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Review On Of Invasive Alien Medicinal Plants Used In Wounds Treatment In Animals South Africa.

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Abstract
The care of wounds in animal species can be a challenging endeavor. Special considerations must be made in regards to the animal's temperament and behavior, anatomy and size, and tendency towards secondary stress-related health problems. Wound healing disorders present a serious both clinical problem of medical health care in South Africa and veterinary health care; most of these disorders lead to complications, high morbidity and mortality rates. However, most of the synthetic drugs currently used for the treatment of wounds are not only expensive but also pose problems such as allergy and drug resistance. In this direction a number of plant drugs are being investigated at present. Many plant drugs have been used in management and treatment of wounds over the years. Plants and their extracts have immense potential in the management and treatment of wounds. In this literature review, we presented the role of invasive alien medicinal plants in wound healing, some of the common medicinal plants, standardization, quality control, safety assessment, and efficacy assessment concerns of herbal medical products.

Keywords: *WHO, Herbal plants, Alien plants, native plants, Wound healing; Antiviral; Immunomodulatory.*

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I. Introduction

Wound is defined as the disruption of the cellular and anatomic continuity of a tissue; it may be produced by physical, chemical, thermal, microbial or immunological insult to the tissue[7] .A wound comprises damage to anatomic structures and functions of the skin, thus resulting in loss of epithelial continuity with or without loss of surrounding connective tissue. [1] The effects of a wound may be in the form of partial ot complete organ dysfunction, sympathetic activation, bleeding, bacterial contamination and cell death. [2] Wound care and maintenance involve a number of measures including dressing and administration of pain killers, use of anti-inflammatory agents, topical and systemic antimicrobia agents and healing drugs [5]

A large number of plants/plant extracts/decoctions or pastes are equally used by rural people and traditional medical practitioners in South Africa for treatment of cuts, wounds, boil and burns. Plants or chemical entities derived from plants need to be identified and formulated for the treatment and management of wounds [6] These natural agents induce healing and regeneration of the lost tissue by multiple mechanisms. The medicinal plants extracts and fractions effectively arrest bleeding from fresh wounds, inhibit microbial growth and accelerate wound healing [3].These phytomedicines are not only cheap, readily available and affordable but also safe compared to synthetic drugs. Records have it that different parts of plants used for wound healing contain some active principles or components that are antimicrobial and nutritive in function [4].

Process of Wound Healing in Animals

Wound healing in animal is typically a well-organized process divided into 3–5 overlapping phases, depending on the classification system: Hemostasis phase, inflammatory phase, debridement phase, repair (proliferative) phase, and maturation phase .Chronic or non-healing wounds do not proceed through the normal phases of wound healing, often unable to make the transition from the inflammatory to the repair phase[181,182] .Knowledge of normal wound-healing physiology provides a framework for understanding factors that impair wound healing and for implementing effective wound management strategies.

Hemostasis (Coagulation) Phase

Immediately following injury to the skin, hemostasis is achieved through vasoconstriction and platelet-mediated activation of the intrinsic clotting cascade, ending in formation of a fibrin clot. Release of proinflammatory cytokines from damaged tissue and the newly formed clot act as potent chemotactic signals to recruit neutrophils, endothelial cells, and fibroblasts to the wound. Formation of the fibrin clot is therefore an important step in promoting onset of the inflammatory and repair phases.[181,182]

Inflammatory Phase

The inflammatory phase is regarded as by improved capillary permeability and penetration of neutrophils, macrophages, and lymphocytes into the wound . Following initial vasoconstriction throughout hemostasis, vasodilation and better vascular permeability develop. improved blood flow and fluid extravasation shared with obstruction of lymphatic drainage source the classic signs of inflammation, including heat, redness, and swelling. This acute inflammatory reaction more often than not lasts for 1–2 days but may persist in a poor wound environment.[181,182]

Debridement Phase

Wound debridement begins with movement of white blood cells into the wound. Platelets within the fibrin plug release growth factors and cytokines, which recruit inflammatory cells to the wound.[182] Circulating neutrophils begin entering the wound within minutes of injury, peaking within the first 24 hours, and are primarily responsible for bacterial phagocytosis. Monocytes accumulate within 12 hours after injury and undergo differentiation to mature wound macrophages under the influence of local cytokines. Macrophages are the dominant inflammatory cell within three to five days of injury and play a pivotal role in transitioning from inflammation to repair. Macrophages are responsible for phagocytosis of apoptotic cells, tissue debris, and microbial organisms. In addition, they release proinflammatory cytokines that propagate the inflammatory response and growth factors that stimulateconversion of mesenchymal cells to fibroblasts and promote collagen synthesis and angiogenesis. [181,183].Lymphocytes appear later, peaking at approximately seven days.

Proliferative (Repair) Phase

The proliferative phase of wound healing is the repair phase that lasts up to *2* days to 3 weeks after the inflammatory phase. The proliferative or repair phase begins approximately 3–4 days after injury and is characterized by fibroplasia, angiogenesis, and epithelialization This phase comprises of three steps viz., granulation, contraction and epithelialisation. In the fibroplasia step fibroblasts form a bed of collagen and new capillaries are produced. Fibroblast produces a variety of substances essential for wound repair including glycosaminoglycans and collagen. Under the step of angiogenesis wound edges pull together to reduces the defects in the third step epithelial tissues are formed over the wound. Epithelialization involves proliferation and migration of epidermal keratinocytes from the wound edges, differentiation of epithelial progenitor cells into a stratified epidermis, and restoration of the basement membrane connecting the epidermis to the underlying dermis.[182,183] Angiogenesis typically occurs five to nine days after initial injury. The existing tissue at the wound edges is pulled inward by contraction, and surrounding skin stretches, decreasing the overall size of the wound. The process continues until the wound edges meet (contact inhibition), tension is high, or myofibroblasts are inadequate.[179]

Maturation (Remodeling) Phase

Maturation typically begins one week after injury following collagen deposition in the wound and is the longest phase of wound healing, continuing for weeks to months after injury .The main activity happening during this phase is strengthening and remodeling of the newly formed collagen. There is reduced proliferation and inflammation and regression of the newly formed capillaries in the wound bed. Type III collagen is replaced by type I collagen. Collagen fibers remodel by aligning with tension lines of the body and gain strength through cross-linking. The scar eventually becomes less cellular, flattens, and softens. Normal tissue strength is never regained, with approximately 80% of the original strength acquired at best[181,182].The wound healing activities of plants have since been explored in ethnophamacology. Many herbal plants have a very important role in the process of wound healing. Plants are more potent healers because they promote the wound healing.

II. Factors Impacting Wound Healing

Both systemic (host) and local factors serve as potential impediments to wound healing. Host factors include age, body condition, nutritional intake, and concurrent disease. Large wounds place animals in a catabolic state, and thus calorie and protein intake should be increased to ensure that nutritional requirements are met. Hypoproteinemia (< 2.0g/dL) and diets deficient in protein have delay wound healing and decrease wound strength. Underlying metabolic disease, such as diabetes mellitus, hyperadrenocorticism, and uremia, delay wound healing as well.[184,186] Many medications are associated with impaired wound healing and reduced wound strength, including corticosteroids and chemotherapeutic agents.[186,187] Chemotherapeutic drugs further delay healing as they specifically target rapidly dividing cells, affecting fibroblast proliferation and wound strength.[188] Nonsteroidal anti-inflammatory drugs have been investigated with regard to their effects on wound healing; however, these medications have not been found to alter the rate of wound healing significantly[186].

The presence of debris, dirt, hair, suture, and necrotic or devitalized tissue act as foreign material, leading to an intense inflammatory reaction that prolongs the inflammatory phase and delays the repair phase.

Accumulation of fluid in the wound bed, as with a hematoma or seroma, inhibits fibroblast migration, encourages infection, and leads to wound ischemia, delaying wound healing and strength formation[184,185].

III. Initial Wound Care And Management

The goal of wound care is to prevent further contamination and convert contaminated or infected wounds into clean wounds for either surgical closure or second intention healing. In order to fully assess an open wound, sedation or general anesthesia may be indicated. Wounds should be lavaged and debrided immediately, after which samples from the deep aspects of the wound are collected for culture and susceptibility. A biopsy should be considered for all chronic or non-healing wounds. Aseptic technique should be utilized when treating wounds, including the use of sterile gloves, instruments, and bandage materials. [189] It should be noted that wound healing is faster under moist and wet conditions. Excessive wetness, however, can be problematic, and thus the ideal wound dressing should absorb exudate without excessively drying the wound.

IV. Some Possible Plants With Wound Healing Activities

As pathogens develop resistant every currently and afterwards the importance of vaccine creation in the clinical researches in plants has increase over the years.. Hence, important organic compounds presents in plants could overstate to reduce side effects associated with the use of synthetic drugs such as hepatotoxicity, hyperglycaemia, hyperlipidaemia, lactic acidosis, lipodystrophy, osteonecrosis, osteopenia, osteoporosis and mild skin rashes. This review describes Alien medicinal plants containing wound healing properties that would generously play an important role in the discovery of novel drugs. Possible plants, which could be evaluated for powerful wound healing combinations or compounds in upcoming days, are discussed below.

V. Alien Medicinal Plants With Wound Healing Activities

Agrimonia Eupatoria

Botanical Description

Agrimonia Eupatoria Belong to the Family of The plant: is slim, erect leafy perennial herb. The stem is about 60-90 cm long, scarcely branched. The herbs deep green, covered with soft silky hairs and when slightly bruised exhaling a peculiar, but pleasant aromatic odour. The whole plant yields a dye. [20]. Leaves**:** Leaves are pinnately compound. Lower leaves 10-18cm; leaflets 6-21 in number coarsely toothed, hairy on both surface very unequal, large ones 5-9 elliptic, ovate or obovate rarely orbicular or minute. 1.3-3.8cm intermixed with a number of much smaller ones. Upper leaves gradually smaller and with few leaflets. Stipules adnate to the base of leafstalk. [19,20]. Flowers: Flowers very numerous 6.0mm in diameter, yellow in colour and terminal spike-like racemes. Each flower in the axial of a small, 3-cleft bract and with two smaller, 3-tootched bracteoles at the tops it stalk. Calyx-tube top-shaped, grooved, bearing outside its mouth a ring of small, hooked bristles; limb 5-lobed. Petal 5, oblong. Stamen 15, Carpels 2, free, enclosed within the calyx tube; styles thread like protruding; stigmas terminal, dilated; ovule solitary. Achenes 1 or 2, in closed in the hardened bristly calyx crowned with a ring of hooked bristles. Fruits and Seed: Fruits pendulous, of 1 or 2 achences in closed in the hardened spinous calyx. Calyx of fruits encircled with a thick whorl of hooked prickles, which attach themselves to anything that comes in their way. Flowers appear in about July and August, soon after the seeds become mature. Each flower contains two seeds. It is astringent and bitter in taste [19,21-24]

Geographical distribution:

The plant is indigenous to middle and northern Europe, temperate Asia and north America [25].

Ethnopharmacology:

Its ancient uses include treatment for catarrh (mucous membrane inflammation with discharge), bleeding, tuberculosis and skin diseases. It has been reported to be useful in gallbladder disorders. [20]. Numerous other reported uses include a dye, flavoring, gargle for performers and speakers, antitumor agent, astringent, edemas, rheumatism; hemorrhoids, bleeding gums, varicose ulcers; laryngitis; pulmonary and cutaneous tuberculosis ,kidney diseases cardiotonic, coagulant, diuretic, sedative, antiasthmatic and for corns or warts [26-27]. It was also used as anti-inflammatory, cholagogue, mild haemostatic, antibacterial, for irritations and infections of the intestinal tract, gallbladder diseases, hyperacidity, colic, urinary disorders (bedwetting, incontinence), sluggish liver, mucus membrane inflammations and externally for ulcerations [27].

Antimicrobialactivities

Antibacterial activity

There are reports on the antibacterial activity of *A. eupatoria* extracts against pathogenic *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli* bacteria and the beneficial effect on wound healing in rats [35]. Similar antibacterial activity against *Staphylococcus aureus* and α-haemolytic *Streptococci* in the

healing process was detected in other studies as well [34].The antibacterial (against *Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli*) and wound healing effects of the extracts of *Agrimonia eupatoria* (aqueous and ethanolic) were studied. The results showed that the ethanolic extract was more effective on inhibiting the tested bacteria than the aqueous extract. *P. aeruginosa* was the most resistant bacteria, while highest inhibition zone appeared against *E. coli* (20 mm). There was a moderate activity agains *S. aureus* with inhibition zone of 15 mm [28]. Preparations of *Agrimonia eupatoria* were screened for antimicrobial activity against selected Gram-positive and Gram-negative bacteria of relevance in wounds using a 96 well plate microdilution method (200, 40 and 8µg/ml). It exerted moderate antibacterial effects [29].

Antiviral effect

Ethanolic extract of *Agrimonia eupatoria* was reported to be active against Columbia SK virus [7,27]. The Inhibitory activity of an aqueous extract of the aerial parts (stems and leaves) of *Agrimonia eupatoria* against hepatitis B virus (HBV) was investigated. The extract prepared at 60 degrees ºC was found to have the greatest effect. The inhibitory activity of *Agrimonia eupatoria* extracts on HBsAg secretion varied over the growing season and was the highest at mid-July. This inhibitory activity suggest that *Agrimonia eupatoria* contain potential antiviral activity against HBV [29,30].

Wound healing effect

Prepared ethanolic extract ointment showed wound healing activity in rats in contrast with fucidin ointment and aqueous extract ointment, hence the wound healing was completed in l0 days by using the ethanolic extract ointment, while the healing was completed in 12 and 14 days for the aqueous extract and fucidin ointments respectively, while, the untreated wound needed more than 16 days for healing completion [28].

Immunomodulatory effect

An aqueous ethanol extract of the herb was tested for immunomodulative activity in the peritoneal cavities of mice. They produced immunostimulant activity resulted in an increase in phagocytic activity and increases in the activities of lysozyme and peroxidase [31].

Cytotoxic Activity

No health hazards or side effects are known with the proper used of the recommended doses. Agrimony is listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates that Agrimony can be added to foodstuffs in small quantities. However, because of the tannin contents, the intake of large quantities caused digestive complain and constipation [32-33].

Lantana camara

Botanical description:

Lantana camara Belong to the Family of Verbenaceae. *L. camara* is a low erect or subscandent vigorous shrub with tetrangular stem, stout recurved pickles and a strong odour of black currents. Plant grows up to 1 to 3 meters and it can spread to 2.5 meter in width. Leaves are ovate or ovate oblong, acute or sub acute, crenate serrate, rugose above, scabrid on both sides. The leaves are 3-8 cm long by 3-6 cm wide and green in colour [37]. Leaves and stem are covered with rough hairs. Small flower held in clusters (called umbels). Colour usually orange, sometime varying from white to red in various shades and the flower usually change colours as they ages. Flowers are having a yellow throat, in axillary head almost throughout the year. The calyx is small, corolla tube slender, the limb spreading 6 to 7 mm wide and divided in to unequal lobes. Stemen four in two pairs, included and ovary two celled, two ovuled. Inflorescences are produced in pairs in the axils of opposite leaves. Inflorescences are compact, dome shaped 2-3 cm across and contain 20-40 sessile flowers. Root system is very stro and it gives out new fresh shoots even after repeated cuttings[36].

Geographical distribution:

L. camara is a tropical origin plant and native to Central and Northern South America and Caribbean. *L. camara* is now spreaded to nearly 60 countries viz, New Zealand,

Mexico, Florida, Trinidad, Jamaica and Brazil. It is reported as alien many African countries including Kenya, Uganda, Tanzania and South Africa [37].

Ethnopharmacology:

L. camara is an important medicinal plant with several medicinal uses in traditional medication system. It is been used to cure many health problems in different parts of theWorld. Leaves are used to treat cuts, rheumatisms, ulcers, catarrhal infection, tetanus, rheumatism, malaria, cancer, chicken pox, asthma, ulcer, swelling, eczema, tumour, high blood pressure, bilious fever, ataxy of abdominal viscera, sores, measles, fevers,

cold and high blood pressure. In Ghana, infusion of the whole plant is used to cure bronchitis and the powdered root in milk was given to children for stomach-ache and as a vermifuge. Lantana oil is used in the treatment of skin,itches, as an anticeptic for wounds. In leprosy and scabies decoctions were applied externally. [37-39].

Antimicrobial activity

Antibacterial activity and Antifungal activity

Different varieties of *L. camara* plants' leaves and flowers were reported for antibacterial activity. Three different solvent extract of leaves and flowers of four different varities of *L. camara* exhibited significant antibacterial activity *E. coli*, *Bacillus subtilis* and *P. aeruginosa* whereas poor antibacterial activity against *Staphylococcus aureus*[40].Ethanolic extracts of *L. camara* leaves and roots were reported for antibacterial activity. The *in vitro* antibacterial activity was performed by microdilution method. The extracts exhibited antimicrobial activity against *Staphylococcus aureus*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Víbrio cholareae*, *Escherichia coli* and two multiresistant strains *E. coli* and *S. aureus.* [41].Methanolic extracts of different parts of *L. camara* were screened for antimicrobial activity against 10 bacteria and 5 fungi by disk diffusion method and broth microdilution method. The leaves extract of *L. camara* showed highest activity against Gram positive *Bacillus cereus* and Gram negative *Salmonella typhi*. [42-44].

Antiviral activity

In Tanzania the root bark extract of Lantana camara showed an in vitro antimalaria test with Plasmodium falciparum[50] .The essential oil containing ß-caryophyllene, geranyl acetate, terpinyl acetate, bornylacetate and limonene remarkably inhibited the growth of many tested against fungi[49] .

Wound healing activity:

Wound healing property of aqueous extract of leaf of *L. camara* was reported in rats. Topical application of the extract on the wound (100 mg/kg/day) significantly enhanced the rate of wound contraction (98%), synthesis of collagen and decreased wound healing time[45]. Ethanol extract of leaf of *L. camara* was reported for wound healing activity in adult male Wister rats. Topical application of the extract over the wound significantly increased the wound healing activity. Histological analyses of healed wounds confirmed the role of extract in healing. [46].

Cytotoxic Activity

L. camara is one among the most toxic plants known so far, possibly within top ten. Reports of *L. camara* toxicity have been reported from Australia, India, New Zealand, South Africa and America. However, the toxicity occurs only on the consumption of high amount of plants material. It is reported that sheep, cattle and goats are susceptible to lantadenes A, B, D and icterogenic acid toxicity, where as horses, rats, neonatal calves and lambs are not susceptible to lantadene A. The prominent clinical sign of poisoning includes photosensitisation and jaundice. Loss of appetite in poisoned animals occurs within 24 hours and decrease in appetite also observed. The most severely poisoned animals die within 2 days of poisoning but usually death occurs after 1 -3 weeks after poisoning. The kidneys are swollen and pale in colour, the gall bladder is grossly distended and the liver is enlarged. The oral toxic dose of lantadene A for sheep is 60 mg/kg is toxic and 1–3 mg/kg by intravenous route. [47, 48].

Psidium guajava

Botanical Description

Psidium guajava L. belong to the Family Myrtaceae *Psidium guajava* is an evergreen shrub like tree which reaches to the height of 6 to 25 ft's. The plant has a wide spreading network of branches. Mostly its branches are curved which display opposite leaves with the small petioles of about 3 to 16 cm.The leaves are wide and clear green in color and have clear and prominent veins [52, 53,70]. The plant produces white flowers with incurved petals having a nice fragrant.Flowers have four to six petals and yellow colored anthers and pollination occurs by the insects. Guava fruit ranges from small to medium sized with 3 to 6 cm length. It has pear like shape and yellow color in ripen condition [54,70]. It has a musky special odor when ripened which is strong but pleasant [51]. Its pulp is slightly darker in color which contains slightly yellowish seeds. The size of seeds is very small and they are easily chewable. They are arranged in regular patterns; their number ranges from 112 to 535 [51, 55,70]. The guava bark is thin and has green colored spots. It is very easy to remove it in long straps.

Ethnopharmacology:

P guajava (Myrtaceae) is widely used in Mexico to treat gastrointestinal and respiratory disturbances and is used as an anti-inflammatory medicine[68,70] Commonly roots, bark, leaves and immature fruits, are used

in the treatment of gastroenteritis, diarrhoea and dysentery. Leaves are applied on wounds, ulcers and for rheumatic pain, while they are chewed to relieve toothache[69,70] .A decoction of the new shoots is taken as a febrifuge. A combined decoction of leaves and bark is given to expel the placenta after childbirth[67] A water leaf extract is used to reduce blood glucose level in diabetics. This hot tea was very common among the local people of Veracruz [68] The leaf of *Psidium guajava* is used traditionally in South African folk medicine to manage, control, and/or treat a plethora of human ailments, including diabetes mellitus and hypertension[65,66]

Antimicrobial activities

Antibacteria activity

The antimicrobial activities of alcohol fruit extracts from guava (Psidium guajava) were compared to those of pineapple (Ananas comosus) and apple (Malus pumila). Eight bacterial strains including Pseudomonas aeruginosa, Klebsiella, Enterococcus faecalis, Shigella flexineri, Enterobacter cloacae, Enterotoxigenic E.coli (ETEC), Enteroaggregative E.coli (EAEC) and Staphylococcus aureus were used for antimicrobial evaluations. Guava has a high antimicrobial activity. Guava leaf's extract doses can reduce the amount of wound[56].

Antifungal activity

P. guajava L. leaf extracts possess high antifungal activity[57-59]

(the hot water extract and the methanol extract were measured for their antifungal activity against *Arthrinium sacchari* M001 and *Chaetomium funicola* M002 strains).[54]

Wound healing

The wound healing properties of a methanolic leaf extract of *Psidium guajava* were determined using the excision wound model. More than 90% wound healing was observed after 14 days post-surgery, whereas 72% healing was observed in the distilled water treated group .[60]

Anti-inflammatory

The essential oil, steam-distilled from leaves of *Psidium guajava*, was given orally to rats to study its effects on the exudative and proliferative phases of the inflammatory reaction (carrageenan induced paw oedema and cotton pellet induced granuloma models). The essential oil (0.8 mg/kg) significantly reduced oedema formation induced by carrageenan while at 0.4 mg/kg and 0.8 mg/kg the oil also significantly reduced granuloma formation induced by cotton pellets.[61] .

Cytotoxic Activity

The water extract of *P. guajava* leaves has no short term harmful effect,[39] and was found to be non toxic to rats and mice at a dose of 5g/Kg. i.e. LD50 was more than 5 g/ kg.[63]The study peformed on the Egyptian plant lately stated that the ethyl acetate extract is not toxic in doses up to 1.40 g/kg body weight, the alcoholic extract up to 2.05 g/ kg,the aqueous extract up to 2.35g/kg and the essential oil up to 0.62 g/kg.[62]Guava tea intake raises no changes in parameters of iron metabolism, liver and kidney functions and of blood chemistry data. In addition hypoglycemia is not caused by excess ingestion of guava tea. [64]

Hypericum perforatum

Botanical Description:

Hypericum consists of herbs and shrubs having yellow or coppery flowers with four to five petals, numerous stamens, and a single pistil [70] and free branching typically range from 40 to 80 cm in height. [70] The stems and branches are densely covered by oblong, smooth margined leaves that range from 1 to 3 cm long and 0.3-1.0 cm wide. The leaves are interrupted by minute translucent spots that are evident when held up to the light. The upper portions of mature plants can produce several dozen five petaled yellow flowers that are typically 1.0-2.0 cm wide. The edges of the petals are usually covered with black dots. Crushed flowers produce a blood red pigment. By late summer, the flowers produce capsules that contain dozens of tiny, dark brown seeds. It thrives in poor soils, and is commonly found in meadows, fields, waste areas, roadsides, and abandoned mines and quarries. [70]

Geographical distribution

Indigenous to Europe and New Zealand, and is naturalized in the northern Africa, South Africa , Asia, Australia, United States of America [72,74,75,76,93]] The plant material is harvested at flowering time[71]

Ethnopharmacology

Symptomatic treatment of mild and moderate depressive episodes (classified as F32.0 and F32.1, respectively, in the *International statistical classification of diseases and related health problems, Tenth revision*

(ICD-10) [77,78,90]Externally for the treatment of minor cuts, burns and skin ulcers [76,91]Topically for viral infections [70]As an antiphlogistic agent in the treatment of inflammation of the bronchi and urogenital tract; treatment of biliary disorders, bladder irritation, the common cold, diabetes mellitus, dyspepsia, haemorrhoids, neuralgia, migraine headaches, sciatica and ulcers [73,76]Also used as a diuretic, an emmenagogue and an antimalarial agent [73,76]

Antimicrobial activities

Antibacterial activity

A methanol extract of Herba Hyperici inhibited the growth in vitro of *Escherichia coli*, *Proteus vulgaris*, *Streptococcus mutans*, *Streptococcus sanguis*, *Staphylococcus oxford* and *Staphylococcus aureus (*MIC 0.31-1.25 mg/ml) [92]However, a decoction or hydroalcoholic extract of *H. perforatum* dried stem was not active against herpes simplex virus 1 or 2, or HIV in vitro (100 µg/ml) [93]

Antiviral activity

In vitro activity of hypericin has been demonstrated against Friend murine leukaemia virus, hepatitis B virus, murine cytomegalovirus, human cytomegalovirus (Davis strain), parainfluenza 3 virus, Sindbis virus, vaccinia virus, vesicular stomatitis virus and equine infectious anaemia virus [94- 99]. Hypericin and pseudohypericin also inhibited herpes simplex virus types 1 and 2, and HIV-1 in vitro ([99-105] Hypericin inhibited the activity of HIV reverse transcriptase in vitro (IC_{50} 0.77 mmol/l) [96,102,106] and inhibited herpes simplex virus, Rauscher murine leukaemia and Friend murine leukaemia viruses in mice after intravenous, intraperitoneal or intragastric administration [102-104].

Wound healing

External application of a 20% aqueous extract of the crude drug to the skin of guinea-pigs and rabbits accelerated healing of experimentally induced wounds (*95*, *96*). Intragastric administration of a 60% ethanol extract of the dried leaves to rats (0.1 ml/animal) accelerated healing of experimentally induced wounds by enhancing the strength and rate of wound contraction and epithelialization [107]

Cytotoxic Activity

Phototoxicity has been reported in cattle after ingestion of *H. perforatum* during grazing. However, the doses were estimated to be approximately 30-50 times higher than normal therapeutic doses [107]. Drug-monitoring studies indicate that side-effects of the herb are rare and mild, and include minor gastrointestinal irritations, allergic reactions, tiredness and restlessness. However, these studies did not last longer than 8 weeks [80,83,90] Clinical studies have suggested that the use of the herb does not affect general performance or the ability to drive [108,109] Due to concerns over phototoxicity to livestock, *H. perforatum* is listed as a noxious weed in seven western states in the United States. Programs promoting its eradication are underway in Canada, California, and Australia.

Datura stramonium

Botanical Description

Datura stramonium is mostly known as Angel's trumpet, Locoweed, Jimson weed or Datura, it belongs to family Solanaceae. The plant rises to the height of about 60-120 cm or more,they are pubescent and branched plant. The leaves dimensions are 8-17x4-13cm, sinuately dentate, minutely puberulose and ovate. The flowers are trumpet-shaped, white to creamy or violet and 6 to 9 cm long [70,110]. Commonly found in temperate and subtropical region [70,111] **.**

Geographical distribution

D. stromonium is probably originated in Caspian Sea territories and spreaded to Europe in the first century. At present it grows in waste places in Europe, Asia, America and South Africa. *D. stromonium* is cultivated in Germany, France, Hungary, South America and throughout the world [70,111].

Ethnopharmacology:

From the ethnomedicinal point of view it has an important medicinal value throughout the world. The leaves and seeds are used in different treatment regime. The leaves of *Datura stramonium* when mixed with mustard oil it helps in treating skin disorders. The extract of flower petals is used in ear pain. Seeds are used in fever, cough,asthma and as purgatives. Seeds are also used intoxicants for its narcotic action [70,113]. In folklore medicine this plant were used because of its analgesic effects in the "Old world" [114]. *Datura stramonium* comprises of different types of phytochemicals including Tannins,Saponins, Alkaloids, Glycoside Flavonoids Steroids and Phenols [115].The bioactive components present in branches and leaves extracts consists of high

anti-microbial and anti-fungal activities [116]. Traditionally the plant is used to treat various diseases and there is a constant search for the medicinal value of plant. *Datura stramonium* has both the toxic effects and medicinal uses [70,112] Since inception of life humans beings use plant for different purposes like food and medicine. Still today a large number of people use different plant for different disease treatments. *Datura stramonium* has most important medicinal use. *D.stramonium* is used frequently as an antiasthmatic treatment [117,118,119] The widely reported medicinal uses include the use of the dried leaves of the plant as an anti-asthmatic agent[120,121,122].As the cure for the asthma mixture of the leaves and seeds is taken orally as a decoction or smoke [123]. Aqueous extract of the seeds are reported to be used in the treatment of gastric pains and indigestion[124].Furthermore, this plant as herbal remedy is also frequently given to pregnant mother with asthmatic complaints. It is used as a medicinal, psychotropic, sacred & antispasmodic[125].

Antimicrobial Activities

Antibacterial Activity

The antimicrobial assay done by disc diffusion method of the crude extract showed antimicrobial activity on pathogenic organisms obtained from burn patients. Silver sulfadiazine (1 mg/ml), DMSO and solvents used for fractionation were also tested simultaneously. The pathogens isolated from Burn ward unit, Child Trust Hospital, Chennai were *Staphylococcus* sp., *Klebsiella* sp., *E. coli*, *Streptococcus* sp., *Pseudomonas* sp., *Salmonella* sp. and *Vibrio* sp. Wound healing was increased due to enhanced epithelialisation[128].

Antiviral

Atropine inhibited only the growth of enveloped viruses independent of the nucleic acid content of the virus. The activity of atropine was checked by plaque reduction test and one step growth experiments. The test viruses included *Herpes Simplex Virus, Influenza virus, New Castle Disease Virus, Sindbis, Vaccinia, Adenovirus, Japanese encephaitis Virus*. Viruses were cultivated on primary chick embryo (CE), HeLa S3, primary monkey kidney cells (MK) [132].Atropine also blocks the glycosylaton of viral proteins of *Herpes* virus and hence the production of new infectious virus particles (virions). Virions formed in the presence of atropine are non infectious [126].

VI. Wound Healing Properties

In vivo healing potential of *Datura alba* alcoholic extract on burn rat wounds were studied [129]. A 10% w/w ointment was prepared and applied topically on thermal wounds. Complete wound healing was observed within 12 days in treated rats against control rats which required about 30 days for healing. Apart from antimicrobial activity, studies were carried out to check rate of wound contraction and histochemical analysis to examine cellular infiltration. Biochemical assays to check collagen and hexosamine content of tissue on various days were carried out by using gelatin zymography.

Anti-inflammatory

The crude extract has enhanced chemotactic effect which attracted inflammatory cells towards the wound site and cellular proliferation was observed by hematoxylin and eosin staining. Increase in cellular proliferation may be due to mitogenic effect of the plant extract. Increase in hydroxyproline content was observed which indicates the increase in collagen synthesis which is essential for wound healing. Matrix metalloproteases (MMP's) such as MMP 9 were expressed in early days, and MMP 2, a 72 kDa gelatinase were also observed. MMP's are helpful in removal of fibrin and eschar which results in formation of peptides which are known to have angiogenic and chemotactic properties. The presence of gelatinase indicates progression of wound healing process [130].

VII. Immunomodulatory Activity

Phytochemical investigations of *D. quercifolia* has led to the isolation and characterization of several *Datura* lactones, which are of with anolide skeleton . [131].Phytochemical investigation yielded a new *Datura* lactone, 1",5!,12!-trihydroxy-6!,7!, 24!, 25!-diepoxy- 20S, 22R with 2-enolide (5) along with two known compounds, 3 and 4. These compounds were evaluated for their immunomodulatory activity by observing the B and T-cell activation and cytokine production from splenocytes.Of the three compounds isolated, Compound 4 showed dose related increase in primary and secondary antibody production, while Compound 5 act as a suppressor where levamisole was use as standard which increases primary and secondary antibody production. Compound 3 showed higher SRBC induced DTH response at a dose of 0.1 mg/kg p.o. BMS (Betamethasone) was used as standard .Compound 3 was checked for the activation of spleen Tcell sub types, CD4 and CD8, selective release of cytokines, IL-2 and TNF-!. It stimulated and showed increase in CD4+ T-cell count and stimulated increase in IL-2 and TNF-! in dose dependent manner (0.01 mg/kg was found more effective) [131].

Cytotoxic Activity

Toxicity studies of ethanol extract of the leaves of *D. stromonium* in rats. Two doses of 50 and 200 mg/kg of the extract were administered to the rats for five weeks. Parameters studied were the indices of liver and kidney function and some biochemical and haematological parameters. Feed intake, final body weight, serum AST, ALT, billurubin, total protein, urea and the electrolyte studied were not affected by the extract administration. Serum creatinine levels were however significantly raised in the rats administered with ethanol extract at the dose of 200 mg/kg body weight. The biochemical and haematological parameters were also affected[198].The effects of acute, subacute and chronic administration of alkaloids atropine and scopolamine, the main constituents of the active principle of *D. stromonium*, with toxic properties, were studied in male Albino Wistar rats. After acute *i.p.* administration of dose 100 mg/kg of total alkaloids to the seeds of *D. stramonium*, there were no remarkable changes in general appearance and no deaths occurred in any experimental group. Twenty four hour after total alkaloids of seeds, a significant reduction in indices of liver, spleen brain and kidney function and some biochemical and haematological parameters were observed. The red blood cells, hematocrit, hemoglobin and white blood cells were significantly higher in the treated groups than the control group. Subacute study for four weeks showed no resulting mortality or signs of toxicity. In chronic study, the synthetic alkaloids administered *i.p.* at daily doses of 4.2 mg/kg of atropine and 1.6 mg/kg of scopolamine, did not produce death. However diarrhoea and hypoactivity were observed. The relative weight of liver was significantly less than that of the control group[199].

VIII. Schinus Terebinthifolius

Botanical Description

Schinus Terebinthifolius belonging to the family Anacardiaceae. The plant grows and propagates from seeding or cutting. The tree is 5-10m high, medium-sized and carries a broad crown. The trunk is covered with a thick bark and the leaves are imparipinnate-composed ranging from 3-10 pairs of aromatic leaflets [134]. The leaflets are wider than those of the plants of the same family such as the *S. molle* and the *S. lentiscifolius*. The male and female flowers are very small, arranged in pyramidal inflorescences. The fruits are drupe-like, globoid, sweet, aromatic, bright and red [134,135]. For having an essential oil that produces a spicy flavor, the fruits are quite used in the French cuisine, known as "poivre rose". In Peru, they are used for syrups, vinegar, and drinks, and in Chile, for wine [136,137]. There is a great deal of studies about such species and their antimicrobial effects. However, there is a wide variety of extracts, protocols, and compounds investigated that can be exploited [138].

Geographical distribution

Originated from South America and its habitat ranged from southern Brazil to Chile and Mexico. [134,135, 136,137].

Ethnopharmacology:

In traditional medicine, including in some states in northeastern Brazil, it is used to treat the skin, mucous membrane injuries as a remedy for ulcers, gastroduodenal disorders, urinary infection, respiratory problems, cancer, diarrhea and arthritis. It has also been used to treat sexually transmitted diseases, uterine inflammation, as antiseptic, antioxidant and anti-inflammatory [139]. The *S. terebinthifolius* Raddi is among the most used plants for dental use, being among the most sold for such an end by indigenous people in Brazil. The decoction of the leaves is commonly used for skin treatment while the decoction of the bark is used for diarrhea, gout and rheumatism [133, 140]. Furthermore, intravaginal compresses with the aqueous extract of such a plant have been used to treat cervicitis and cervicovaginites [134, 140].

On the other hand [142] has been observed that the cure rate for bacterial vaginosis by the vaginal gel out of an extract of aroeira was lower than the one obtained by metronidazole gel, regardless of being observed rare and non-severe side effects in the studied groups. Many of these uses have been proven by scientific research [140,142-143]. The decotation of the leaves is used in hypertension, depression and irregular heartbeat treatment. The decotation of the bark is, in turn, used in rheumatic pains and backaches [144]. Other extracts of the bark are used as a home medication for the treatment of diseases from both the urinary and respiratory system. They are applied in postpartum baths as anti-inflammatory and healing, in treating cervicitis, genital discharge, hemoptysis and uterine hemorrhage. The leaves and the fruit are also used in the wash water of wounds and ulcers [145].

Antimicrobial activity

Antibacterial Activity

Medicinal plants have been man's most important natural resource to treat microbial infections [133]. Some plants of the Anacardiaceae family present antimicrobial and antioxidant properties. The ethanol and aqueous extracts of the *Spondias mangifera* (Anacardiaceae) showed antimicrobial activity against gram-positive bacteria viz. *Bacillus subtilis* and *Staphylococcus aureus* and important antioxidant activity. Saponins, flavonoids

and tannins were positive for both extracts. Alkaloids were detected only in methanol extract [159]. As for the antimicrobial activity of the *S. terebinthifolius*, many studies confirm its therapeutic property. Accordingly to [45], in a study of some species of Cuban plants, the species that showed the most effective antimicrobial activity was the *S. terebinthifolius* Raddi acting against the *Staphylococcus aureus*. In another study by [46], alcoholic and aqueous extracts of the *S. terebinthifolius* incorporated into gels presented antimicrobial activity against standard strains of the *S. aureus* ATCC 6538, ATCC 9144. As investigated by [154], the ethanol extract of the *S. terebinthifolius* barks is effective as an antimicrobial agent against gram-positive and gram-negative microorganism.

Anti-fungal

The antifungal properties of eight plant extracts used in Brazilian traditional medicine were tested by [160] against the fungi *Candida albicans*, *Candida krusei*, *Candida tropicalis*, *Candida parapsilosis*, *Candida glabrata*, *Sporothrixschenckii* and *Cryptococcus neoformans*. The dichloromethane and ethyl acetate partitions derived from ethanol extract (80%) of the leaves and stems of *S. terebinthifolius*, proved to be the most active of the species examined with MICs in the range 15-125 mg/ml. The same authors also conducted a study with the pathogenic fungus *Paracoccidioides brasiliensis* responsible for paracoccidioidomycosis a lung disease prevalent in countries in South America and often fatal. The extracts have shown activity against the fungus, and two active components were identified as schinol and 4'-ethyl-4-methyl-2,2 ', 6,6'-tetrahidroxi-[1,1'-biphenyl]-4, 4'-dicarboxylate, the first being the most active (MIC between 7.5 and 125 g/mL as fungus strain) [161, 162].

Antivirial Activity

Crude hydroethanolic extract from the stem bark of *S. terebinthifolius*, as well as its fractions and isolated compounds, showed anti-HSV-1 (Herpes simplex virus type 1) activity and exhibited potential for future development treatment against orofacial infections associated with HSV-1[164].

Wound healing activity

Some researches [154] within the studies about the therapeutic effects of the hydroalcoholic extracts of the *S. terebinthifolius* leaves applied topically to the oral mucosal wound healing process of rats concluded that the extract of the *S. terebinthifolius* reduced the intensity of the inflammatory process. The studies [153] described the wound healing action, respectively, in bladder, stomach and skin surgical wounds of rats.

Anti-inflammatory

It was concluded that the *S. terebinthifolius* extract acts by accelerating the reparation process of the epithelial tissue stimulating the keratinization and also acting for the reparation of the connective tissue, reducing the intensity of inflammation and accelerating angiogenesis and collagen maturation which are healing characteristics. In scientific studies with the *S. terebinthifolius* stem barks, it was detected the presence of tannins which gives it astringent, disinfectant and anti-inflammatory action [154,155]. The essential oil of vegetative parts of the aroeira proved nonsteroidal anti-inflammatory activity through the inhibition of phospholipase A2 by competitive inhibition of the specific enzyme [157]. The aroeira wound healing activity was also directly related to triterpenes present in the fruits of the plant [158].

Cytotoxic Activity

The crude essential oil from leaves showed cytotoxic effects in several cell lines, mainly on leukemia and human cervical carcinoma. Fractions composed mainly of α- and β-pinenes as well as those composed of individually pinenes showed effective activities against all tested cell lines [165]. The turucallane triterpenoids ((Z)-masticadienoic and (E)-masticadienoic acids and (Z)-schinol), isolated from leaves of *S. terebinthifolius*, as well as some semi-synthetic derivatives were cytotoxic and demonstrated antiparasitic (antileishmanial and antitrypanosomal) activity [163].

Catharanthus roseus

Botanical Description

Catharanthus roseus is a long-lived (perennial) sub-shrub or herb, usually erect, 30-100 cm high and at least somewhat woody at the base, sometimes sprawling. White latex is present. [70] Stems are cylindrical (terete), longitudinally ridged or narrowly winged, green or dark red, pubescent at least when young. Leaves opposite, borne on short petioles, 2.5-9.0 cm long, usually elliptical to obovate (egg-shaped in outline but with the narrower end at the base), green with paler veins. The leaf tip is rounded to acute with a tiny point extending from the midrib. Stems and leaves usually with hairs (pubescent), sometimes hairless [70,169] Flowers borne in leaf axils; either singly or paired on very short stalks (pedicels). Sepals 5, 2-6 mm long, narrow, usually with hairs (pubescent). Corolla with a long narrow tube and lobes that spread perpendicular to the tube and almost flat.;

corolla tube greenish, usually at least 2.2 cm long, with the inside of the mouth often dark pink or sometimes yellow, pubescent inside the throat with rings of stiff hairs below the mouth and anthers; corolla lobes 5, pink to white or pinkish purple, 1.0-2.8 cm long, obovate. Anthers 5, attached to the inside of the corolla tube in the upper portion and concealed within it The fruit is a follicle, 2.0-4.7 cm long, with numerous small black seeds. [70,167]

Geographic distribution

Catharanthus roseus originates from Madagascar, but for centuries it has been cultivated as an ornamental throughout the tropics and occasionally in the subtropics; it has become naturalized in many regions[70]

Ethnopharmacology

The plant has historically been used to treat a wide assortment of diseases. It was used as folk remedy for diabetes in Europe for centuries.[70,167] In India, juice from the leaves was used to treat wasp stings. In Hawaii, the plant was boiled to make a poultice to stop bleeding. In china, it was used as an astringent, diuretic and cough remedy.[70,168] In central and south America, it was used as a homemade cold remedy to ease luncongestion and inflammation**.** Throughout the Caribbean, an extract from the flowers was used to make a solution to treat eye irritation and infections. It also had a reputation as magic plant, European thought it could ward off evil spirits, and the French referred to it as "violet of the sorcerers." Western researchers finally noticed the plant in 1950's when they learn of a tea Jamaican were drinking to treat diabetes. They discovered that the plant contains a motherlode of useful alkaloids (130 in all at last count). Some, such as catharanthine, leurosine sulphate, lochnerine, tetrahydroalstonine, vindoline and vindolinine lower blood sugar level, however, others act as haemostatics (arrest bleeding) and two others, vincristine and vinblastine have anticancerous properties. Periwinkle also contains the alkaloids reserpine and serpentine, which are powerful tranquilizers. [70,173]

Antibacterial Activity:

Benzene extract of dried flowers at a concentration of 50% on agar plate was active on *Proteus*, *Pseudomonas*, *Shigella* and *Stphylococcus* species, however, benzene extract of leaves at a concentration of 50% on agar plate was active on *Proteus*, *Pseudomonas*, *Salmonella*, *Shigella* and *Staphylococcus* species.[176] Ethanol (70%) extract of dried leaves on agar plate was active on *Bacillus megaterium* and *Staphylococcus albus* and inactive on *Bacillus cereus* and *Staphylococcus aureus*.[177] Total alkaloids of root at a concentration of 500.0 mcg/ml in broth culture were inactive on E.coli, *Salmonella lyphosa* and *Shigella dysenteries.*14 Water extract of entire plant on agar plate at a concentration of 1:4 was inactive on *Salmonella paratyphi*. [175]

Antifungal Activity:

Acetone and water extracts of dried aerial parts at a concentration (50%) on agar plate was inactive on *Neurospora crossa.*[170] Hot water extract of dried leaves in broth culture was active on *Trichophyton mentagrophytes.*16 Hot water extract of dried stem in broth culture was active on *T. mentagrophytes* and weakly active on *T. rubrum.*[171] Leaves and roots on agar plate were active on *Pythium aphanidermatum*.[172]

Wound healing

Significant wound-healing activity was observed in animals treated with the *C. roseus* leaf extract compared with those who received the reference standard and placebo control treatments. The effects of the EtOH extract of *C. roseus* leaves, at a dose of 100 mg kg−1 day−1 on wound-healing activity in rats. In the excision wound model, *C. roseus*-treated animals showed a significant reduction in the wound area (*P*b0.002) and period of epithelization. In the incision wound model, *C. roseus*-treated animals demonstrated high skin-breaking strength up to 435.0±4.53. In the dead space wound model , the EtOH extract-treated animals showed significantly increased levels of hydroxyproline content (*P*b0.008) as compared with the control group of animals. A significant increase was observed in the weight (*P*b0.001) of the granulation tissue in the animals treated with the extract. [166]

Anti-Inflammatory Activity

Ethanol extract (95%) of dried leaves was administered intraperitoneally to rats at a dose of 4000.0 mg/kg was active 65% inhibition was noticed in Edema. [174]

Antiviral Activity

Water extract of callus tissue in cell culture was active on Tobacco Mosaic Virus.[178]

Cytotoxic Activity

Alkaloid fraction of dried leaves in cell culture was active on CA-9KB, ED50 0.0435 mcg/ml.[179] Chloroform extract and culture filtrate of callus tissue in cell culture at dose of 50.0 gm (dry wt of plant) were active on Leuk-L12 [169] culture, water extract.

Ricinus communis

Botanical Description

Leaves are alternate, curved, cylindrical, purplish petioles, sub peltate, drooping, stipules large, ovate, yellowish, united into a cap enclosing the buds, deciduous, blade 6-8 inches across, palmately cut for three quarters of its depth into 7-11 lanceolate, acute, coarsely serrate segments, smooth blue green, paler beneath, red and shining when young. Flowers are monoecious, large, arranged on the thick rachis of an oblong, spicate panicle, which is at first terminal but becomes lateral by the growth of an axillary bud beneath it;male flowers shortly stalked, on branched peduncles at the base of the panicle, pedicels articulated about the middle; female flowers sessile, at the upper part; bracts broadly triangular. Fruit is blunt, greenish, deeply-grooved, tricoccus capsule, less than an inch long, with the prominences of the ovary becomes sharp, weak, spreading spines, 3-celled, dehiscing loculicidally and septicidally into 6 valves. Seeds are ovoid, flattened, nearly ⅝ inch long by ¼ broad, smooth shining, pinkish- grey, prettily mottled with dark brown, caruncle large, subglobular, raphe faintly raised, running down centre of ventral surface, embryo large in axis of the endosperm, cotyledons foliaceous, broadly ovate, with a cordate base, veined **[191]**. Roots are light in weight almost straight with few rootlets, outer surface dull yellowish brown, nearly smooth but marked with longitudinal wrinkels**[192]**.

Ethnopharmacology

Castor oil is often given orally, alone or with quinine sulphate to induce labour in pregnancy at term. The oil can be used as a vehicle for parenteral administration of steroidal hormones**[193]**. Castor oil is a mild and most efficient purgative, and is well adapted for infants and young children, the puerperal state, and in irritable conditions of the alimentary canal or of the genito-urinary organs. It is one of the safest and most reliable purgatives we possess for the relief of obstinate constipation. The leaves have been also recommended in the form of a decoction or poultice, as an application to the breasts of women to increase the secretion of milk. The decoction has also been reputed to act as a lactagogue and emmenagogue when administered internally**[191]**. Castor cake is used as manure in India. It is rich in nitrogen and other minerals, and has been found to be suitable as a manure for paddy, sugarcane, tobacco etc. Leaves are occasionally fed to cattle.

Fresh juice of leaves is reported to be used as an emetic in the poisoning by narcotics like opium; it is also considered useful in jaundice. Leaves are considered lactagogue and are applied as poultice over the breasts or taken internally in the form of juice. Roots are administered in the form of a decoction for lumbago and allied complaints, in the form of a paste for toothache. Root bark is reported to be a powerful purgative. Castor stems on digestion with lime yield pulps suitable for the production of straw-boards.**[193]**.

Anti-bacterial

The hexane and methanol extracts (200mg/ml) of roots of *Ricinus communis* showed good activity against pathogenic bacterial *Bacillus subtilis* ATCC6051, *Proteus vulgaris* ATCC 6380, *Salmonella typhimurium* ATCC 23564, *Pseudomonas aeruginosa* ATCC 25619, *Escherichia coli* K-12 and *Staphylococcus aureus.* Aqueous extracts showed no antimicrobial activity against any of the pathogens. Methanol extracts (200mg/ml) were found to be prominent against *E.coli.* **[190]**.

Anti-fungal

The hexane and methanol extracts (200mg/ml) of roots of *Ricinus communis* showed good activity against pathogenic *Candida albicans* and *Aspergillus niger.* Aqueous extracts showed no antimicrobial activity against any of the pathogens. Hexane extracts (200mg/ml) showed prominent antimicrobial activity against *Candida albicans* and *Aspergillus niger* fungal strains. Methanol extracts (200mg/ml) were found to be prominent against *Aspergillus niger*. **[190]**.

Anti-Inflammatory activity

Anti-inflammatory and free radical scavenging activities of the methanolic extract of root of *Ricinus communis* (Euphorbiaceae) Linn. was studied in Wistar albino rats. The methanolic extract at doses 250 and 500 mg/kg *p.o.* exhibited significant ($P < 0.001$) anti-inflammatory activity in carrageenin induced hind paw edema model.

The extract at the dose of 500 mg/kg *p.o.* also exhibited significant ($P < 0.001$) antiinflammatory activity in cotton pellet granuloma model. The methanolic extract showed significant free radical scavenging activity by inhibiting lipid peroxidation initiated by carbon tetrachloride and ferrous sulphate in rat liver and kidney

homogenates. The extract enhanced free radical scavenging activity of stable radical 2,2-diphenyl- 1-picryl-hydrazyl (DPPH), nitric oxide and hydroxyl radical in *in-vitro* assay methods.**[194]**.

Cytotoxic Activity:

Ricin is a heterodimeric protein from the seeds of R. communis. It has cytotoxic activity by virtue of its ability to fatally disrupt protein synthesis. The cell entry process by ricin is postulated to be a 10 step process, which culminate into the protein synthesis disruption. A single molecule of ricin reaching the cytosol can kill the cell due to this. Therapeutically, it can be used to specifically target and destroy cancer cells.**[195]**. The leaves on the other hand, have another range of cytotoxic phytochemicals which induces apoptosis via translocation of phosphatidyl serine to the external surface of cell membrane and loss of mitochondrial potential. These compounds included three monoterpenoids: 1,8-cineole, camphor and alpha-pinene and a sesquiterpenoid: beta caryophyllene.**[196]**. The *Ricinus communis* agglutinin I (RCA I), was found to preferentially binds to and is internalized by tumour endothelial cells leading to VEGFR-2 down-regulation, endothelial cells apoptosis and tumour vessel regression. It has no effect on normal blood vessels**.[197]**.

Comparison between Native plants and Alien plants

Biological invasions are currently one of the most important environmental issues brought by globalization [11] and one of the major threats to biological diversity [18]. Facilitated by human activities intentionally or unintentionally, the biological invasions have been the result of species exchanges between many regions throughout the world[9,10,17] .The increase in threats caused by invasive species on ecosystems have led to many studies focused on why some species significantly succeed in new environments where they are not native[8,14,16].The Enemy Release Hypothesis (ERH) postulated that invasive plants benefit from a direct release from natural enemies resulting in an increase in distribution and abundance[15].Hence, increasing of the vegetative and reproductive biomass in invasive (*S. vulgaris)* plants indicates that the invasive plants performed better and had higher competitive ability than the native plants. Higher vegetative and reproductive biomasses in invasive populations have been also reported in some previous studies on invasive plants (*Senecio* genus)[12,13].There use in medicinal plants of animals and human increase or create a new natural enemy in a form of traditional practitioners and medicinal plants trader who cause some if not most native plants to exiting or to be endanger species. This could also help the government to control invasive alien species to a reasonable environmental threshold if the medicinal part of the invasive plants are properly expose to these sector of the population as a an alternative control measure to invasive plants.

Comparison between Synthetic and Herbal Medicine

Synthetic drugs deal with symptoms caused by specific diseasesor pathogen as understood by scientific pathology, however, a herbal medicine usually direct towards aiding the body's own healing process. Herbal medicines usually act gently, "suppor" the systems and processes that have become deficient or attempt to help remove excesses that have become preponderant. Symptom relief is only a section of medicinal plants therapeutic strategies. For example, arthritic is usually treated with steroid anti-inflammatory drugs which have widespread distressing adverse effects. The approach of herbs to these conditions causes moistening of dry synovia, prompt of flow in the affected regions, facilitation of elimination via kidneys and hepatic/biliary routes, dietary alteration of metabolism, etc. (200-204).

In this regard, a pharmaceutical drug is usually designed to elicit a specific reaction and its "side or adverse effects" are usually traded as a "risk" against the "benefit" of the primary effect. Herbal medicines usually tend to have several broad complementary or synergistic actions on physiological systems at the same time which are usually in the same general therapeutic direction, and often non-specific. Furthermore, these actions are rarely adverse effects. Herbal medicine actions are too complex and usually cannot be adequately described using the vocabulary of "medication" action terms such as diuretic (201-206). The rational integration of herbal medicine into modern medical practices, including cancer therapy, should be accomplished on a scientific basis, taking into an account the interrelated issues of standardization , quality control, safety assessment, and efficacy assessment.

Standardization and quality control of herbal crude drugs – Processes and procedures

Standardization of herbal medicines is the process of prescribing a set of standards or inherent characteristics, constant parameters, definitive qualitative and quantitative values that carry an assurance of quality, efficacy, safety and reproducibility. It is the process of developing and agreeing upon technical standards. Specific standards are worked out by experimentation and observations, which would lead to the process of prescribing a set of characteristics exhibited by the particular herbal medicine. [150-152], Hence standardization is a tool in the quality control process.According to WHO [150,151], standardization and quality control of herbals is the process involved in the physicochemical evaluation of crude drug covering aspects, such as selection and handling of crude material, safety, efficacy and stability assessment of finished product, documentation of safety

and risk based on experience, provision of product information to consumer and product promotion. Authentication- Each and every step has to be authenticated, area of the collection, parts of the plant collection, the regional situation, as phytomorphology botanical identity, microscopic and histological analysis(characteristic features of cell walls, cell contents, starch grains, calcium oxalate crystals, hairs, fibers, vessels etc.) Several studies of the histological parameters are list of palisade ratio, vein islet number, vein termination, stomatal number, stomatal index, trichomes, stomata, quantitative microscopy, taxonomic identity, foreign matter. Loss on drying, swelling index, foaming index, ash values and extractive values, Chromatographic and spectroscopic evaluation[63], Determination of heavy metals, pesticide residues, Microbial contamination, Radioactive contamination. The parameter stability of herbal formulations that includes pharmacognostic parameters, physicochemical parameters, phyto-chemical parameters, microbiological assay and chromatographic analysis. [67]

Safety assessment

Herbal medicines are generally regarded as safe based on their long-standing use in various cultures from generations to generations. However, there are case reports of serious adverse events after administration or maladministration of herbal products. In a lot of cases, the toxicity has been traced to contaminants and adulteration, some of the plants used in herbal medicines can also be extremely toxic [67,180]. As a whole, herbal medicines can have a risk of adverse effects and drug-drug and drug-food connections if not properly assessed. Assessment of the safety of herbal products, therefore, is the first main concern in herbal research. These are various approaches to the evaluation of safety of herbal medicines. Most of the plants if not all have been tested for toxicity which back up thier used by generations in different countries other than South Africa .The toxic effects of herbal preparation may be attributed mainly to the following: intrinsic toxicity of plant constituents and ingredients and industrialized malpractice and contamination. [63,141]Evaluation of the toxic effects of plant constituents of herbal formulation requires detailed phyto-chemical and pharmacological studies. It is, however, safe to assume that, based on human experiences in various cultures, the use of toxic plant ingredients has already been largely eliminated and recent reports of toxicity could largely be due to misidentification and overdosing of certain constituents [149].

Assessment of efficacy

Herbal medicines are inherently different from conventional pharmacological treatments, but presently there is no way to assess their efficacy other than by currently used conventional clinical trial methodologies, in which efficacy is conventionally assessed by clinical, laboratory, or diagnostic outcomes: Clinical outcomes include parameters such as improved morbidity, reduced pain or discomfort, improved appetite and weight gain, reduction of blood pressure, reduction of tumor size or extent, and improved quality of life. [63,180] For most if not all the herbal pants in this review have reduce the wound on animals trials and in laboratory have shown good control of wound infection pathogen. Laboratory /other diagnostic outcomes include parameters such as reduction of blood glucose, improvement of hemoglobin status, reduction of opacity as measured by radiological or imaging techniques, and improvement in electrocardiogram (ECG) findings. [67] Implementation of a standardized approach for the herbal practitioners and collection of the prospective data necessarily creates an interventional design which, if planned properly, may closely resemble single-blind randomized trials. Even if it differs from double-blind randomized trials in the degree of rigor, the design may be the optimum, both biologically and economically, for rapid evaluation of herbal products. Standardization, however, may sometimes be incompatible with the existing legislative framework and caution is needed regarding the ethical implications of such studies. [67]

IX. Conclusion And Future Prospectives

Synthetic medicine has benefited considerably from Herbal Medicine in two areas: treatment with similar effects and treatment with different effects from those of Herbal medicine. The application of, and research into, natural products are far away from acceptable. A amount of challenges require to be resolved in the future. For example, synergistic effects may exist among the compounds that transpire in natural products; however, the modes and mechanisms of action are rarely very clear. It is, therefore, needed to make full use of such synergetic effects toward improving the usefulness of treatment. However, it is also mandatory that any adverse effects of natural products be correctly decrease to meet up protection standards.

People needs to learn more from natural products and traditional medicines. In order to promote the development of contemporary medical research on natural products, humans have to face up to various difficulties and challenges. Important information resource on natural products and Herbal medicine is mixed in a large number of myths and useless rumours. Furthermore, one plant or formula of natural products and Herbal medicine contains a great quantity of chemical constituents, bio active, invalid, and possible synergistic components.

Therefore, great effort should be made at initial to remove the dross and take the essence precious experience of natural products and Herbal medicine

Furthermore, in several cases, the role of single compound from natural products and Herbal medicine is paid much attention to the expense of combination which in turn are capable of even dropping side effect. However, as a matter of fact, one advantage of Herbal medicine therapeutics is the "synergism"; that is, often multiple components in Herbal medicine play a synergistic role which is greater than that of the individual Synthetic. Synthetic cannot treat some complex diseases effectively, such as cardiovascular disease, cancer, diabetes, respiratory combine with immunodeficiency's. Thus, the treatment has seen a shift to the "multi-drugs and multi-targets" mode for combination therapies.Herbal medicine with tested cytoxicity, antibacteral , antifungal, antiviral and immunomodulatory activity could pave a way for development of reasonably a drugs with addressable side effect.

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Conflict Of Interest

The author declares that he has no conflict of interest.

Authors' Contributions

The author declares that this work was done by the author named in this article.

Ethics approval and consent to participate

Not applicable.

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