1984), Samuelsson *et al.* (1992)
Synadenium sp.	sap	fresh wounds	Kokwaro (1993, p. 112)
Synadenium cupulare		infected wounds, boils	Nwude and Ebong (1980)
Graminae			
Cynodon dactylon	extract	wound healing	Subramanian and Nagarajan (1988)
Saccharum officinatum		stomatitis, aches, strings.	Hedberg *et al.* (1983b)
Sasa albomarginata		wound healing, needs Vit C to work	Shibata *et al.* (1980).
Guttiferae			
Hypericum perforatum		wound healing	Fedorchuk (1964), Rao *et al.* (1991)
Icacinaceae			
Rhaphiostylis beniniensis	leaves	sores	Dalziel (1956, p. 292)
Lamiaceae			
Leonotis mollisima	root	wounds, snake bites, festering sores	Hedberg *et al.* (1983a), Kokwaro (1993, p. 121)
Leonotis nepetaefolia	leaves	ulcers	Watt and Breyer-Brandwijk (1962, p. 520)
Plectranthus sp.	leaves juice	fresh wounds, scabies, antibacterial	Chhabra *et al.* (1984), Kokwaro (1993, p. 126)
Salvia haematodes	fruit, root	wound healing	Akbar (1989)
Lauraceae			
Persea americana	fruit pulp	fresh wounds, bruises, sores, analgesic, scar remover growth promotor	Watt and Breyer-Brandwijk (1962, p. 532), Gazit and Blumenfeld (1972), Ortiz de Montellano (1975), Browner (1985), Ramirez *et al.* 1988), Werman *et al.* (1991)
Leguminosae			
Abrus precatorius	seed	fresh wounds	Adjanohoun *et al.* (199 , p. 219, 233)
Acacia farnesiana	bark, leaves	sores	Dalziel (1956, p. 207)
Acacia fischeri	root	fresh wounds	Kokwaro (1993, p. 136)
Acacia polyacantha	leaves	sores	Kokwaro (1993, p. 138)
Cassia acutifolia	leaves	fresh wounds, burns	Dalziel (1956, p. 179)
Cassia alata	leaves	infected wounds	Palanichamy *et al.* (1991)
Cassia nigricans	leaves	external ulcers	Adjanohoun *et al.* (1993, p. 105, 347)
Crotalaria deserticola	leaves	fresh wounds	Kokwaro (1993, p. 144)
Crotalaria pallida	leaves	fresh wounds	Kokwaro (1993, p. 146)
Crotalaria cleomifolia	leaves	anti-burn	Kokwaro (1993, p. 144)
Mimosa tenuiflora	bark	burns, abrasion wounds	Tellez and Dupoy (1990).
Pongamia pinnata	leaves	wound healing	Subramanian and Nagarajan (1988)
Smithia ochreata	whole plant	fresh wounds	Dalziel (1956, p. 261)
Tephrosia paucynga	leaves, root	fresh wounds	Kokwaro (1993, p. 156)
Liliaceae			
Allium sativum[a]	Bulb	wound healing in perforated ear drum	Singh *et al.* (1984).
Aloe aculeata	juice	anti-burn	Suga and Hirata (1983)
Aloe africana	juice	anti-burn	Suga and Hirata (1983)
Aloe ammophila	juice	anti-burn	Suga and Hirata (1983)
Aloe arborescens[a,c,*]	fresh leaves, juice	anti-burn	Kameyama and Shinho (1979)

Table 5.1. Cont'd

Family/Plant Name	Part used	Wound Type/Uses	Ref.
Liliaceae cont'd			
Aloe arenicola	juice	anti-burn	Kameyama and Shinho (1979)
Aloe candelabrum	juice	anti-burn	Kameyama and Shinho (1979)
Aloe castanea	juice	anti-burn	Kameyama and Shinho (1979)
Aloe comosa	juice	anti-burn	Kameyama and Shinho (1979)
Aloe ferox	juice	anti-burn	Kameyama and Shinho (1979)
Aloe gariepiensis	juice	anti-burn	Kameyama and Shinho (1979)
Aloe globuligemma	juice	anti-burn	Kameyama and Shinho (1979)
Aloe lettyal	juice	anti-burn	Kameyama and Shinho (1979)
Aloe nyeriensis	juice	anti-burn	Kameyama and Shinho (1979)
Aloe perryi	juice	anti-burn	Kameyama and Shinho (1979)
Aloe saponaria	fresh leaves	anti-burn	Kameyama and Shinho (1979)
Aloe speciosa[*]		wound healing acceleration	Kameyama and Shinho (1979)
Aloe spectabilis	juice	anti-burn	Kameyama and Shinho (1979)
Aloe species		anti-burn	Anon. (1980), Winters *et al.* (1981), Suga and Hirata (1983)
Aloe transvalensis	juice	anti-burn	Kameyama and Shinho (1979)
Aloe vanbalenii	juice	anti-burn	Kameyama and Shinho (1979)
Aloe vera[a]	leaves	burns, roentgen dermatitis, wound healing after dental surgery complete regeneration of skin, new hair growth, complete restoration of sensation, lack of scar tissue	Collins and Collins (1935), Kesten and Laughlin (1936), Rattner(1936), Loveman (1937), Crewe (1939), Mandeville (1939), Rowe (1940), Rowe *et al.* (1941), Barnes (1947), Lushbaugh and Hale (1953), Goff and Levenstein (1964), El Zawahry *et al.* (1973), Cobble (1975), Northway (1975), Ship (1977), Hegazy *et al.* (1978), Sayed (1980), Davis *et al.* (1987, 1988, 1989, 1991, 1994), Lerner (1987), Rodriguez-Bigas *et al.* (1988), Crowell *et al.* (1989), Kivett (1989), Verma *et al.* (1989), Egawa *et al.* (1990), Fulton (Jr.)(1990), Kaufman *et al.*(1990), Thompson (1991), Heggers *et al.* (1993), Hormann and Korting (1994), Patel and Mach (1994), Udupa *et al.*(1994), Bouthet *et al.* (1995)
Aloe volkensii	extract	anti-burn	Suga and Hirata (1983)
Aloe wickensii	extract	anti-burn	Suga and Hirata (1983)
Loganiaceae			
Strychnos cocculoides	root	sores	Kokwaro (1993, p. 158)
Lythraceae			
Lawsonia inermis	leaves	wound healing acceleration	Malekzadeth and Shabestrari (1989)
Malvaceae			
Abutilon fruticosum	root	fresh wounds	Kokwaro (1993, p. 161)
Hibiscus aponeurus	leaves, stem	anti-burn	Kokwaro (1993, p. 165)
Hibiscus flavifolius	leaves, root	anti-burn	Kokwaro (1993, p. 165)
Sida ovata	bark	fresh wounds, ear inflammation, bactericide	John (1984), Kokwaro (1993, p. 168)
Meliaceae			
Azadirachta indica[*]	leaves	wound healing acceleration	Davis *et al.* (1991)
Trichilia heudelotti[**]	bark	sores	Dalziel (1956, p. 329)
Menispermaceae			
Cissampelos pareira	root	fresh wounds, boils, burns, insect and snake bites	Hedberg *et al.* (1983a), Jain and Puri (1984), Martinez (1984), Shah and Jain (1988), Anesini and Perez (1993), Kokwaro (1993, p. 172)
Tinospora caffra	leaves	fresh wounds	Kokwaro (1993, p. 172)
Moringaceae			
Moringa pterygosperma	stem	pyoderma	Caceres and Lopez (1991)
Nyctaginaceae			
Boerhavia diffusa	root	abscesses, hemostatic, antibacterial, anti-inflammatory, ulcers	Dalziel (1956, p. 43), Mudgal (1975), Anon. (1978b), Dabral and Sharma (1983), Olukoya *et al.* (1993)
Passifloraceae			
Adenia digitata	root	ulcers	Watt and Breyer-Brandwijk (1962, p. 826)
Pedaliaceae			
Sesamum indicum	leaves	sores, ulcers, dog bites	Watt and Breyer-Brandwijk (1962, p. 832), Ortiz de Montellano (1975), Kumar and Prabhakar (1987)
Phytolaccaceae			
Phytolacca dodecandra	leaves juice	fresh wounds, dog bites, rabies, skin lesions, ulcers, anti-inflammatory	Watt and Breyer-Brandwijk (1962, p. 837), Abebe (1986), Desta (1993)
Piperaceae			
Peperomia pellucida	whole plant	sores	Dalziel (1956, p. 16)
Piper betle	leaves	wounds	Santhanam and Nagarajan (1990)

Table 5.1. Cont'd

Family/Plant Name	Part used	Wound Type/Uses	Ref.
Plantaginaceae			
Plantago lanceolata	leaves	epithelialization	Monastyrkaya and Petropavlovskaa (1953)
Plantago major	leaves	wounds	Nikol'skaya (1954), Mironov *et al.* (1983)
Plantago psyllium	extract	wounds	Nikol'skaya (1954)
Poaceae			
Chloris virgata	leaves	fresh wounds	Kokwaro (1993, p. 253)
Cymbopogon dieterlenni	whole plant	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 470)
Saccharum officinarum	whole plant	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 484)
Polygalaceae			
Polygala arenaria	whole plant	fresh wounds	Dalziel (1956, p. 27)
Heinsia crinata	root, leaves	fresh wounds	Kokwaro (1993, p. 193)
Polygonum cuspidatum		anti-burn	Anon (1978b)
Polyporaceae			
Fomes rimosus	plant ash	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 1113)
Portulacaceae			
Portulaca foliosa	whole plant	fresh wounds	Kokwaro (1993, p. 194)
Rubiaceae			
Chasssalia albiflora	fruit	fresh wounds	Kokwaro (1993, p. 201)
Crossopteryx febrifuga	bark	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 898), Hedberg *et al.* (1983b)
Sarcocephalus esculentus	bark, root	fresh wounds	Dalziel (1956, p. 412)
Scrophulariaceae			
Limnophilia conferta	extract	wound healing acceleration	Reddy (1991)
Rhamphicarpa herzfeldiana	leaves	fresh wounds	Kokwaro (1993, p. 219)
Solanaceae			
Nicotiana rustica	leaves	sores	Adesakin, personal communication
Withania somnifera	leaves	sores, snakebite, scabies, inflammation, festering boils, deobstruent, ulcers, anti-inflammation, analgesic	Anon. (1946), Dalziel (1956, p. 435), Arseculeratne *et al* (1985), Shah and Gopal(1985), Begum and Sadique (1987), Nagaraju and Rao (1990)
Tiliaceae			
Grewia occidentalis	stem	sores	Kokwaro (1993, p. 230)
Grewia similis	bark	sores	Kokwaro (1993, p. 231)
Umbelliferae			
Centella asiatica[a,c,*]	whole plant	external ulcers, postphlebitic syndrome, suppurating wounds, wound healing promotion, analgesic, antifungal, anti-inflammatory, sores, aches, abscesses cuts, fractures	Yantadilaka and Raktavat (1950), Rastogi *et al.* (1960), Burkill (1966), Pasich *et al.* (1968), Poizot and Dumaz (1978), MacGregor and Greenwood (1980), Holdsworth *et al.* (1983), Jain and Puri (1984), John (1984), Singh (1986), Morisset *et al.* (1987), Tenni *et al.* (1988), Arpaia *et al.* (1990), Sakina and Dandiya (1990), Montecchio *et al.* (1991), Adjanohoun *et al.* (1993, p. 39, 321)
Centella coriacea	fresh herb	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 1035)
Ferula pseudooreoselinum	root	anti-burn	Dzhumazhanov (1959)
Verbenaceae			
Clerodendron glabrum	leaves	fresh wounds, fractures	Arnold and Gulumian (1984), Weniger *et al.* (1986),
Priva cordifolia	leaves	anti-burn	Kokwaro (1993, p. 242)
Verbena officinalis	leaves	fresh wounds, ulcers, bleeding, analgesic, insect and snake bites, anti-inflammatory	Watt and Breyer-Brandwijk (1962, p. 1054), Le Grand (1989)
Vitex leucoxylon	stem bark	fills wounds dead space	Sarma *et al.* (1990)
Vitex rufa	bark, leaves	ulcers	Dalziel (1956, p. 458)
Vitaceae			
Cissus quadriangularis	leaves	fresh wounds	Watt and Breyer-Brandwijk (1962, p. 1058), Adjanohoun *et al.* (1991)
	leaves	external ulcers, fractures, aches	Watt and Breyer-Brandwijk (1962, p. 1058), Udupa and Prasad (1964), El-Hamid (1970), Chopra *et al.* (1976), Nagaraju and Rao (1990)
Rhoicissus tridentata	sap	sores, wound healing promotion, cuts, anesthetizer	Al-Yahya (1985), Holdsworth and Rali (1989),Kokwaro (1993, p. 246)
Zingiberaceae			
Aframomum melegueta	leaves	fresh wounds	Adjanohoun *et al.* (1991, p. 301)
Curcuma aromatica[c]	rhizome	granulation tissue	Santhanam and Nagarajan (1990)
Curcuma longa[c]	rhizome	granulation tissue	Kumar *et al.* (1993)
Anchomanes difformis	stem, juice	fresh wounds	Adesakin, personal communication
Sphaerocentrum jollyanum	stem bark	sore	Adesakin, personal communication

Table 5.1. Cont'd

Family/Plant Name	Part used	Wound Type/Uses	Ref.
Miscellaneous			
Achatina fulica[**,***]	slimy juice from giant African snail	heals circumcision, wounds	Sofowora (1996)
Apis mellifera[**,***]	honey from bees	it is believed in some parts of Nigeria that a wound that does not heal with honey may never heal	

* Wound healing plant already in clinical use
** Mucilage-containing plant and carbohydrate derived natural products with wound-healing properties
*** Not of plant origin

[a] Plant already tested on humans
[b] Plant with outstanding wound healing effects on animals but not tested on humans
[c] Plant from which the active wound healing chemical compound has been isolated/characterized/patented

Table 5.1. includes 11 plants that have been tested in humans. Many of the active products and their biological activity have been patented. The most widely used genus of all the plants is *Aloe*. The genera tested in humans are distributed in the families as follows: Liliaceae (3), Asteraceae/Compositae (2), Boraginaceae (2), Convolvulaceae (1), Umbelliferae (1), Leguminosae (1), Crassulaceae (1).

Wound healing after traditional surgery

A few examples of surgical operations carried out in African traditional medicine and the treatment for which involve plants are:

Bone Setting - A traditional bone setter is a specialist skilled in the treatment of fractures. The bone setter ties splints and medicaments to the fracture. The fractured part is laid flat and immobilized and herbal dressings are placed on the fracture, examples of herbs used include a decoction of *Cissus quadrangularis* (Vitaceae) leaf which is drunk three times daily and used to bathe the affected parts. The plant has actually been demonstrated to have wound and fracture healing activity (Udupa and Prasad 1964; Chopra *et al.* 1976).

Treatment of burns - In African traditional medicine burns are treated with herbal preparations which produce a soothing effect. For example papaya juice ointment is applied by some practitioners to produce a gradual removal of dead tissue, after this process is completed and the healthy granulation tissue appears, the burn is treated with a herbal medication especially to promote wound healing (Sofowora 1996).

After some surgical operations certain types of diet are forbidden to ensure that there is rapid healing up of wounds, *e.g.* no "okro" soup prepared from *Hibiscus esculentus* or other slimy foods including *Corchorus olitorius* leaves is permissible after traditional circumcision until the wound is healed (Sofowora 1996).

After the traditional abstraction of bullets from wounds sustained by warriors, herbal medication (usually oily preparations) as dressings and heat therapy are applied to such wounds to aid healing.

Circumcision - Other surgical operations carried out by the traditional medical practitioners include circumcision of the male. This is carried out with care using a cold knife and keeping the penis cold to effect some vasoconstriction and reduce blood loss during the operation. Local or general anesthetics are rarely applied. A few drops of spent traditional (from plant) dye (*i.e.* dye which has already been used for dyeing native cloth) is splashed onto the surface probably for its antimicrobial effect. A little later (this is common in all cases) a giant African snail (*Achatina fulica*) is broken open at the base of its shell to release the slimy juice which is allowed to drop directly onto the cut surface. No more dressing is applied on that day. On the second day a preparation of palm oil containing some herbs is applied to the wound with the aid of a feather. The sore heals within 2-3 weeks, if the wound is not damaged.

Tribal marks - In the treatment of wounds resulting form tribal marks, spent dye is also utilized immediately after the incisions are made. Two days later, palm oil is applied with the aid of a feather and the wound area kept dry. On the third day the patient bathes and rubs the sore with a face towel and native soap (sometimes mixed with maize pap to absorb the fluid oozing from the sores). Maize pap, gum or mucilage may be acting as a wound sealing plug as well. After cleansing the wounds, various herbs which have astringent, hemostatic or antimicrobial properties *e.g. Hoslundia opposita, Dissotis rotundifolia, Ehreta cymosa, Solanum nodiflorum*

and *Ocimum gratissimum* are wrapped in banana leaf, heated in hot ash and the leaf juice squeezed onto the sores once or twice daily. Healing is effected within 3 weeks. The tribal marks are often pressed into shape with a thumb during the healing period to avoid keloid (hardened tissue swelling) formation. In traditional medicine herbal preparations are used to dissolve away keloids instead of removal by surgery as in orthodox medicine.

The traditional surgical patients are advised against eating slimy foods *e.g.* vegetable soup made from *Corchorus olitorus* leaves during the healing process because it is believed that such foods when taken internally prevent rapid healing of sores. It is noteworthy to state here that slimy items from natural sources including mucilages, gums and slimes from snails have been used externally in wound healing (Elliot 1994), whereas they are forbidden for internal consumption in Western Nigeria and other parts of Africa (Sofowora 1996).

Possible mode of action of some wound healing plants from Africa

As earlier mentioned, the mechanism or mode of action of wound healing agents in the plants used for wound healing vary. A correlation of the possible mode of action of some of these plants is provided below. The active wound healing agent(s) reported in several wound healing plants and which provide justification for their use is shown in Table 5.2.

1. The juice of *Aristolochia bracteata* (Aristolochiaceae) is used in the treatment of foul and neglected ulcers. The leaves of a related species *A. elegans* was found to contain among other compounds, aristolochic acid and allantoin (Sofowora 1996). Allantoin is one of the wound healing agents listed in Table 5.2. The antimicrobial activity of *A. bracteata* may explain its traditional use for treating sores. The presence of allantoin is contributory.
2. After circumcision, a shoot of *Pergularia daemia* (Asclepiadaceae) is wilted over fire and the warm juice is squeezed onto the circumcision wound, probably as an antiseptic, anesthetic or analgesic. A poultice of the leaves of the plant is applied to boils and abscesses in India and Ghana and it is applied to sore eyes. The paralytic effect of the extract of *P. daemia* on cockroaches within 2-4 days could possibly indicate that the plant has anesthetic properties which will be beneficial as a soothing agent in circumcision (Sofowora 1996). The plant *P. daemia* also possesses antimicrobial activity which could explain its use in the treatment of wounds and abscesses. The plant also has mild analgesic effect when administered intraperitonially or orally.

   Kalanchoe crenata (Crassulaceae). The crushed leaves or the juice expressed after heating the leaves of *K. crenata* are mixed with shea butter or oil and rubbed on abscesses or other swellings or applied to ulcers and burns. Juice from dried leaves are squeezed out and applied to septic wounds (Sofowora 1996). Its main constituents include malic acid and α-tocopherol found in the green callus.

α-Tocopherol has also been reported to possess wound healing activity see Table 5.2.

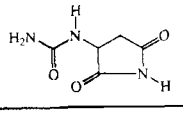
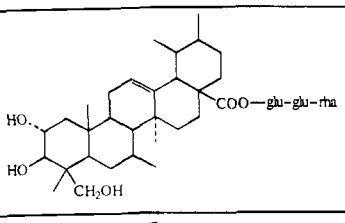
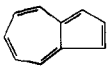
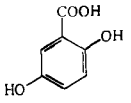
3. In Ghana, *Euphorbia hirta* leaves are used in sore and wound healing. It is used in East Africa to treat boils (Sofowora 1996). In East Africa, The Malay peninsula and Liberia the latex is used in treating conjunctivitis and ulcerated cornea. The Toukouleurs and Wolofs also use the latex externally as antiseptic and for sore healing. At one time in southern Malawi it was used in eye treatment, but it is no longer so commonly used. The plant contains flavonoids, triterpenes, mucilage and some acids *e.g.* ellagic acid (Sofowora 1996). Ellagic acid may be responsible for the wound healing properties (see Table 5.2). Ellagitannin derivatives have been isolated from the leaf of a Chinese specimen of *E. hirta*. Antiulcer activity was demonstrated by a chromatographic fraction of *E. hirta* from Taiwan. The fraction contains amongst others, protocatechic acid and gallic acid which may be responsible for the antiulcer and wound healing activities.

4. *Moringa pterygosperma* (Moringaceae) root and root bark are used by the Indians to treat mouth sores. The root contains a gum which is made up of bassorin and enzymes. The plant also contains cytokinins, zeatin and zeatin riboside (Sofowora 1996) which have some effects on wound healing activities as normal cell growth promotors. The plant has antimicrobial activity (against a wide range of micro-organisms) which corroborates the traditional use of the plant in gargles for sore mouth. An intramuscular injection or local administration of spirochin (Sofowora 1996) is antiseptic and prophylactic against wound infections, even in patients with already marked infection. It has analgesic and antipyretic effects.

5. In Angola, the crushed bark of *Ximenia americana* (Oleaeceae) is applied to sores of domestic animals and in west tropical Africa the pulverized bark and root are used as a dressing for ulcers, etc. The main constituents of the whole plant include hydrocyanic acid. The bark yields 16-17% of tannins (Sofowora 1996). These tannins may be responsible for its wound healing activity. See Table 5.2. for wound healing tannins.

6. *Borreria verticillata* (Rubiaceae) is used in Casamance for the treatment of whitlow and boils, by applying a paste obtained by pounding the leaves in a mortar with the extract of *Carapa procera*. The volatile oil it contains is rich in terpenes, phenolics and aromatic polycarboxylic acids. Azulene is present in the oil and this compound has also been reputed to possess wound healing activity. See Table 5.2. The high boiling components of the volatile oil showed strong antimicrobial activity against Gram positive and Gram negative bacteria (Sofowora 1996).

Table 5.2. Wound healing active chemical compounds and their sources

Chemical Compound	Wound haling Activity	Plant/Source	References
 Allantoin	wound healing accelerator	synthesized from uric acid	Thompson (1991)
[a]Aloe Carboxypeptidase	anti-burn	*Aloe arborescens* var. *natalensis*	Obata *et al.* (1993).
 Asiaticoside	wound healing accelerator	*Centella asiatica*	Velasco and Romero (1976)
 Azulene	anti-inflammatory	*Anthemis nobilis*	Takeda *et al.* (1983)
 Benzoic acid	antifungal, anti-inflammatory	wide spread in nature	Yamasaki and Saeki (1967)
 2,5-Dihydroxy-benzoic acid	anti-inflammatory	wide spread in nature	Yamasaki and Saeki (1967)

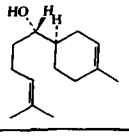
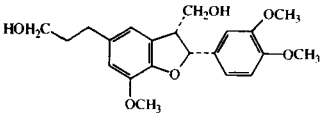
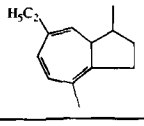
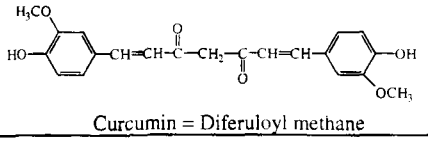
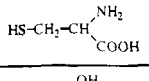
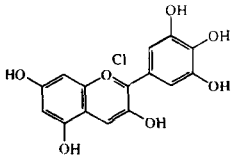
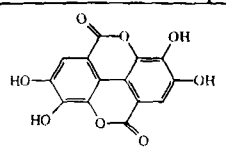
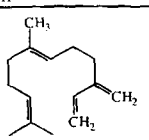
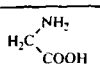
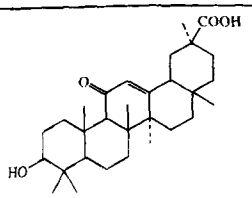
 α–Bisabolol	anti-burn	*Anthemis nobilis*	Zita and Steklova (1955)
 Dimethyl-cedrusin	simulates fibroblast collagen synthesis	*Croton* sp.	Santhanam and Nagarajan (1990). Pieters (1992)
 Chamazulene	anti-burn	*Anthemis nobilis*	Zita and Steklova (1955)
 Curcumin = Diferuloyl methane	wound healing accelerator	*Curcuma aromatica* *Curcuma longa*	Deodhar *et al.* (1980), Santhanam and Nagarajan (1990), Kumar *et al.* (1993)
 Cysteine	wound healing accelerator	wide spread in proteins	Harvey and Gibson (1984).
 Delphinidin chloride	wound healing accelerator	wide spread in plants	Conti *et al.* (1992).
[a]Echinacin B an extract	anti-hyaluronidase	*Echinacea angustifolia*	Bonadeo *et al.* (1971)

Table 5.2. Cont'd

Chemical Compound	Wound haling Activity	Plant/Source	References
 Ellagic acid	hemostatic, anti-inflammatory	*Castanea* sp., *Eucalyptus* sp.	Egawa *et al.* (1990).
Essential oil	wound healing accelerator	*Chromolaena odorata*	George (1974).
 ß-Farnesene	anti-burn	Essential oils (*Chamomile*)	Zita and Steklova (1955)
 Glycine	wound healing accelerator	Gelatin, silk fibroin	Harvey and Gibson (1984).
 Glycyrrhetinic acid	cicatrizant	*Glycyrrhiza glabra* and its varieties	Vevron and Giustiniani (1988).

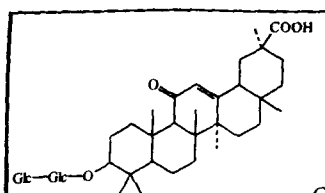
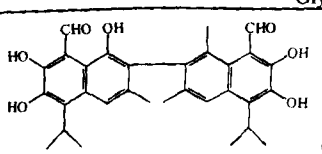
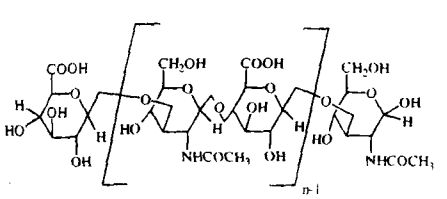
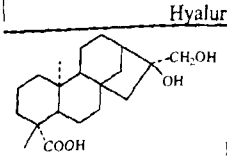
 Glycyrrhizin	wound healing accelerator	*Glycyrrhiza glabra* and its varieties	Davydova *et al.* (1992).
 Gossypol	antimicrobial	*Gossypium barbadense*, *Thespesia populnea*	Aizikov *et al.* (1977)
 Hyaluronic acid	wound healing accelerator	connective tissue	Peacock, and van Winkle (1976), Bleacher *et al.* (1993)
 16ß, 17-Dihydroxy-kauran-19-oic acid	wound healing accelerator	*Siegesbeckia pubescens*	Han *et al.* (1975).

Table 5.2. Cont'd

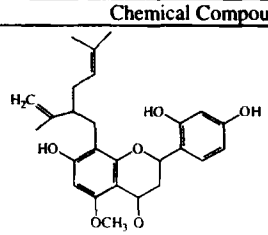
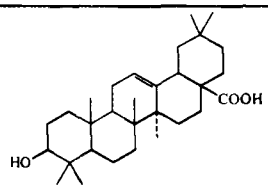
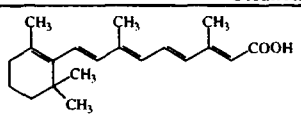
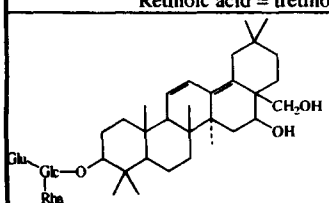
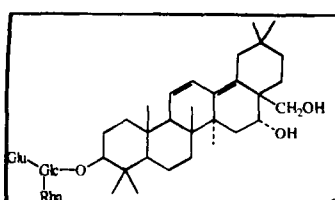
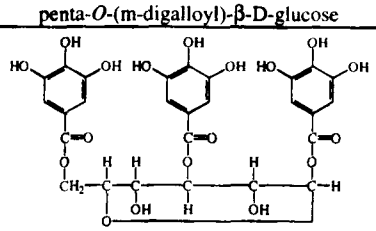
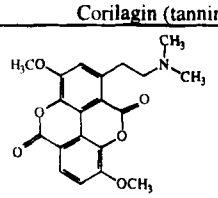
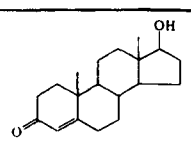
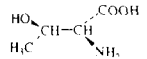
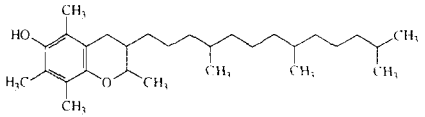
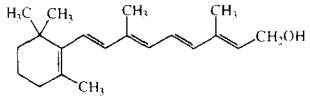
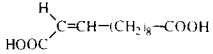
Chemical Compound	Wound haling Activity	Plant/Source	References
 Kurarinone	antiulcer	*Sophora flavescens*	Yamahara *et al.* (1990)
 Oleanolic acid	wound healing promotor	Wide spread	Tamai and Yamahora (1992).
 Retinoic acid = tretinoin	keratolytic	synthesized from vitamin A	Trease and Evasns (1989)
 Saikosaponin B1	wound healing accelerator	*Bupleurum falcatum*	Nishiyama and Akutsu (1992), Hostettmann and Marston (1995).
 Saikosaponin B2	wound healing accelerator	*Bupleurum falcatum*	Nishiyama and Akutsu (1992) Nishiyama and Akutsu (1993) Hostettmann and Marston (1995)
Tannic acid ($C_{76}H_{52}O_{46}$) = penta-*O*-(m-digalloyl)-β-D-glucose	anti-burn	*Pinus caribaea*	Bope *et al.* (1948)
 Corilagin (tannin)	anti-burn	*Pinus caribaea* *Aleurites fordii* *Acalypha wilkesiana*	Bope *et al.* (1948) Nonaka *et al.* (1990), Olugbade *et al.* (1996).
 Taspine	anti-burn, anti-inflammatory, cicatrizant	*Croton lechleri*	Vaisberg *et al.* (1989) Pieters (1992) Porras-Reyes *et al.* (1993)
 Testosterone	wound closure	testes of bull/synthesis	Morton and Malone (1972)

Table 5.2. Cont'd

Chemical Compound	Wound haling Activity	Plant/Source	References
 DL-Threonine	wound healing accelerator	wide spread in proteins	Harvey and Gibson (1984)
 α-Tocopherol	improves skin integrity	embryos of cereals, many seed oils, alfalfa, lettuce	Bernhard (1988).
 Vitamin A = Retinol	wound healing accelerator, improves skin integrity	Butter/Egg yolk, fish liver (not in plants)	Gao *et al.* (1992)
 Traumatic acid	wound hormone	Bean pod tissue or *Aloe* sp	Freytag 1954)

[a] = Already in clinical use.

The structure-activity relationships (SAR) of wound healing chemical compounds isolated from plants and animals

The chemical compounds with wound healing activity are not restricted to a particular chemical group. They are, however, mostly proteins, amino acids, terpenes, flavonoids, alkaloids, quinonoids, tannins, steroids, carbohydrates or coumarins. Branched chains, uronic acid moiety and pyran rings are fairly common in the diverse structures. So also are polyhydroxyl and acidic functional groups.

Most of the Wound Healing agents are acids, and/or triterpenes. This would suggest a pharmacodynamics based essentially on the presence of at least one carboxylic acidic group, and a structure-activity relationship based on the presence of some terpene and carboxylic acid moieties.

The fact that many growth regulators in plants *e.g.* gibberelins are acidic and terpenoid in nature seem to support this suggestion. The gibberelic acids are biosynthesized via kaurenoic acid which, by a multi-step ring contraction, furnishes the gibbane ring system (Trease and Evans 1989). A kaurenoic acid derivative has been reported to have wound healing properties (Han *et al.* 1975). (see Table 5.2). Abcissic acid (Trease and Evans 1989) and traumatic acid (Devlin and Witham 1986; Freytag 1954) are also involved in cell upkeep, proliferation, elongation phases etc. (Trease and Evans 1989) which are really responsible for re-epithelialization and wound closure. Traumatic acid is abundant in *Aloe* species which are highly reputed for the treatment of wounds and burns (Freytag 1954).

Cell division hormones-cytokinins - have a more specific effect on cell division. These include kinetin (not found in plant, but in the sperm of herrings) and zeatin which has been found in the embryo of maize, at the milky stage. Other derivatives of zeatin have been found in many woody plants (Trease and Evans 1989). Cytokine and TGF (transforming growth factor) play an important role in wound healing (Bleacher *et al.* 1993; Meyer 1958; Sullivan *et al.* 1995). Induced cell cytokinins are believed to be the major promotors in cellular division and hormonal control of morphogenesis (Devlin and Witham 1986). Excessive amounts of these compounds cause scarring in adult wounds, whilst fetal wounds heal without scar due to deficiency or lack of these compounds in the foetus.

Many pentacyclic saponins and their genins have been shown to affect the cell as antiexudative (Hostettmann and Marston 1995) preventing spread. They may be acting as antihyaluronidase or as hyaluronic acid or related compounds since these compounds have been applied to wounds (Bleacher *et al.* 1993). Some of the wound healing compounds listed in Table 5.2. are saponins or aglycones of saponins.

Many triterpene saponins and their aglycones have been reported to possess antiulcerogenic, anti-inflammatory, fibrinolytic, antipyretic, analgesic and antiedematous activities (Hostettmann and Marston 1995). Antiulcerogenics - skin and gastric *e.g.* glycyrrhetinic and glycyrhizic acids, both of which constitute Biogastrone acid (Elks and Ganellin 1990) which is used in the treatment of ulcers and as an anti-inflammatory also in skin diseases are well known. The saponins are reported to act by promoting mucous formation (Hostettmann and Marston 1995).

This property favours wound healing by preventing wound desiccation as well as furnishing important growth factors.

Conclusion

The profiles of fetal proteoglycans, collagens and growth factors are different from those in adult wounds. High level of hyaluronic acid and its stimulation is more rapid and there is highly organized collagen deposition (Bleacher *et al.* 1993; Broker and Reiter 1994). Growth factors are characteristically less prominent in fetal wounds. Topical application of wound healing promoting agents *e.g.* regulated amounts of growth factor to wounds may soon be possible.

The traditional surgical patients are advised against eating slimy foods *e.g.* vegetable soup made from *Corchorus olitorus* leaves during the healing process because it is believed that such foods when taken internally prevent rapid healing of sores. It is noteworthy to state here that slimy items from natural sources including mucilages, gums and slimes from snails have been used externally in wound healing (Elliot 1994), whereas they are forbidden for internal consumption in Western Nigeria and other parts of Africa (Sofowora 1993).

Acidic firoblast growth factor (aFGF) has also been found to be one of the most effective wound healing components of the human system. It has potential therapeutic applications for promoting the healing of dermal ulcers, especially in healing-impaired individuals (Popp *et al.* 1995) and has been recommended for that use.

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