Phyto-Extracts in Wound Healing

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ABSTRACT - Data generated through systematic investigation, carried out on the evaluation of phyto-extracts on wound healing research during the last 20 years have been compiled. About 450 plant species having wound healing properties have been identified. The present knowledge of the wound healing process comprise coagulation, inflammation, proliferation, formation and accumulation of fibrous tissues, collagen deposition, epithelialization, contraction of wound with formation of granulation tissues, remodeling and maturation. The constituents of the plant extracts modulate one or more of the above stages. It was the endeavor to identify the active constituents responsible for antimicrobial activity, free radical scavenging properties, stimulators of enhanced collagen production and/or angiogenesis promoters with identification of lead scaffold chemical structures. Multiple phytochemicals concentrated and blended in optimal concentrations, are expected to be available in future years to carry out multi-tasking efforts in wound healing as more knowledge about the properties of the key constituents are unveiled.

INTRODUCTION

Wounds can be major causes of physical disabilities and may lead to losses of many productive man-hours. Wounds are essentially the disruption of functional continuity of cells and tissues at the site of injury, and can be caused by insults to the tissue sites by physical, chemical, microbiological or immunological process. Humans and all animals have *in situ* capabilities of healing wounds in their body parts through continuous tissue repair and tissue regeneration. However, such capabilities are impaired by age, stress situation, obesity, sex, habits of the patient(such as smoking , alcoholism etc.), conditions of health and immunity status, severity and types of wounds, patient's medication status , disastrous nature of the assault- environment around the site of the wounds and potentials of serious microbial infection (1). Curing of acute and chronic wounds proceed through common basic phases of hemostatis, inflammation, proliferation, fibroplasias, collagen deposition, epithelialization, contraction, remodeling and maturation.

Phases in Wound Healing

During the wound healing process, a series of events encompass the repair especially through the presence and actions of activated platelets, neutrophils and macrophages. Increased vascular permeability and angiogenesis are the consequences of the healing, where multiple cellular and cytokine-mediated events are recruited. The endothelial cells are up-regulated by the actions of secreted soluble factors from the activated cells which include the fibroblast growth factors, transforming growth factors, epidermal growth factors and vascular endothelial growth factors among others (2 - 4). The platelets also get activated by the contents from the vascular wall; the main activators such as fibronectin, fibrillar collagen and other matrix proteins cause the kick-off.

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The inflammed skin tissues at the wound site release several prostaglandins, some of which are considered to be the mediators for platelet activation and functioning (5-7). Once activated, the platelets commence aggregation and adhesion; concomitantly these release several mediators including chemotactic factors as well as adhesive proteins. Each factor has a role in the healing cascade (8-10). The mast cells surrounding the blood vessels at the wound site release histamine proteases, tumor necrosis factor, leukotrins and cytokines. These work as chemotactic signals for the recruitment of white blood cells or leukocytes (11) at the site of the wound. While coagulation of blood and vasoconstriction at the wound site are events completed in minutes, the repair process of polymorphonuclear cell migration manifested through vasodilation and inflammation followed by epithelialization, granulation and new tissue formation take about a week. Usually by the end of the first week, fibroblasts are the main cells accumulating at the wound. These cells are involved in differentiation in the wound healing process (12). During the initial phases usually type III collagen is synthesized and laid down at the wound site; during the later phase the stronger type I collagen gets produced (13). Type III collagen, which were in abundance during the proliferation stage gets degraded and is replaced by type I collagen during the maturation stage (14). The collagen fibers get cross-linked by the action of specific enzymes, properly rearranged and aligned for providing maximum rigidity and toughness (15). The maturation phase can vary from three weeks to two years. If the healing process does not move in a foreseeable manner, then the wound may turn into a chronic wound (16).

Direction of Wound Healing Research using Active Phyto-Extracts

The basic understanding that platelets and the fibrins produced from fibrinogen at the wound site set off several biochemical processes which include collagen synthesis, cell migration, fibroplasias and angiogenesis have been significantly investigated. (17-21). The events at the wound site, especially those including release of platelet factors and others such as cell adhesion, cell proliferation, mitogenesis, angiogenesis, fibroplasia, epithelialization, wound contraction, maturation and remodeling of the wound site have been researched upon by several investigators. The platelets are the cause of release of more than sixty biologically active substances (9) and that each such factor is involved at specific time and in specific concentrations, contributing to specific activities in the wound healing process cascade, recruiting different cell types and coordinating complex interactions among the different actors during the wound healing process. Several factors appear and disappear at different stages of the healing cascade and their quantification along with the identification of involved cells has not yet been generally possible. The complexity of the situation can be gauged when one realizes that there is considerable variation in the concentration of such factors in healthy individuals; the quantities of transforming growth factor (TGF), vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF) as an example, in blood samples obtained from 20 different donors showed substantial variation (9). More understanding of the wound healing process especially in terms of quantification of factors are expected to evolve in the coming years. In this context, quantitative insight into the interaction of the various components of the plant extracts with the particularized substances present at the wound site needs also to be studied to scientifically assess their worth. Such studies would require semi-quantitative if not quantitative analysis of the active substances present in different classes of plant extracts. This area is yet to evolve although the usefulness of various kinds of plant extracts in curing wounds of different types is real and many of the plant extracts have been in use in traditional practices for several years in different societies.

Active Plant Parts Studied for Wound Healing

During the last two decades, there has been increased interest to assess the utility of plant extracts in wound healing and to gain more insight into the active constituents that promote or modulate the healing process. We have reviewed the literature for the last 20 years. Table 1 provides information about the plants along with their families, which had shown wound healing properties studied in different models; the table also contains information about those wound healing plants that are extensively used in folk medicine.

Based on the information furnished in the literature, the main effects of the active constituents of the plant extracts towards wound healing are summarized as under:

1) Phyto-chemical constituents contributing to antimicrobial activity
2) Phyto-chemical constituents working as antioxidants and as free radical scavengers
3) Active components having enhanced mitogenic activity (contributing to increased cell proliferation), angiogenesis, enhanced collagen production and increased DNA synthesis.

Ideally, active substances present in the plant extracts are anticipated to interfere with one or more phases of the wound healing process in a positive manner in proper sequence and at the right time frame to show improved efficacy. There should also be minimization of substances that deteriorate the healing process. Since in actual experiments and usage, all the plant products as cited in the table have shown efficacious results, there are increased needs to isolate and investigate each active ingredient that has a positive role in the healing process. Unfortunately, such data presently are not plentiful. The active ingredients obtained from the plant materials have been analyzed for the presence of alkaloids, carbohydrates, glycosides, terpenoids, diterpenes, sesquiturpenes and phytosterols, phenolic compounds and multiple kinds of tannins, proteins, flavonoids, saponins, lignins, alkaloids and essential oils. (29,32,37,60,98,99 ,139 ,155,357,389,457,500). The identification of secondary metabolites in plant extracts that could bind to cellular receptors at wound site to initiate modulation of wound healing process was recently revived (501). In a couple of investigations, the principal active ingredients have been isolated to study especially their anti-microbial properties e.g. terpenes and terpenoids like gentiopicroside, sweroside and swertiamarine from *Gentiana lutea*; certain pentacyclic triterpenes (502-503) ; essential oil containing concentrates of eucalyptol (28) ; flavones such as kaempferol and quercetin and their derivatives (473); phenylpropanoid glycosides like verbascoside and teupolioside (504); cyanogenic glycosides such as sambunigrin as well as gallic acid and its derivatives (496).Wound healing substances isolated from *Termalia arjuna* were tannins (457); oleanoic acid from *Anredra diffusa* (70); polysaccharides from *Opuntia ficus-indica* (365)*;* shikonin derivatives including deoxyshikonin, acetylshikonin, 3- hydroxyl isovaleryl shikonin and 5,8-O-dimethylacetylshikonin from *Onosma argentatum* (361); asiaticoside, asiatic acid and madecassic acid from *Centella asiatica* (146-147)*;* quercetin , isorhammetin and kempferol from *Hippophae rhamnoides* (261) ; and curcumin from *Curcuma longa* (168). The list of well-charaterized newer active ingredients is increasing with a galloping speed.

Wound repair process follows a set of biochemical reactions. At the wound site, increased amounts of superoxide anion radicals are produced by activated platelets, neutophils and the macrophases as well as by the fibroblasts, stimulated by the pro-inflammatory cytokines during the inflammation phase. These radicals are part of the inate immune system and are generated to destroy the invading microbes at the wound site. However, the oxidative stress requires careful manipulation and control as increased amounts are detrimental to the surrounding tissues and can cause heavy damage. While the system has its checks and measures in place and utilizes superoxide dismutases, catalases, glutathione peroxidases and peroxiredoxins, secreted by the adjoining cells, the impairment of such cells in certain wounds calls for use of extraneous agents that are more appropriate radical scavengers, working in synergy or independently. Several plants extracts containing proanthocyanidins, polyphenolic flavonoids and polyphenols in such situations are expected to provide enabling support to the healing process initially by the moderation of superoxide anions and later by enhancing the expression of vascular endothelial growth factor (VEGF), thereby enhancing angiogenesis and flow of blood as the repair process advances. The plant components having some such properties are described further below.

Among the soluble compounds in the plant extracts, the flavonoids, quinones, phenolic acids and phenyl propanoids have been found to possess considerable anti-microbial as well as anti-oxidant properties. A large number of flavonoids having the general structure as given in Figure 1 were found to possess antimicrobial and/or antioxidant properties.

Flavonoids are strong scavengers of reactive oxygen species .In wounds there is a tendency for sharp rise in the concentration of reactive oxygen species due to the activation of platelets, neutrophils, macrophages, lymphocytes and fibroblasts at different time points of the healing process. Infection from microbes also adds to the woes. In such situations, plant flavonoids would benefit the healing process by modulating the concentrations of reactive oxygen species. Quantitative information and correlationships are yet inadequate however.

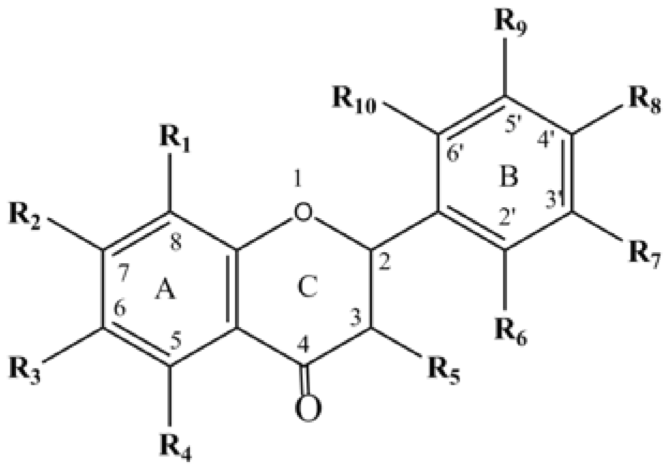

Figure 1: General structure of Plant Flavanoids showing anti-microbial and/or anti-oxidant properties

Apigenin (R1=R3=R5=R6=R7=R9=R10=H, R2=R4=R8=OH) and its glucoside derivatives ; **Chalcone** (R1=R3=R5=R6=R7=R9=R10=H and ring C etherial bond between 1 and 2 opened up with OH in ring A and a double bond between 2 and 3 in ring C); **Chrysoeriol** (R1=R3=R5=R6=R7=R10=H, R2=R4=R8=OH, R9=-O.CH_3) and its gluside derivatives; **Cyanidin** (R1=R3=R6=R7=R10=H, R2=R4=R5=R8=R9=OH, oxo structure at 4 replaced by a double bond between 4 and 3 carbon atom); **Daidzein** (R1=R3=H, R2=R4=OH, C ring R5 substituted by p-hydroxy phenyl and position 2 of C ring replaced by H); **Diosmin** (R1=R3=R5=R6=R9=R10-H, R4=R7=OH, R8=-O.CH_3 and R2 with -O-6-O-(6-deoxyalpha-L-mannopyranosyl)beta-D-glucopyranosyloxy)**); Hesperidin (**R1=R3=R5=R6=R7=R10=H, R4=R9=OH, R8=-O.CH_3 and R2 with -O-6-O-(6-deoxyalpha-L-mannopyranosyl)beta-D-glucopyranosyloxy**); Kaempferol** (R1=R3=R6=R7=R8=R9=H, R2=R4=R5=R8=OH) and its glucoside derivatives; **Luteolin(**R1=R3=R5=R6=R7=R10=H, R2=R4=R8=R9=OH) and its glucoside derivatives**; Naringenin** (R1=R3=R5=R6=R7=R9=R10=H, R2=R4=R8=OH)**; Patuletin (**R1=R6=R9=R10=H, R2=R4=R5=R7=R8=OH, R3=-O.CH_3) and its derivatives**; Pelargonidin** (R1=R3=R6=R7=R9=R10=H, R2=R4=R5=R8=OH, =C=O of ring C replaced by =CH- and O of ring C assumes a positive charge), **Quercetagetin (**R1=R6=R9=R10=H, R2=R3=R4=R5=R7=R8=OH**), Quercetin** (R1=R3=R6=R7=R10=H, R2=R4=R5=R8=R9=OH); **Vestitol** (R1=R3=R4=H, Ring C position 4 oxo structure replaced by CH_2 and ring C R_5 H replaced by 2-hydroxy 4-methoxyphenyl group).

Plants such as *Allamanda cathartica* (50), *Artemisia absinthium* (77), *Coronopus didymus* (176), *Cuminum cyminum* (187), *Flaveria trinervia* (233), *Heliotropium indicum* (253-255), *Hippophae rhamnoides* (261-263), *Ipomoea Carnea* (277), *Jatropha curcas* (187, 281,283), *Lawsonia alba* (298), *Litsea glutinosa* (307), *Rosmarinus officinalis* (416), *Moringa oleifera* (336-338), *Olea europaea* (357-359), *Pedilanthus tithymaloides* (376), *Sambucus ebulus* (422), *Scorzonera* (427-428) species and many others are used extensively in traditional practices in wound healing and these plants are also rich in a wide range of flavonoid compounds.

Anthocyanins synthesized in plants via the phenylpropanoid pathway are compounds based on flavylium ion which is a kind of oxonium ion. Anthocyanins have strong radical scavenging properties and many of these compounds also exhibit anti-bacterial properties. Some of the compounds found in wound healing plants are described with general formula as in Figure 2.

Anthocyanins from Black Soyabean seed coat (*Glycine max*) was found to have enhanced wound healing properties (243). Extracts from *Anadenanthera colubrina* rich in proanthocyanidins were effective in cutaneous wound healing in rats (62). *Caralla brachiata* rich in proanthocyanidins is also expected to be useful for such purposes.

Several soluble quinones present in the roots of plants such as *Alkanna tinctoria, Arnebia densiflora and Arnebia euchroma* and many others were also found to possess antimicrobial propertie (49, 79, 80); these also had some antioxidant properties. The general structures of such soluble quinones are indicated schematically in Figure 3:

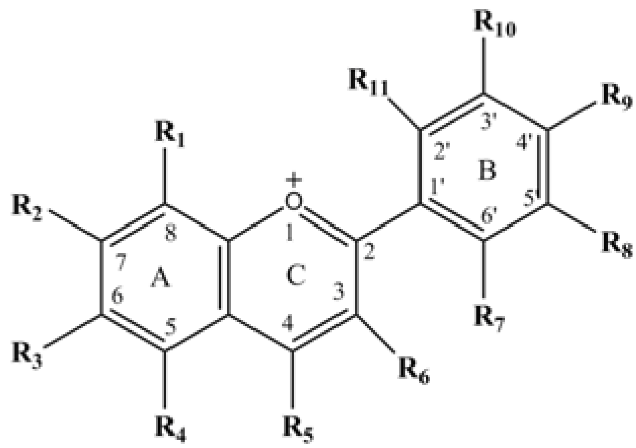

Figure 2: **General structure of Plant Anthocyanins showing anti-microbial and/or anti-oxidant properties**

Aurantinidin (R1=R5=R7=R8=R10=R11=H, R2=R3=R4=R6=R9=OH) and its 3-glucoside derivatives; **Cyanidin** (R1=R3=R5=R7=R8=R11=H, R2=R4=R6=R9=R10=OH) and its 3-glucoside derivatives; **Delphinidin** (R1=R3=R5=R7=R11=H, R2=R4=R6=R8=R9=R10=OH) and its 3-glucoside derivatives; **Europinidin** (R1=R3=R5=R7=R11=H, R2=R6=R8=R9=OH, R4=R10=-O.CH_3) and its 3-glucoside derivatives; **Luteolinidin** (R1=R3=R5=R6=R7=R8=R11=H, R2=R4=R9=R10=OH) and its 3-glucoside derivatives; **Malvidin** (R1=R3=R5=R7=R11=H, R2=R4=R6=R9=OH, R8=R10=-O.CH_3) and its 3-glucoside derivatives; **Pelargonidin** (R1=R3=R5=R7=R8=R10=R11=H, R2=R4=R6=R9=OH) and its 3-glucoside derivatives; **Peonidin** (R1=R3=R5=R7=R8=R11=H, R2=R4=R6=R9=OH, R10=-O.CH_3) and its 3-glucoside derivatives; **Petunidin** (R1=R3=R5=R7=R11=H, R2=R4=R6=R9=R10=OH, R8=-O.CH3) and its 3-glucoside derivatives; **Rosinidin** (R1=R3=R5=R7=R8=R11=H, R4=R6=R9=OH, R2=R10=-O.CH_3) and its 3-glucoside derivatives

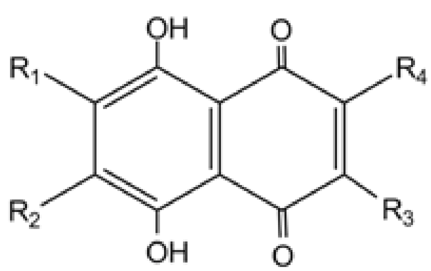

Figure 3: **General structure of Plant Quinones showing antimicrobial and antioxidant properties**

Alkannin (R1=R2=R4=H, R3=CH_3.CH(OH).CH_2.CH=CH.$(CH_3)_2$; **Alpha-methylbutylalkannin** (R1=R2=R4=H, R3=-CH_2-CH(O.CO.CH.(CH_3).(C_2H_5)); **Teracrylalkannin** (R1=R2=R4=H, R3=-CH_2.CH.(O.CO.C(CH_3)=C$(CH_3)_2$)); **Beta-hydroxyisovalerylalkannin** (R_1=R_2=R_4=H, R_3=-CH_2-CH(O.CO.CH_2.C(OH)$(CH_3)_2$)); **Beta-acetoxyisovalerylalkannin** (R_1=R_2=R_4=H, R_3=-CH_2-C(O.CO.CH_2.C.O.CO.CH_3)$(CH_3)_2$); **Shikonin:** (R_1=R_2=R_4=H, R_3=-CH_2-CH(OH).CH_2.CH=C$(CH_3)_2$); **Beta-hydroxyisovalerylshikonin** (R_1=R_2=R_4=H, R_3=-CH_2.C(O.CO.CH_2.C(OH).$(CH_3)_2$).CH_2.CH=C$(CH_3)_2$); **Deoxyshikonin** (R_1=R_2=R_4=H, R_3=-CH_2.CH_2.CH_2.CH=C$(CH_3)_2$)

Structures of several of these compounds with ocurenace and biological properties have been reviewed (503). Emodin from *Rheum officinale* Baill showed encouraging results of repair of excision wounds in rats (413). Embelin from extracts of leaves of *Embelia ribes* Burm was effective in healing wound in excision, incision and dead space model on Swiss Albino rats (213).

Terpenoids of different structures including the monocyclic and the multicyclic ones have been identified to possess antimicrobial activity; these compounds are anticipated to manifest their antimicrobial effects through the process of synergy with other compounds present in the plant extract. Besides the monocyclic terpenoids, several dicyclic, tricyclic and the pentacyclic terpenoids of plant origin have been identified which possess considerable antimicrobial activities. Terpenoids are present in essential oils of a variety of trees, citrus fruits and herbs. Wound healing activities of *Achillea* species like *Achillea biebersteinii* (28) *, A. millefolium* (31)*, A. oxyodonta* (29)*, A. setacea* and *A. teritifolia* (506), *A. vermicularis* (29) *etc., Achyranthes aspera* (32-33)*, Allamanda cathartica* (50)*, Alternanthera sessilis* (59)*, Anredera diffusa* (70), *Arnebia densiflora* (79)*, Berberis lycium* (96)*, Caesalpinia benthamiana* (116)*, Celastrus paniculatus* (141)*, Centella asiatica* (146-149)*, Cissus quadrangularis* (159)*, Croton bonplandianum* (182)*, Croton stellatopilosus Ohba* (183)*, Elephantopus scaber* (211) *, Heliotropium indicum* (254-255)*, Laurus nobilis* (50)*, Paullinia pinnata* (375)*, Vernonia arborea Hk.* (480) *etc.* are substantially attributed to the presence of a wide range of terpenoids. Since the structures of each group of terpenoids including mono and multi-cyclic ones vary considerably, a generalized structure could not be assigned to describe a general class of terpenoids having antimicrobial activities. However, assessing the chemical structures of terpenoids present in the above plants for identifying specific mono or multi-cyclic skeletons for *in-vitro* modification with a view to develop newer compounds is anticipated to be facilitated from the study of the listing of plants.

Phenolics including tannins, substituted cinnamic acids, phenolic acids and phenyl propanoids have also shown antimicrobial as well as antioxidant properties. Tannins from Phyllanthus muellerianus (380), *Terminalia arjuna* (457)*, Terminalia avicennioides* (458)*, Terminalia bellirica* (459)*, Terminalia chebula* (460) and *Terminalia coriacea* (461) are reported to promote wound healing. Tannins are polyphenolic compounds containing considerable numbers of hydroxyls, carboxyls and other hydrophilic structures and are considered to be macromolecules. All natural tannins could not be included in one generic structure although there are considerable resemblances in chemical properties among different tannins.

A number of substituted cinnamic acids of the general structure schematically represented in Figure 4, have been isolated from plant extracts having antimicrobial properties.

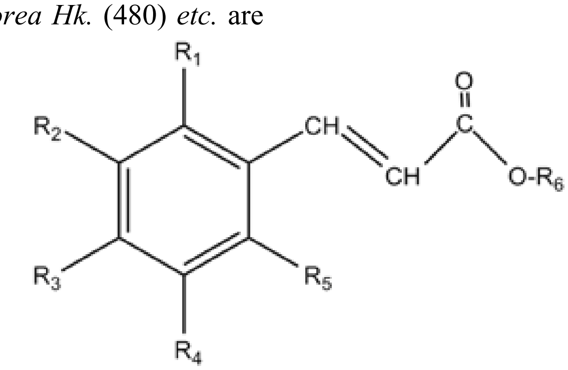

Figure 4: **Substitued Cinnamic acids obtained from plants and plantt parts**

Caffeic acid(R1=R4=R5=R6=H, R2=R3=OH**)** and esters**; Chlorogenic acid**(R1=R4=R5=H, R2=R3=OH, R6=3-alkoxy ester of 1,4,5 trihydroxycyclohexane carboxylic acid) and esters;**Ferulic acid**(R1=R4=R5=R6=H, R2=-O.CH_3,R_3=OH)

Caffeic acid, chlorogenic acid and ferulic acid are documented to have wound healing activities (507-509); these substances also work as free radical scavengers. Plant materials like *Buddleja globosa* (110) leaves containing caffeic acid derivatives, *Scorzonera cana var. jacquiniana* and *S. eriophora* (427) containing chlorogenic acids and *Angelica sinensis* (510) containing ferulic acid have been found to be effective in wound healing.

Several phenolic acids were also found to possess sound antimicrobial properties. In addition, many phenolic acids also had profound radical scavenging properties. Since the structures of phenolic acids vary considerably, it was not possible to represent all of them with one generic structure. However, plants such as *Ageratum conyzoides* (44,46), *Emblica officinalis* (214), *Punica granatum* (30,404), *Salvia hypoleuca* (420), *Schinus lentiscifolius* (423), *Strobilanthes crispus* (446), *Quercus infectoria* (407), *Ximenia Americana* (496) contain tannins and gallic acid and these have excellent wound healing activituies. Various mixed phenolic acids are present in plants such as gall nuts, tea leaves, oak bark etc. (511); although these plant materials have not been used in wound healing, it is anticipated that use of these would have beneficial effects as radical scavengers and therefore could be useful in wound healing.

Phenyl propanoids, especially in the form of glycosides, are natural polyphenols which are widely distributed in the plant kingdom. The roots and aerial parts of the families of Asteraceae, Labiateae, Liliceae, Oleaceae and related ones contain phenylpropanoid glycosides (sometimes also incorporating glucose, galactose and rhamnose in these compounds). Such substances are powerful antioxidants. Utilizing plant cells from *Ajuga reptans* and *Syringa vulgaris* two phenylpropanoid glycosides namely teupolioside and verbascoside were producued which had profound anti-inflammatory and wound healing properties (504).

Water soluble alkaloids including quinazolines, isoquinazolines, indole derivatives including betalains and eumelanins from a diverse range of plants have been found to possess antioxidant properties and many of these have also antimicrobial characteristics. *Adhatoda vasica* (36), *Adhatoda zeylanica* (38), *Berberis lycium* (512), *Catharanthus roseus* (139) etc. are rich in certain alkaloids which have antimicrobial properties. These plant extracts are useful in wound healing purposes and are traditionally used by various societies. Since the compounds from such plants considerably vary in chemical structure, a generalized structure for all these alkaloids could not be presented. However, presently much work is being done to synthesize newer antimicrobial compounds utilizing quinazoline and indole backbones (513-515).

Several natural heteropolysaccharides such as arabinogalactans and rhamnogalacturonans are present in large quantities in certain plants. Hot water extracts of *Alstonia boonei* De Wild (57), *Biophytum petersianum* Klotzch (99), *Cochlospermum tinctorium* Perr (517), *Glinus oppositifolius*(242), *Opuntia ficus-indica* (364, 365), and *Parquetina nigrescens* (57) containing mainly water soluble polysaccharides have been used in traditional practices for treating external wounds. Although exact structure activity relationships are not yet understood, it is believed that the polysaccharides accelerate the phases of reepithelialization and remodeling by influencing interactions in the cell matrix and by moderating the deposition of laminin (365). Polysaccharides are also believed to exhibit immunomodulatory action on the cells around the wound site (57), which stimulate cell proliferation.

Mitogenic properties are anticipated to enhance healing process as phytochemicals possessing such properties exhibited in a structured manner are expected to enhance cell division. Whole plant extracts from *Achyrenthus aspera* (33) and 'Cal-proteins' from *Calatropis procera* (123) were believed to posssess constituents having mitogenic activities. Extracts of *Calendula officinalis* flowers have increased proliferation potential for endothelial progenitor cells (518). Extracts of leaves from *Datura alba* (195) and *Euphorbia heterophylla* (220) are believed to have strong mitogenic potentials contributing to the healing process. In most of the claims however, the specific compounds responsible for the mitogenic activities have not been identified. Like mitogens, substances promoting angiogenesis would also promote healing process by supply of blood around the wound sites. Extracts of *Aloe vera* (54), *Alternanthera brasiliana* (58), mixtures of extracts from *Astragali radix* and *Rehmanniae radix* (519), *Bidens pilosa* and *Ocimum suave* (97), B*lechnum orientale* (100), *Boessenbergia rotunda* (101), *Butea monosperma* (114), C*alendula officinalis*

(118), *Cinnamomum zeylanicum* (157), *Cordia macleodii* (175), *Echium amaenum* (206), *Equisetum arvense* (15) etc. have been shown to promote angiogenisis around wound site. Angiogenesis promoting compounds with specific structures following a pattern have not yet been identified. Increase in DNA and total collagen at wound site with time by the application of phytoextracts substantiate the beneficial effects and are measures of enhancement of healing process linked to the phytoextracts. Extracts from *Achillea biebersteinii* (29), *Achillea kellalensis* and *Punica granatum* (30), *Adhatoda vasica* (37), *Alkanna tinctoria* (49), *Annona squamosa* (67), *Arnica Montana* and *Artemisia absinthium* (77), *Bauhinia purpurea* (94), *Bulbine frutescens* and *Bulbine natalensis* (111), *Butea monosperma* (112), *Calotropis gigantea* (121), *Capparis zeylanica* (25), *Cassia occidentalis* (138), Curcumin from *Curcuma longa* (190), *Desmodium gangeticum* (198), *Elaeis guineensis* (210), *Elephantopus scaber* (211), *Eucheuma cottonii* (216), *Ficus racemosa* (228), *Gynura procumbens* (249), *Heliotropium indicum* (255), *Hyptis suaveolens* (273), *Indigofera asphalathoides* (275), *Jasminum sambac* (280), *Kalanchoe pinnata* (289), *Leonotis nepetaefolia* (299), *Martynia annua* (315), *Moringa oleifera* (336), *Nigella sativa* (347) etc were claimed to be responsible for facilitated healing as evidenced by increased DNA production and total collagen enhancement at wound site with time. However, in all these cases individual specific chemical entities having the properties of enhancing the wound healing process have not been described. Enhanced healing in all these cases probably arises from synchronized action of multiple active ingredients present in the phyto extracts.

CONCLUDING REMARKS

Wound healing is a complex but highly regulated process. Healing of all kinds of wounds follows common steps of recovery. Microbial colonization is often inescapable. Infections of wounds from potentially pathogenic bacteria in most situations of causation of wounds are inevitable. Therefore, the utmost aim is to restore the host-bacterial balance by ensuring that the wound is cleaned up and antimicrobial agents are used with moisture retentive bandages. At the same time as oxidative stress during the initial healing process is high, the next objective is to use agents that scavenge the excess of reactive oxygen anions generated at the wound site and rationalize their concentration. Other objectives are to stimulate the adjoining tissues in the wound so that the processes of cell proliferation, remodeling and maturation are facilitated. The plant kingdom is rich in chemical constituents for mitigating these objectives acting especially as antimicrobial agents as also as the free radical scavengers, and several compounds have since been isolated. The steps of tissue repair involving interactions of neutrophills, macrophages, fibroblasts and other cells at the wound site along with deposition of collagens with proper laying out around the wounds are complex processes and require understaning of multiple interactions with several agents. Concomitantly, formation of new blood vessels through the process of angiogenesis to ensure continuous supply of nutrients and healing supplements also require detailed understaning. In all these processes, several compounds from the plant extracts would work synergistically to provide the desired effect and therefore such phytochemicals concentrated and blended in optimal concentrations from multiple sources are expected to be available in the future years to carry out multi-tasking efforts in wound healing of all kinds as more knowledge about the properties of the key constituents and the healing processes are unveiled.

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Table 1. (Plant name with Family and the plant parts used/studied for wound healing properties in different models)

Plant Name	Plant Family	Plant part used/ studied	Assessment Methods/Animal Wound Models where applicable *	Reference No.
Abrus precatorius L.	Fabaceae	Leaves	Used in Folk medicine to treat Cuts and Wounds	22
Abutilon indicum Linn	Malvaceae	Whole plant	Excision and Incision models in Wistar Albino Rats	23
Acalypha fruticosa	Euphorbiaceae	Aerial Part	Excision and Dead space models in Rats	24
Acalypha indica	Euphorbiaceae	Whole Plant	Excision and Incision models in Rats	25
Acalypha langiana	Euphorbiaceae	Leaves	On External Human Wounds	26
Acanthus ebracteatus	Acanthaceae	Stem	Incision model in Balb/c mice	27
Achillea biebersteinii Afan.	Asteraceae	Essential Oil from Whole Plant	In-vitro anti-microbial assay	28
		Roots	Excision and Incision in Sprague-Dawley rats and Albino mice	29
Achillea kellalensis	Asteraceae	Flowers	Excision model in Wistar Rats	30
Achillea millefolium L	Asteraceae	Leaves	Excision, Incision and Dead Space models in Wistar Albino Rats	31
Achyranthes aspera	Amaranthaceae	Leaves	Excision and Incision model in Albino Rats	32
			Excision and incision models in Albino Rats	33
Acorus calamus Linn.	Araceae	Leaves	Excision and Incision model in Rats	34
Actinidia deliciosa	Actinidiaceae	Fruit	Burn model in Wistar Rats	35
Adhatoda vasica	Acanthaceae	Leaves	Excision model in Wistar Rats	36

			Excision model in Swiss Albino mice	37
Adhatoda zeylanica	Acanthaceae	Leaves	Used in Traditional medicine	38
Adiantum capillus veneris	Pteridaceae	Leaves	In-vitro anti-oxidant assay	39
Aegle marmelos	Rutaceae	Root	Excision and Incision model in Wistar Albino Rats	40
		Seeds	Excision and Incision model in Wistar Rats	41
		Leaves	Excision model in Albino Rats	42
Ageratina pichinchensis	Asteraceae	Whole Plant	Rat Model inflammation inhibition	43
Ageratum conyzoides	Asteraceae	Leaves	Excision models in Wistar Rats	44
		Leaves	Excision model in Sprague Dawley Rats	45
		Roots	Excision model in Albino Rats	46
Albizzia lebbeck	Fabaceae	Root	Incision, Excision, Dead Space models in Rodents	47
Alchemilla vulgaris	Rosaceae	Whole plant	Certain cell lines and Excision in rats	48
Alkanna tinctoria	Boraginaceae	Whole Plant	Skin Burn Injury in Rabbits	49
Allamanda cathartica L.	Apocynaceae	Leaves	Excision and Incision models on Sprague Dawley rats	50
Aleurites moluccana L.	Euphorbiaceae	Leaves	Excision and Incision models in Rats	51
Allium cepa L.	Liliaceae	Tubers	Excision, Incision and Dead Space models on Wistar Albino rats	52
Aloe arborescens Miller	Xanthorrhoeaceae	Leaves	Incision in rats and rabbit	53
Aloe barbadensis	Liliaceae	Leaves	Excision model on Sprague-Dawley rats	54
Aloe ferox Miller	Xanthorrhoeaceae	Leaves	Incision in rats and rabbit	53
Aloe littoralis	Asphodelaceae	Leaves	Burn and Incision	55

			models on Wistar Rats	
Aloe vera	Xanthorrhoeaceae	Leaves	Excision mpdel in Rabbits	56
Alstonia boonei De Wild	Apocynaceae	Stem Bark	Used in Traditional Practicies for wound healing	57
Alternanthera brasiliana Kuntz	Amaranthaceae	Leaves	Excision and incision wound models on Sprague Dawley Rats and In vitro CAM assay	58
Alternanthera sessilis (Linn.) R. Br. Ex DC	Amaranthaceae	Leaves	Excision, Incision and Dead space models on Albino Rats	59
Amaranthus spinosus	Amaranthaceae	Whole Plant	In-vitro Anti-microbial and anti-oxidant assay	60
Ammannia baccifera L.	Lythraceae	Leaves	Excision and Incision models on Wistar Albino Rats	61
Anadenanthera colubrina var. cebil	Fabaceae	Bark	Incision and Excision models on Rats	62
Anagallis arvensis L.	Myrsinaceae	Whole Plant extract	Biochemical Test, inhibitor of COX-1 aqnd COX-2	63
Anagallis foemina Mill.	Myrsinaceae	Whole Plant extract	Biochemical Test, inhibitor of COX-1 aqnd COX-2	63
Andrographis Peniculata	Acanthaceae	Whole Plant	Excision model on Albino Rats	64
Angelica sinensis	Apiaceae	Whole Plant	Human fibroblast cell proliferation assay	65
Annona muricata	Annonaceae	Stem bark	Excision model on Albino Rats	66
Annona squamosa	Annonaceae	Leaves	Excision wound model on diabetic rats	67
Anogeissus latifolia	Combretaceae	Bark	Excision and Incision model on Sprague – Dawley rats and Anti-microbial activity	68
Anogeissus leiocarpus	Combretaceae	Leaves	Excision model on Albino Wistar Rats	69
Anredera diffusa	Basellaceae	Whole plant	On external wound in mice	70
Anthocephalus cadamba	Rubiaceae	Whole plant	Excision and Incision model in	71

			Wistar Rats	
Aralia echinocaulis	Araliaceae	Whole Plant	Angiogenesis and Cell proliferation assay in rats	72
Argyreia nervosa	Convolvulaceae	Leaves	Excision model in Wistar Rats	73
Arisaema leschenaultii Blume.	Araceae	Tubers	Excision, Incision and Dead Space model in Wistar Albino Rats	74
Aristolochia bracteolata	Aristolochiaceae	Leaves	Excision, Incision and Dead Space models in Rats	75
		Leaves	Excision model in Wistar Albino Rats	76
Artemisia absinthium	Asteraceae	Aerial Parts	Cell line assay and in-vitro antioxidant assay	77
Ajuga chia	Lamiaceae	Whole Plant	Excision model in Mice	78
Arnebia densiflora (Nordm.) Ledeb.	Boraginaceae	Roots	Incision model on Wistar Albino Rats	79
Arnebia euchroma	Boraginaceae	Roots	Burn model in Wistar Rats	80
Arrabidaea chica Verlot	Bignoniaceae	Leaves	Incision model in Rat	81
Artocarpus heterophyllus Lam	Moraceae	Leaves	Excision model on Albino mice	82
Asparagus Racemosus	Liliaceae	Roots	Excision and Incision on Wistar Rats	83
Aspila africana	Asteraceae	Leaves	Excision model in Albino Rats	84
Astragalus membranaceus (Astragali Radix)	Fabaceae	Roots	Incision model on Diabetic Rat	85
			Studies on Human Skin Fibroblast cell line for ECM prompotion	86
Astilbe thunbergii	Saxifragaceae	Rhizome	Burn model in Mice	87
Atropa belladonna L.	Solanaceae	Leaves	Incision model on Sprague-Dawley rats	88
Avena sativa L.	Poaceae	Whole Plant	Excision on Mice and Incision on Rats	89
Azadirachta indica	Meliaceae	Oils from *Azadirachta indica* and *Hypericum perforatum*	Human Scalp wound	90

Bacopa monnieri wettest	Scorphulariaceae	Whole Plant	Excision, Incision and Dead Space in Swiss Albino Rat	91
Baliospermum montanum (Willd.)	Euphorbiaceae	Roots	Excision on Albino Rats	92
Barleria cuspidata	Acanthaceae	Leaves	Excision and Incision on Albino Rats	93
Bauhinia purpurea	Caesalpiniaceae	Leaves	Excision, Incision, Burn and Dead Space models on Sprague Dawley Rats	94
Bauhinia variegata	Fabaceae	Lectin from seeds	Incision model in Mice	95
Berberis lycium	Berberidaceae	Roots	Excision, Incision and Dead Space in Swiss Albino Rat	96
Bidens pilosa	Asteraceae	Leaves	Excision model on on Wistar Albino Rats	97
Biophytum *petersianum* Klotzsch.	Oxalidaceae	Whole Plant	Human complement system exvaluation	98
		Aerial Part		99
Blechnum orientale Linn	Blechnaceae	Leaves	Excision model on Sprague-Dawley rats	100
Blepharis maderaspatensis (L.) B.Heyne ex Roth.	Acanthaceae	Leaves	Excision and Incision on Wistar Albino Rats	61
Boesenbergia rotunda (L.)	Zingiberaceae	Rhizome	Excision model in Rats	101
Bolax gummifera	Apiaceae	Whole Plant	Anti-microbial activity studies	102
Bombax malabaricum	Bombacaceae	Bark	Excision, incision and burn models on Wistar Rats	103
Borassus flabellifer L.	Arecaceae	Fruit	Human Beings	104
Brassica juncea Linn	Cruciferae	Leaves	Excision model on Wistar Albino Rats	105
Bridelia ferruginea	Euphorbiaceae	Stem bark	Excision model in Rats	106
			Anti-microbial activity studies and in-vitro antioxidant assay	107
Bryophyllum pinnatum (Lam.)	Crassulaceae	Leaves	Incision, Excision and Deadspace in Swiss Albino Rats	108
Buchanania lanzan	Anacardiaceae	Fruit	Excision, Incision and Dead space models in Albino	109

			Rats	
Buddleja globosa	Scrophulariaceae	Leaves	Fibroblast Assay	110
Bulbine frutescens	Asphodelaceae	Leaves	Excision and Incision on Pigs	111
Bulbine natalensis	Asphodelaceae	Leaves	Excision and Incision model in Pigs	111
Butea monosperma	Fabaceae	Bark	Excision model in Rats	112
		Stem bark	Excision, Incision and Dead space in Wistar Rats	113
		Flower	Excision in Wistar Albino Rats in Wistar Albino Rats	114
		Stem bark	Excision, Incision and Dead space model in Wistar Albino Rats	115
Caesalpinia benthamiana	Caesalpiniaceae	Root Bark	In-vitro anti-oxidant assay	116
Calendula officinalis	Compositae	Flower	Excision model in Rats	117
		Flowers	CAM Assay and Excision model in Wistar Rats	118
Calotropis gigantean	Apocynaceae	Flowers	Excision and Incision models in Wistar Albino Rats	119
		Root Bark	Excision, Incision and Dead space models in Wistar Albino Rats	120
		Leaves	Excision and Incision models in Wistar Albino Rats	121
		Latex	Excision and Incision models in Wistar Albino Rats	122
Calotropis procera (Ait.) R. Br.	Asclepiadaceae	Stem bark	Excision model in Swiss Albino Mice	123
Camellia sinensis	Theaceae	Leaves	Incision in Wistar rats and Anti-oxidant assay	124
Capparis zeylanica	Capparaceae	Roots	Excision and incision model in Albino Rats	125
		Whole plant	Excision model in Wistar Albino	126

			Rats	
Carapa guianensis L.	Meliaceae	Leaves	Excision, Incision and Dead Space models in Sprague Dawley Rats	127
Carica candamarcensis	Caricaceae	Fruit	Burn model in rodents	128
Carica papaya	Caricaceae	Latex	Burn model in Swiss Albino mice	129
		Roots	Excision and Incision model in Swiss Albino Rats	130
		Fruit	Excision model in Mice	131
		Leaves	Excision model in Sprague Dawley Rats	132
		Fruit	Excision and Dead space models in Sprague Dawley Rats	133
Carissa spinarum Linn.	Apocynaceae	Root	Burn model in Mice	134
Carthamus oxycantha	Asteraceae	Whole Plant	Irritant activity assessed on rabbit skin	135
Caryocar coriaceum Wittm.	Caryocaraceae	Fixed oil of the plant	Excision model on mice	136
Cassia fistula	Fabaceae	Levaes	Human wounds	137
Cassia occidentalis L.	Fabaceae	Leaves	Excision, Incision and Dead Space models in Wistar Albino Rats	138
Cassia tora	Caesulpinaceae	Leaves	Excision model in Wistar Albino Rats	76
Catharanthus roseus	Apocynaceae	Flower	Excision, Incision and Dead Space models in Sprague Dawley Rats	139
Cecropia peltata L.	Urticaceae	Leaves	Excision model in Sprague Dawley Rats	140
Celastrus paniculatus	Celastraceae	Leaves	Excision, Incision and Dead space models in Swiss Albino Rats	141
Celosia argentea Linn.	Amaranthaceae	Leaves	Rat burn wound model	142
Cenostigma macrophyllum Tul.	Fabaceae	Fixed oil of plant from seeds	Excision model in Wistar Rats	143
Centaurea iberica Trev. Ex Spreng.	Asteraceae	Aerial Parts	Excision and Incision models in mice and rats	144

Centaurea sadleriana Janka	Asteraceae	Aerial Parts	Burn wound in rats	145
Centella asiatica	Apiaceae	Whole Plant extract	Excision model in Rats	146
		Whole Plant extract	Excision model in Sprague-Dawley rats	147
		Aerial part	Excision, Incision and Dead space in Wistar Albino Rats	148
		Whole plant	Proliferation of RCE cells	149
Centratherum anthelminticum Linn.	Asteraceae	Seeds	Excision and Incision model in Wistar Albino Rats	150
Centrosema pubescens	*Fabaceae*	Leaves	Excision and Incision model in Albino Rats	151
Chamomilla recutita	Asteraceae	Flowers and Aerial parts	Incision on tongue of Wistar rats	152
Choerospondias axillaris	Anacardiaceae	Bark	Human subjects with burn injury	153
Chromolaena odorata	Asteraceae	Leaves	Excision model in Sprague Dawley Rats	154
		Leaves	Hemostatic activity determination in Wistar Albino Rats	155
Cichorium intybus L.	Asteraceae	Aerial parts, leaves and roots	Incision and Excision in rats	156
Cinnamomum zeylanicum	Lauraceae	Whole Plant	Excision model in Wistar Rats	157
Cissus multistriata	Vitaceae	Leaves	Excision model in Albino Rats	158
Cissus quadrangularis	Vitaceae	Whole Plant	Excision and Incision model in Albino Rats	159
Cleome rutidosperma DC	Capparidaceae	Roots	Excision and Incision models in Wistar Albino Rats	160
Cleome viscose	Cleomaceae	Leaves and whole plant	Excision model in Rats	161
Clerodendron splendens G. Don	Verbenaceae	Aerial Part	Excision and Incision model in Sprague Dawley Rats	162

Clerodendrum infortunatum L.	Lamiaceae	Leaves	In vitro (DPPH) as well as in rat models	163
Clitoria ternatea L.	Fabaceae	Seed and Root	Excision, Incision and Dead Space models in Wistar Albino Rats	164
Cocculus hirsutus	Menispermaceae	Leaves	Excision model in Rabbits	165
		Leaves	Excision model in Wistar Albino Rats	166
Cocculus pendulus (J.R.& G.Forst.) Diels.	Menispermaceae	Levaes	Excision models in Wistar Albino Rats	167
Cocos nucifera	Arecaceae	Young Coconut Juice	Incision model in Wistar Rats	168
Colutea cilicica Boiss. & Bal.	Fabaceae	Flowering parts and fruits	Excision and Incision models in Sprague-Dawley rats	169
Combretum Imberbe	Combretaceae	Leaves	Fungal wounds of immunocompromised Wistar Rats	170
Combretum smeathmanni	Combretaceae	Whole plant	In vitro cell culture model- Fibroblast and Keratinocytes proliferation assay	171
Commelina diffusa	Commelinaceae	Whole plant	In vitro antimicrobial and antioxidant activity assessment	172
Copaifera langsdorffii	Fabaceae	Oleo resin from bark	Excision and incision in rat model	173
Cordia dichotoma Frost. F.	Boraginaceae	Fruits	Excision, Incision and Dead space models in Wistar Albino Rats	174
Cordia macleodii Hook. f & Thoms.	Boraginaceae	Leaves	Excision, incision and Dead space in Wistar Albino Rats	175
Corchorus olitorius	Oceanopapaveraceae	Whole Plant	Anti-microbial and anti-oxidant assay	60
Coronopus didymus	Brassicaceae	Whole plant	Wound healing in Rats	176
Cratylia mollis Mart	Fabaceae	Seeds	Healing of lesions in immunocompromised mice	177
Crinum zeylanicum L.	Amaryllidaceae	Bulbs	Excision model in	178

			Wistar Rats	
Crocus sativus	Iridaceae	Pollen	Thermal burn wound treatment in rats	179
Crossandra infundibuliformis	Acanthaceae	Leaves	Excision model in Wistar Albino Rats	180
Crotalaria verrucosa	Fabaceae	Whole Plant	Excision, Incision and Dead space in Rats	181
Croton bonplandianum	Euphorbiaceae	Leaves	Excision model in Wistar Albino Rats	182
Croton stellatopilosus Ohba	Euphorbiaceae	Plaunotol isolated from plant was tested	Fibroblast proliferation assay to assess wound healing capacity of the compound	183
Croton zehntneri	Euphorbiaceae	Leaves	Excision woumnd in Swiss mice	184
Cucumis sativus	Cucurbitaceae	Fruits	Excision model in Swiss Albino mice and Wistar rats	185
Cudrania cochinchinensis	Moraceae	Leaves	In vitro cell culture method to assess fibroblast cell proliferation	186
Cuminum cyminum	Apiaceae	Seeds	Excision, Incision and Dead Space models in Albino Rats	187
Curculigo orchioides	Hypoxidaceae	Root tuber	Excision model in Wistar albino rats	188
Curcuma aromatica Salisb.	Zingiberaceae	Rhizome	Excision model in Swiss albino mice	189
Curcuma Longa	Zingiberaceae	Procured Curcumin	Gamma radiation-induced wound healing in mice	190
		Rhizomes	Excision, Incision and Dead Space model in Albino Wistar Rats	191
Cynodon Dactylon	Poaceae	Leaves	Excision model in Swiss Albino mice	192
		Whole plant	Excision, Incision and Dead Space model in Albino Wistar Rats	191
Cyperus rotundus Linn.	Cyperaceae	Tubers	Excision, Incision and Dead Space model in Wistar Rats	193
Daphne oleoides subsp. Kurdica	Thymelaeaceae	Aerial part sof the plant	Excision and incision model in rodents	194

Datura alba	Solanaceae	Leaves	Burn model in Albino Rats	195
Davallina Orientalis	Asclepidaceae	Whole plant	Bone healing model in mice	196
Dendrophthoe falcata (L.f) Ettingsh.	Loranthaceae	Aerial parts	Excision and Incision models in Rats	197
Desmodium gangeticum	Leguminosae	Aerial Part	Excision, Incision and Dead space models in Wistar Rats	198
Desmodium gyrans	Leguminosae	Leaves	Excision model in rabbits	199
Dianthus caryophyllus	Caryophyllaceae	Flower buds	In vitro assessment for antibacterial properties	200
Dissotis theifolia	Melastomataceae	Stem	Excision model in Albino rats	201
Dodonea viscosa	Sapindaceae	Leaves	Excision, Incision and Dead space in Rats	202
		Whole Plant	Anti- microbial and Anti-inflammatory activities	203
		Whole Plant	Excision and Incision models in Wistar Albino rats	204
Echinacea pallida	Asteraceae	Roots	Punch Biopsy (Excision) model in SKH-1 mice	205
Echium amaenum	Boraginaceae	Flowers	Excision model in Wistar Rats	206
Eichornia crassipes	Pontederiaceae	Leaves	Excision model in Wistar Rats	207
Elaeagnus angustifolia	Elaeagnaceae	Fruit	Excision in Sprague-Dwaley rat	208
Elaeagnus angustifolia	Elaeagnaceae	Flowers	Healing on rabbit scar	209
Elaeis guineensis Jacq	Arecaceae	Leaves	Excision model in Rats	210
Elephantopus scaber Linn.	Asteraceae	Leaves	Excision, Incision and Dead Space models in Swiss Wistar Rats	211
Eleusine coracana	Poaceae	Seeds	Excision rat model	212
Embelia ribes Burm.	Myrsinaceae	Leaves	Excision, Incision and Dead space models in Swiss Albino Rats	213
Emblica officinalis	Phyllanthaceae	Fruit	Excision wound	214

			model in rat	
Equisetum arvense	Equisetaceae	Leaves	Excision model in Wistar Albino Rats	215
Eucheuma cottonii	Areschougiaceae	Whole Seaweed	Excision model in Sprague Dawley Rats	216
Eugenia jambolana	Myrtaceae	Bark	Burn model in Wistar Albino Rats	217
Eugenia malaccensis	Myrtaceae	Seeds	Incision of skin in mice model	218
Euphorbia caducifolia	Euphorbiaceae	Latex	In vitro CAM assay; incision and excision in mice model	219
Euphorbia heterophylla	Euphorbiaceae	Leaves	Excision model in Wistar Albino Rats	220
Euphorbia hirta	Euphorbiaceae	Whole plant	Burn model in Wistar Albino Rats	221
Fagonia schweinfurthii	Zygophyllaceae	Whole plant	Excision wound model in Albino rats	222
Ficus amplissima Smith	Moraceae	Leaves	Excision and incision model in rats	223
Ficus asperifolia Miq.	Moraceae	Bark	Fibroblast growth stimulation and antioxidation effect	224
Ficus benghalensis	Moraceae	Bark	Excision and incision models in Wistar Albino Rats	225
		Roots	Excision and Incision models in Wistar albino rats	226
		Roots	Excision, Incision and Dead space models in Wistar albino rats	227
Ficus racemosa	Moraceae	Roots	Excision and Incision models in Wistar albino rat	228
		Fruit	Excision models in Albino Rats	229
Ficus religiosa	Moraceae	Leaf	Excision and Incision models in Wistar albino rats	230
		Leaves	Excision, Incision and Burn models in Sprague dwaley	231

			rats	
Flabellaria paniculata	Malpighiaceae	Leaves	Excision model in Wistar Rats	232
Flaveria trinervia	Asteraceae	Leaves	Excision model in Albino mice	233
Galinsoga parviflora	Asteraceae	Whole Plant	Fibrobalst proliferation assay and test for anti-microbial activity	234
Ganoderma lucidum	Ganodermataceae	Whole Plant	Ulcers in abdomen of rats	235
Gentiana lutea	Gentianaceae	Rhizome	Excision, resutured Incision and Dead space models in Rodents	236
		Whole plant	CAM assay	237
Geranium macroprrhizum	Geraniaceae	Above and undergroun d parts	In-vitro (radical scavenging) and in-vivo (hepatoprotective effect)	238
Ginkgo biloba	Ginkgoaceae	Leaves	Dead space and Excision models in Rats	239
Ginseng Radix Rubra	Araliaceae	Saponin from Roots	Incision wound model and Angiogenesis in human umbilical vein endothelial cells	240
			Fibronectin synthesis	241
Glinus oppositifolius	Molluginaceae	Whole Plant	Traditional use in wound healing	242
*Glycine max (*Black Soybean)	Fabaceae	Seed coat	Incision model in Sprague Dawley Rats	243
Glycosmis arreabo	Rutaceae	Leaves	Excision and Incision models in Rats	244
Gossypium arboreum L.	Malvaceae	Leaves	Fibroblast growth stimulation and antioxidation effect	224
Gossypium herbaceum	Malvaceae	Leaves	Excision, Incision and Dead Space models in Wistar albino rats	245
Grewia tiliaefolia	Tiliaceae	Stem bark	Excision, Incision and Dead space models in Wistar Rats	246

Gymnema sylvestre	Asclepiadaceae	Whole plant	Excision and burn models in Albino mice	247
		Leaves	Excision, Incision and Dead space models in Rats	248
Gynura procumbens	Asteraceae	Leaves	Excision model in Sprague Dawley Rats	249
Hamamelis virginiana	Hamamelidaceae	Polyphenol s	Effect on wond healing impairing myeloperoxidase and collagenase	250
Hamelia patens Jacq.	Rubiaceae	Whole plant	Incision models in Sprague Dawley Rats	251
Helichrysum graveolens (Bieb.) Sweet	Asteraceae	Flowers	In-vitro anti-inflammatory and antioxidant activities and Incision and Excision models in Rodents	252
Heliotropium indicum	Boraginaceae	Whole Plant	Excision and Incision models in Rats	253
		Whole plant	Incision wound model in human lung cell culture	254
		Leaves	Excision (normal and infected), incision, and dead space models in Wistar Albino Rats	255
Hemidesmus indicus	Apocynaceae	Roots	Excision model in Wistar Rats	256
Hemigraphis colorata	Acanthaceae	Leaves	Excision model in Swiss Albion mice	257
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Senna alata L	Fabaceae	Leaves	Excision in rats	430
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Sesbania grandiflora	Leguminosae	Bark	Excision in Wistar Albino Rats	432
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Thymus kotschyanus	Lamiaceae	Aerial parts	In vitro assessment for antibacterial properties	200
Tinospora cordifolia Willd.	Menispermaceae	Roots	Excision and Incision in Albino mice	463
Toddalia Asiatica Linn.	Rutaceae	Stem bark	Excision and Incision model in Wistar Rats	464
Tragia involucrata	Euphorbiaceae	Roots	Excision in Rats	465
Tribulus terrestris	Zygophyllaceae	Leaves	Excision, Incision and Burn in Albino Wistar Rats	466
Trichosanthes dioica Roxb.	Cucurbitaceae	Fruit	Excision and Incision in Rats	467
Tridax Procumbens L.	Asteraceae	Leaves	Excision in Mice	468
Trifolium canescens	Fabaceae	Aerial parts	Incision and Excision models in Rodents	469
Typha domingensis Pers.	Typhaceae	Female flower inflorescen ce	Incision and Excision in Mice and Rats	470

Typha latifolia L.	Typhaceae	Fruit	Dermal fibroblast and epidermal keratinocyte proliferation assay	471
Uncaria rhynchophylla	Rubiaceae	Roots	Human Umbelical cell proliferation assay	472
Urena Lobata	Malvaceae	Leaves	Anti-microbial and Anti-oxidant assay	473
Vaccinium macrocarpon	Ericaceae	Seeds	Excision wound model in rats	474
Vanda roxburghii R.Br	Orchidacea	Whole plant	Excision wound model in rats	475
Verbascum mucronatum Lam.	Scrophulariaceae	Flowers	Excision and Incision model in mice and rats	476
Verbascum thapsus	Scrophulariaceae	Flower	Excision in Rabbits	477
Verbena officinalis	Verbenaceae	Bark	Excision in Rats	478
Vernonia arborea Buch.-Ham.	Asteraceae	Bark	Excision, Incision and Dead Space in Wistar Rats	479
Vernonia arborea Hk.	Asteraceae	Leaves	Excision, Incision and Dead space in Wistar Rats	480
Vernonia scorpioides	Asteraceae	Leaves	Incision in Guinea Pigs	481
Vinca rosea	Apocynaceae	Leaves	Excision in Diabetic Rats	482
Viscum Articulum Brm.	Santalaceae	Whole plant	Excision, Incision and Dead space in Albino Rats	483
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Vitex leucoxylon	Verbenaceae	Stem Bark	Incision in Rodents	485
Vitex negundo	Verbenaceae	Leaves	Excision and Incision in Wistar rats	486
Vitex trifolia L.	Lamiaceae	Leaves	Excision, Incision and Dead space wound model in Sprague-Dawley rats	484
Vitis vinifera	Vitaceae	Grape seed extract	Excision in Balb C mice	487
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Vitis Vitigenia	Vitaceae	Leaves	Excision and Incision in Wistar	488

			Albino Rats	
Waltheria douradinha	Malvaceae	Whole plant	Fibrobalst proliferation assay and test for anti-microbial activity	234
Warbugia ugandensis	Canellaceae	Leaves	Excision in Albino Rats	489
Wattakaka volubilis (L.f.) Stapf	Asclepiadaceae	Leaves	Excision, Incision and Dead space in Albino Rats	490
Wedelia biflora L.	Asteraceae	Leaves	Excision, Incision model in Wistar Albino Rats	491
Wedelia trilobata L.	Asteraceae	Leaves	In vitro anti-oxidant assays	492
Withania coagulans	Solanaceae	Fruit	Excision contraction parameters in Diabetic rats	493
Wrightia arborea (Dennst.) Mabb	Apocynaceae	Leaves	Excision and Incision in Wistar Albino Rats	494
Wrightia tinctoria (Roxb) R. Br	Apocynaceae	Leaves	Excision and Incision in Wistar Albino Rats	495
Xanthium cavanillesii	Asteraceae	Fruit	Fibroblast proliferation assay and Anti-microbial assay	234
Ximenia Americana	Olacaceae	Leaves	In vitro anti-oxidant assays and enzymes-inhibition assays	496
Zanthoxylum chalybeum	Rutaceae	Roots and Leaves	Excision in Wistar Albino Rats	489
Zingiber officinale	Zingiberaceae	Roots	Abrasion in Male CD Hairless Rats	497
Ziziphus nummularia L.	Rhamnaceae	Leaves	Excision, Albino Rats	498
Zizyphus oenoplia	Rhamnaceae	Fruits	Excision, Incision and Dead space, Albino Wistar Rats	499

*Wherever animal models were used, these have been reported as Excision, Incision, Burn and/or Dead space model, as applicable.

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