II. REVIEW OF LITERATURE

The medicinal plants have been regarded as sacred and used by early civilization to treat sickness and to embellish man’s well being. Plants have provided large kind of potent drugs to alleviate suffering from diseases. In spite of spectacular advances in synthetic drugs in recent years, some of the plant origin have still retained its importance and are remarkably effective because of the easy availability, low cost and comparatively being devoid of serious toxic effects. In spite of tremendous advances made in the modern medicine, there are still a large number of ailments for which suitable drugs are yet to be found. There is an urgent need to develop safer drugs for the treatment of serious ailments. The Vedic literatures also mentioned the identity and utility of herbs/herbal products in treating human ailments. Only a few plants have been subjected to rigorous phytochemical and pharmacological studies and many of the plants are yet to be investigated.

The knowledge of the biological activities and the chemical constituents of plant are desirable, not only for the discovery of new therapeutic agents, but also disclosing the value of new sources of economically useful materials. Thus a careful and extensive study on medicinal plants is necessary to identify newer plant products to evaluate the efficacy of the compound to combat the diseases.

This chapter focused on the critical review on in vitro, phytochemical and pharmacological aspects pertaining to *Elephantopus scaber*.

*In vitro* studies

The earlier botanist pondered as to how the complexity in a plant could be dissected out into individual cell and tissue types, so that these could be subjected to direct experimental control, free from complex interactions occurring in the intact plant.
In 1939, Schwann’s Cell Theory proposes that each living cell of an organism if provided with proper environment, would be capable of independent development gave birth to the concept of ‘totipotency’. It should be possible to reproduce an organism from any one of its nucleated cells, since all the information needed to specify an organism is contained in its DNA. With this concept in the middle of the present century a new experimental tool has emerged, known as Plant Tissue Culture.

The first major breakthrough in plant tissue culture, in the sense of achieving long term cultures of unorganized tissue masses called callus, was with the explants of cambium tissue isolated from tobacco (White, 1939), potato and carrot (Nobecourt, 1939; Gautheret, 1939 and Van Overbeek, et al., 1941) reported that isolated embryos of Datura could grow and develop on a medium supplemented with coconut milk.

For the first time in Berlin, Haberlandt (1902) originated the concept of Cell Culture. He attempted to cultivate the isolated plant cell in vitro on an artificial medium (Knop’s solution containing peptone, asparagin and sucrose). In 1954 Muir, et al., developed a successful technique for the culture of single isolated cells, known as paper raft nurse technique. Attempts were made during this period for single cell culture by hanging drop and agar plate method. Jones et al., (1960) demonstrated that a single isolated cell could divide and regenerate as a whole plant.

In the late 1940’s, control and induction of organogenesis in callus culture was established. Skoog and Tsui (1948) demonstrated that manipulation of the nutrient medium could induce caulogenesis (shoot initiation) in segments and callus of tobacco. The chemical capable of stimulating cell divisions was identified as 6-furfurylaminopurine, (Kinetin) a degraded product of herring-sperm DNA. (Miller, et al., 1955). Later, Skoog and Miller (1957) have
demonstrated the chemical regulation of organogenesis in callus cultures. They demonstrated that shoot and root initiation in tobacco callus cultures could be regulated by a suitable ratio between auxin and cytokinin in the medium. Followed by them, much progressive work has been demonstrated in the induction of organs from plant tissue and organ cultures. (Reinert, 1959; Street, 1966; Torrey, 1966; Halperin, 1969; Murashige, 1977; Narayanaswamy, 1977; Bonga, 1977; Bajaj, 1986; Pollard Jeffrey, 1990; Macown and Amos, 1992; Callow, et al., 1997 etc.)

With the introduction of the concept of hormonal control of organogenesis formation, the numbers of impressive basic nutrient media were formulated by White (1934), Heller (1953), Gamborg et al., (1968) and the contribution of Murashige Skoog (1962) were ever recognizable for their nutrient medium formulations.

The regeneration of complete plantlets derived from callus was achieved in many herbaceous species like *Torenia fournieri* (Bajaj, 1972) and *Solanum nigrum*, *Solanum dulcamara* and *Solanum khasianum*, Bhatt, et al., 1979 maintained the leaf callus of *Chrysanthemum manifolium* for nine years and compared the regenerative potentialities of long term culture with one month old leaf callus. They found that 15% of the plantlets regenerated from long-term culture possessed abnormalities such as proliferation of apical buds, variable shape of leaf and stunted growth. The remaining 85% were characterized by excessive growth of lateral shoots.

Whole plant regeneration from the agronomically important monocots such as *Oriza sativa*, *Zea mays*, *Pennicetum*, *Panicum*, *Lolium*, *Festuca* and *Dactylis* has been successfully achieved. (Brown and Thorpe, 1986)
Plant synthesizes various medicinally important secondary metabolites such as alkaloids, glycosides, steroids, flavonoids, volatile oils, etc. It has been demonstrated that secondary metabolites synthesized by a plant can also be synthesized by its cell cultures (Routein and Nickell, 1956; Klein, 1960; Ellis, 1983; Klapheck, 1983; Curtin, 1983). In 1980, Nickell et al., has listed a variety of plant species capable of producing secondary metabolites in culture such as, atropine from *Atropa belladonna*, diosogenin from *Diosorea deltoidea*, digitoxin from *Digitalis purpurea* and ephedrine from *Ephedra gerardiana*.

Hence, the tissue culture technique could be used as a tool for rapid multiplication and enhanced production of medicinally important active constituents.

The first secondary metabolite to be commercially produced is shikonin, which has found market as a biological lipstick. Cell immobilization techniques, where the plant cells are immobilized on a matrix or entrapped in it, have recently been exploited for harvesting secondary metabolites from plant cells (Brodelius and Mosbach, 1982; Brodelius and Nilsson, 1983).

Nakagawa and Tabata (1989) noticed that the *in vitro* derived calli of *Thalictrum minus* showed enhanced production of secondary metabolites when compared to *in vivo* plants.

Krishna (1996) cultured the various explants of hepato- protective medicinal species *Boerhaavia erecta* and *B. rependa* and achieved regenerations from all the explants. The therapeutic efficacy of the *in vitro* derived calli was comparatively screened with *in vivo* plant explants against CCl₄ induced toxic hepatitis.
Cassells, et al., (1999) have noticed that, *Arnica montana* an endangered medicinal species does not gave stable yield of pharmaceutical compounds in commercial plantations. While the *in vitro* derived regenerants produce enhance quantity of secondary metabolite when compared to *in vivo* plants.

Tiwari, et al., (2000) described a protocol for rapid and large-scale clonal propagation of the valuable medicinal herb *Centella asiatica* by enhanced axillary bud proliferation from nodal segments. Although bud break was dependent in benzyladamine supply the synergistic combination of BAP and NAA induced the optimum frequency of shoot formation as well as shoot number.

Khanam, et al., (2000) have studied the effects of cytokinin/auxin combinations on organogenesis, shoot regeneration and tropane alkaloid production in *Duboisia myoporoides*.

Nagaraj and Krishna (2003) have achieved rapid regeneration of plantlets from leaf callus of an anti-hepatitis plant *Andrographis alata*. The therapeutic efficacies of the *in vitro* regenerants were evaluated on toxic hepatitis in experimental animals.


Similarly many hepatoprotective and wound healing plant species have been subjected to *in vitro* studies to achieve rapid regeneration of plantlets, such as *Flaveria terinarvia* (Sudarshana and Shantama, 1991), *Diospyrus cardifolia* (Krishna, 1996), *Phyllanthus amarus* (Kiran Ghanti, et al., 2004), *Celastrus paniculatus* (Maruthi, et al., 2004), *Eclipta alba* (Archana and

Asha Sankar, *et al.*, (2001) studied the ephedrine synthesis in *in vitro* static and suspension cultures of leaf, stem and root calli of four species of *Sida rhombifolia, Sida retusa, Sida acuta,* and *sida cordifolia.* Asilbekova (2001) has studied the composition of triacylglycerines from photosynthetic tissues of *Ruta graveolens* grown *in vivo* and *in vitro* with respect to chain length and unsaturation. De. B, *et al.*, (2003) reported the regeneration of adventitious shoots from young leaves of *Datura metel* and detected number of steroidal compounds. Filippini, *et al.*, (2003) obtained the production of anthocyanin from a stable cell suspension line of *Catharanthus roseus.* Pooja Bhatnagar, *et al.*, (2004) have increased the production of secondary metabolite, solasodine by *solanum laciniatum* using plant tissue culture. Solasodine contents in the regenerated shoots were found to be 10 times higher than the callus culture, which is used as the best starting material for the synthesis of steroid drugs.

Binoy Jose and Satheeshkumar (2004) have established *in vitro* mass multiplication of plants through shoot culture for *Ophiorrhiza mungo* for the production of quinoline alkaloid, camptothecin that is used in the treatment of colon, head, breast and bladder cancers.

Sundravelan, *et al.*, (2004) have established the callus culture from the leaves of *Nothapodytes foetida* for the production of camptothecines and 9-methoxy camptothecine, anti-tumour drugs used in the treatment of colon, head, breast and bladder cancers on MS media supplemented with picloram, N\(^6\)-benzyladenine and gibberellic acid.
Critical review of the literature indicated that, although *Elephantopus scaber* possess high medicinal value, it has not yet been subjected to *in vitro* studies. So, an attempt was made in the present investigation to derive protocol for the rapid regeneration from plantlets from different explant cultures.

**Phytochemical studies**

As early in the period 1493-1541, the great philosopher Poracelsun said that the purpose of chemistry is not to make gold, but to cure diseases. This can be considered as one of the major turning point in the history of drugs. At the end of eighteenth century and the beginning of nineteenth century, many scientists worked on natural products and described the procedure for the isolation of active constituents from the crude drugs. Simultaneously these led to the development of the biologically active constituents that are also chemically synthesized in the large quantities by plant precursors.

In the last 50 years a phenomenal growth occurred in phytochemistry. These developments have not only changed the face of biochemical research, integrated pharmacology and clinical pharmacology, but have made the discovery of drugs. Many Indian researchers like, Nadakarni (1954), Chopra (1956), Kirthikar and Basu (1991), Nayar and Shastry (1982) have done laborious and commandable work in compiling the details of Indian Medicinal Plants. However, many of the medicinal plants are yet to be subjected to rigorous phytochemical studies.

The Asteraceae members attracted researchers for the aromatic and therapeutic characteristics.

Morris Kupchan, *et al.* (1969) have reported the isolation and structural elucidation of two Elephantin and Elephantopin, compounds from *Elephantopus elatus*. Kuo-Hsiung Lee, *et al.* (1975) have isolated
deoxyelephantopin an active principle responsible for the significant inhibitory activity against the Walker 256 carcinoma in rats, from chloroform extract of the plant *Elephantopus carolinianus* Willd. Kuo-Hsiung Lee, *et al.*, (1980) have worked on the isolation and structural elucidation of the three novel cytotoxic anti-tumour germacranolides, molephantin, molephantinin and phantomolin from the ethanolic extracts of *Elephantopus mollis*. The extract also yielded three known triterpenes β-amyrin acetate, lupeol acetate and epifridelanol as well as stigmasterol.

Banergee, *et al.*, (1986) have reinvestigated on the medicinal plants *Elephantopus mollis* and *Centratherum punctatum* and isolated sesquiterpene lactones.

Jakupovic, *et al.*, (1987) have investigated five new lactones in addition to elephantopin and isoelephantopin from *Elephantopus angustifolius* and also derivative of deoxyelephantopin from *Elephantopus mollis*. The structures were elucidated by high field NMR spectroscopy.

Bioassay guided (P-388 lymphocytic leukemia cell line) separation of a CH$_2$Cl$_2$/MeOH extract of *Lychnophora antillana* led to the isolation of two cytostatic (P-388) germacranolides designed lychnostatins 1 and 2. Structural elucidation was based initially upon high field (400 MHz) NMR and electron impact MASS spectral interpretations and by X-ray crystal structure determinations. (Pettit, *et al.*, 1990)

Abdel Sattar, *et al.*, (1996) have isolated two new germacranolides, 9 alpha-hydroxy-1-beta, 10 alpha-epoxyparthenolides and parthenolid-9-one, in addition to the known 9 alpha-hydroxy parthenolide, 9 beta-hydroxy parthenolide, 10 alpha-epoxyparthenolide from *Anvillea garcinii*. The structures of the new compounds were elucidated from their spectral data.
and by chemical derivatization. The *in vitro* anti-tumor and anti-HIV were evaluated.

Hayashi, *et al.*, (1999) have reported the structures and absolute stereochemistries of the germacranolides, tomenphantins A and B from *Elephantopus tomenosus*. $^1$H and $^{13}$C NMR spectroscopic data, chemical transformation and single crystal x-ray analysis were used in these determinations.

Kisiel and Barszcz (2000) have isolated five germacrane and guaiane type sesquiterpene lactones including two previously described taraxinic acid derivatives and three lactones identified as 11β, 13-dihydrolactucin, ixerin D and ainslisside and phenolics from the roots of *Taraxacum officinale*.

Alejandro, *et al.*, (2000) have worked in search for new sources of sesquiterpene lactones, from six *Centaurea* species. They evaluated the antifungal activity of (+)-costunilide, (-)-dehydrocostus-lactone, (-)-lychnopholide and (-) eremantholide C.

Similarly the Asteraceae members were subjected to rigorous phytochemical investigations such as, *Artemisia sylvatica* (Yoo, *et al.*, 2000); *Artemisia caruifolia* (Ma, *et al.*, 2001); *Tridax procumbens* (Ali and Jahangir 2002); *Chamomilla recutita* (Syamasundar, *et al.*, 2002); *Saussurea lappa* (Sun, *et al.*, 2003); *Wedelia paludosa* (Filho, *et al.*, 2004) etc.

**Pharmacological studies**

Presently there has been more demand all over the world regarding the use of the herbal drugs in the place of modern drugs. Even after 58 years of independence, a large population of India had faith on herbal medicaments, but
scientifically cannot merely accept the use of the plants for specific disorders, unless, corroborated by clinical studies. The way in which the drug acts and the manner in which important organ of the body are stimulated has to be proved through clinical experimental evidences.

The present study was concentrating on the wound healing, hepatoprotective and anti-inflammatory studies.

**Wound**

Wound has been defined as disruption of normal tissue structure and function. Wounds can result from injurious processes beginning either internally or externally to the involved organs. It may be caused by mechanical violence, with or without a loss of continuity. Wounds can be produced by physical, chemical, electrical or microbiological insult to tissue.

**Types of wound**

**Incised wound** - The majorities of the incised wounds are caused by a sharp knife or glass and are relatively clean. Structures will be damaged only along the track of penetration with minimal injury to tissues on either side. In the management of these wounds, after suitable exploration these wounds may be closed by primary suture, if possible within 6 hrs of injury. Damaged tendons, nerves and major blood vessels should be repaired at the time primary surgery.

**Lacerated wounds** - Wounds with jagged edges are commonly seen in road traffic accidents. It is frequently dirty and contaminated with organic
In the management of these wounds, within 6 hrs of injury, all the dead tissues and organic matter from the wound are removed to avoid the risk of infection.

**Crushed and devitalized wounds** - Industrial and severe road accidents and also war injuries account for the majority of these wounds. In the management of these wounds, excision of all dead tissue and prevention of tissue tension must be done. All the necrotic muscle along with the driven organic matters must be removed. Tension beneath the deep fascia must be relieved by a long fasciotomy incision and depending on the condition delayed primary suture can be performed. In the practical management of the severely injured, simple first aid principles account for saving lives than surgery. Each wound is treated on an individual basis.

**Wound healing**

Wound healing is the process by which a damaged tissue is restored, as closely as possible, to its normal state. It represents a highly dynamic integrated series of cellular, physiologic and biochemical events, which occur exclusively in whole organisms. It depends upon the reparative abilities of the tissue, the type of damage, the extent of damage and general state of health of the tissue and the organisms in which the tissue exists. In acute wounds, the healing occurs through an orderly and timely process leading to restoration and functional integrity, while chronic wounds fail to follow this course and are often associated with underlying pathology.
Wound healing is a complex biochemical and cellular event, which can be affected by local and systemic factors. The Local factors are, infection, adequate blood supply, foreign body and tissue characteristics. The systemic factors are- age, nutrition, hematological disturbance, diabetes, renal failure, jaundice, malignancy, steroids, cytotoxic drugs, whole body irradiation and Marfan’s syndrome.

The processes of wound healing are-

- Hemostasis
- Inflammation
- Epithelization
- Wound Repair

Hemostasis- This is the first step in the process of healing and occurs by the following mechanisms, viz., reflex vasospasm, secures hemostat of small blood vessels and clotting mechanism. Most wounds are accompanied by some degree of hemorrhage because blood vessels are damaged. Under these circumstances the free blood comes into contact with exposed collagen and with factors released from damaged cells, and clot formation occurs. This mechanism involves the clotting factors and platelets. The injury to the endothelial cells exposes the highly thrombogenic sub-endothelial connective tissue and leads to the formation of platelet plug. There is a simultaneous activation of the coagulation sequence and hemostasis results. Platelets are the first cells to appear at the wound site and release certain substances termed as cytokines.
The order of arrival of cells at the site of wound are- platelets, neutrophils, monocytes and lymphocytes.

Cytokines are considered as wound hormones, which are produced not only by platelets but also by other cells like neutrophils, lymphocytes, macrophages, endothelial cells and smooth muscle cells. Cytokines have a well-defined role in the process of wound healing.

Inflammation- Damage to the body’s tissues triggers a defensive response called Inflammation. During inflammation the local blood flow increases leading to the characteristic local heat (Calor) and redness (Rubor). There is slowing of the circulation accompanied by an increased permeability of capillaries, with exudation of protein rich fluid into the interstitium. Leucocytes marginate to the periphery of the vessel lumen and then emigrate into the interstitium. Cellular events are dominant in this stage and follow a chronological order. The platelets are the first cells to arrive at the site of inflammation. The neutrophils and red blood cells follow them. A fibrin network forms over the wound.

During inflammation, concentrations of some protein changes. These proteins, whose concentration changes markedly during inflammation, are called acute phase proteins. Acute phase proteins include complement, cytokines and several specialized proteins such as fibrinogen for clotting and kinins for vasodilation.
Inflammation and wound repairs proceed simultaneously with successive formation of granulation tissue, synthesis of wound collagen and ground substance. Wound contraction and finally scar formations are the final stages in wound healing process.

**Epithelization**- Epithelium is the most frequently injured tissue, as it covers external surfaces of the body, epithelization refers to the complete coverage of wound surface by generated epithelial cells. These cells undergo morphological changes, proliferation and migration to cover the wound.

**Wound repair**- This is the final stage in the healing process, although it starts as early as 24 hrs after the injury.

The components of wound repair are-

- Granulation tissue formation
- Wound contraction
- Collagen/Matrix formation
- Scar tissue formation

**Granulation tissue formation (Cellular phase)**- Granulation tissue is primarily composed of fibroblasts and small, new blood vessels. The undifferentiated mesenchymal cells of wound margin modulate themselves into fibroblast after injury and mainly contribute to this phase of healing. The fibroblasts start migrating into the wound gap along with the fibrin strands. Injury activated chemotactic factors play a considerable role in this phase,
causing proliferation of fibroblasts, epithelial and endothelial cells. These chemical signals (chemotactic factors) also lead to the alterations in metabolism movement, growth and differentiation of cells involved in healing process (Irwin, 1975).

Wound contraction- Wound contraction is defined as the inward movement of the edges of an open wound, secondary to the forces generated within that wound (Idem, 1967) leading to the decrease in wound size. This process is of considerable importance in healing of excision wounds. Wound contraction begins between 8 and 10 days after injury. It is controlled both by the fibroblasts and by the extracellular matrix, and is due to the fibroblasts applying tension to the surrounding tissue matrix. Contraction makes a much greater contribution to closure of full thickness wounds in rats than in man, which adds to the difficulty of extrapolating from experimental studies to the clinical situation.

Collagen formation- This is the major component of extracellular tissue including soft tissue, ligaments and tendons. It starts with appearance of collagen in the wound by third day after wounding. The main function of collagen is to support or provide strength and shock absorption. Collagen is composed of three polypeptide chains. It is unique as it contains amino acids, hydroxyproline, proline and glycine. Formation of the collagen is a stepwise process with the sequence: Immature protocollagen – Tropocollagen – Stable tropocollagen—Cross linkage.

Matrix- The matrix is produced by fibroblasts and has various components including collagen, elastin, proteoglycans, hyaluronic acid,
laminin and fibronectin. These have different functions including expansion and contraction of tissue, regulation of connective tissue and cell adherence. The stage of collagen and matrix formation merges imperceptibly into the stage of scar formation.

**Scar tissue formation**- Scar is a metabolically active and dynamic tissue. Wound contraction is an essential component in scar formation. Scar replaces the damaged tissue in higher animals, because the healing by regeneration has almost been lost in them. In man only a few internal organs (liver, pancreas, and salivary glands) can regrow. Where as, in lower vertebrates, complete regeneration with regrow of lost extremity like tail is possible (Francis, 1977).

Scar remodeling implies a process of reorientation of collagen fibres and may continue for up to a year or more. During the maturation of the scar, the collagen, which is type III (granulation tissue), is converted to Type I collagen (universaly distributed). At this time, the actual collagen content is highest, but during the next year of scar maturation, molecular reorientation of the collagen and its chemical cross-linking strengthen the healing tissues.

The phenomenon of over healing leads to the formation of hypertrophic scar and keloid. Over this year, hypervascularity subsides and the scars fade to a normal skin color. Scars almost contract and flatten during this period.

The use of plants for healing of wound is as old as Homosepiens evaluation. Even the animals were also get healed their wounds by consuming specific plant species. Plant and the plant products are the immediate available
medicine for healing wound. In Indian system of medicine many plant species are being used for healing wounds. Many investigators have clinically evaluated the effect of crude extracts on healing of excision, incision and dead space wound models on experimental animals.

Udupa, et al., (1991) studied the effects of indigenous drug, *Tridax procumbens*, on developing granulation in rats. Subcutaneously harvested granuloma tissue formed on dead space wound was removed on 4-day interval up to 32 days of wounding. Lysyl oxidase activity, protein content, specific gravity and breaking strength were all increased in drugs treated animals as compared to controls. A fall in the Lysyl oxidase activity was observed in drug treated animals after day 8. The drug may be having a dual role, one a stimulatory (direct) effect in the initial phase of wound healing and the other a depressant (indirect) effect in the later stage.

The same author (1991) evaluated the effect of the fresh juice of the indigenous drug *Aloe vera* (0.2 ml/100g -i.p.) for its wound healing properties in rats. Wound healing effects were studied on incision (skin breaking strength), excision (percentage of wound contraction and epithelization time) and dead space (granuloma breaking strength as biochemical parameters) wound models. Tamalli, et al., (1996) reported the aqueous suspension and seeds extract of *Trigonella foenum graecum* promoted significant wound healing activity in rats. The suspension was more effective than the extract.

The positive influence of *Aloe vera* on the healing of full-thickness wounds in diabetic rats was reported by Chitra, et al., (1998). Full thickness excision/incision wounds were created on the back of rats, and treated either by topical on the wound surface or by oral administration of the *Aloe vera* to the rat. Wound granulation tissues were removed on various days and the collagen,
hexosamine, total protein and DNA contents were determined, in addition to the rates of wound contraction and period of epithelialization. Measurements of tensile strength were made on treated/untreated incision wounds. The results indicated the *Aloe vera* treatment of wounds in diabetic rats may enhance the process of wound healing by influencing phases such as inflammation, fibroplasias, collagen synthesis maturation and wound contraction.

Mallikarjuna Rao and Roy (1999) assessed the effect of grape seed oil (GSO) on collagenation, wound contraction and epithelization phases of wound healing in male Wistar rats. Three wound models viz., incision and dead space wounds for collagenation phase and excision wounds for wound contraction and epithelization phases were employed for the study. GSO significantly promoted the collagenation phase by healing despite causing significant reduction in wound granulation and collagen content. In excision wounds, it promoted wound contraction.

Similarly Somashekar Shetty, *et al.*, (1999) evaluated the wound healing effect of *Ocimum sanctum* at the dose of 0.1ml/100 g on different wound models.

Topical applications of methanolic extract of leaves of *Hypericum mysorens*, (5% and 10%) was evaluated for wound healing potential in excision and incision wound models in rats. Both the concentrations have showed significant wound healing responses (Mukherjee, *et al.*, 2000).

Suguna (2000) studied the influence of *Phyllanthus emblica* extract on dermal wound healing in rats. Full thickness excision wounds were made on the back of rat and *Phyllanthus emblica* extract was administered orally and topically. The granulation tissue formed was used to estimate collagen,
hexosamine, protein and DNA. The extract increased cellular proliferation and collagen synthesis at the wound site. Quicker and better maturation and cross-linking of collagen were observed in the extract treated rats. The results show that \textit{P. emblica} produced different beneficial effects on the various phases of wound repair.

Hemmati and Mohammadian (2000) investigated the effects of mucilage of Quince seeds on wound healing in rabbit. Mucilage extracted from the Quince (\textit{Cydonia oblonga}) seeds in moderately warm water, was applied to the wound area in rabbits twice daily at concentrations of 5, 10 and 15\% (w/w) of the mucilage in eucerin. Healing determined by reduction in wound area, was most rapid effective (13 days) in animals treated with 10\% mucilage. \textit{Quince seed} mucilage proved to hasten wounds more rapidly than a commercial wound healing cream (1\% phenytoin) or eucerin cream without mucilage.

An aqueous extract of \textit{Buddlea globosa} leaves, used traditionally in Chile for wound healing, was tested for the ability to stimulate growth of fibroblasts \textit{in vitro} and for anti-oxidant activity in the same fibroblast cell system challenged with hydrogen peroxide. Low concentrations of the extract gave an increase in fibroblast growth, which was not statistically significant, but cytotoxicity was observed at concentrations greater than 50 \textmu g/ml. The extract showed strong anti-oxidant effect and fractional led to the isolation of three flavonoids and two caffeic acid derivatives, each of which was shown to contribute to the anti-oxidant effect at concentrations below 10 \textmu g/ml. These activities would accelerate the healing of wounds (Mensah, \textit{et al.}, 2001).

Suguna (2002) assessed the effect of topical administration of an alcohol extract of the leaves of an evergreen plant, \textit{Terminalia chebula}, on the healing of rat dermal wounds, \textit{in vivo}. \textit{T.chebula} treated wounds healed much faster as indicated by improved rates of contraction and a decreased period of
epithelization. A significant increase in total protein, DNA and collagen contents in the granulation tissues of treated wounds was observed. The levels of hexosamine and uronic acid in these tissues also increased up to day 8 post wounding. Reduced lipid peroxide levels in treated wounds, as well as ESR measurement of anti-oxidant activity by DPPH radical quenching, suggested that *T. chebula* possessed anti-oxidant activities. The tensile strength of tissues from extract treated incision wounds increased by about 40%. In addition, *T. chebula* possessed antimicrobial activity and was active largely against *Staphylococcus aureus* and *Klebsiella*. The beneficial effects of *T. chebula* in the acceleration of the healing process have been advocated.


The extensive screening of plants for wound healing profile indicated that various phases of wound healing are apparently independent but, interlined and run concurrently. Many investigators were also attempted the isolation of active costitutents and screening of that constituent on different wound healing profiles. These constituents become the basic nucleus of wound healing profile and upon which synthetic drugs can be produced.
The Asteraceae members are the chief source of sesquiterpene lactones that are reported for antibacterial (Kubo, et al., 1994) and antifungal activity (Alejandro, et al., 2000).

The *Elephantopus scaber* is an aromatic Asteraceaeen herb, showed the positive test for sesquiterpene lactones. So in the present investigations different crude extracts of *Elephantopus scaber* and the isolated sesquiterpene compound were concurrently evaluated for its wound healing activity.

**Liver**

The liver is the heaviest gland of the body in human beings, which is responsible for metabolism of chemicals, and for the regulation of man's internal chemical environment. Exogenous and endogenous chemicals are adsorbed, concentrated and then processed by the liver into more usable, storable or excretable form. Hence, it plays a vital role in metabolism and elimination of various compounds.

Liver is one of the most frequently exposed organs and is more susceptible to the toxic injuries induced by certain agents and any damage to hepatic cells disturbs body’s metabolism. But so far, it has been almost impossible to evaluate exactly the factors that make substance toxic to the liver. Several studies, however, demonstrate that how chemically stable compounds produce serious tissue lesions in man and experimental animals including cancer of the liver, hepatic necrosis and other injuries. Certain drugs like tetracycline, paracetamol, antitubercular drugs, oral contraceptives of hormonal origin, chemicals used as food preservatives and agrochemical are of great threat to the integrity of the liver. In addition, alcohol consumption, cigarette smoking and tobacco chewing are found to aggravate the above said problems. Undernutrition and malnutrition are other important causes of liver damage in the developing countries. Thus, liver is expected not only to perform functions,
but also it has to protect itself against the hazards of harmful medicines and chemicals. In spite of tremendous scientific advancement in the field of hepatology in recent years, the problems cannot be completely overcome.

The major clinical manifestation of liver disorders is jaundice. Despite the extraordinary capacity for regeneration, a slight injury may lead to fatal complications. Hepatocellular jaundice may occur due to the liver cell damage caused by viruses, bacterial toxins, hepatotoxic chemicals and radiations. There is no rational therapy available in western medicine as such for the cure of this disease, usually supportive measures are practiced.

Therefore, damage to the liver inflicted by hepatotoxic agents is of great importance. There is an ever-increasing need for an agent, which could protect liver against such damage, and which facilitates or promotes regeneration of parenchyma cells after damage and thereby arrests the growth of fibrous tissue.

The chief functions of the liver are-

**Formation of bile**- All the hepatic cells continually form a small amount of secretion of bile. This is secreted into the minute bile canaliculi, which lie between the double layer of cells in the hepatic plates and the bile then flows peripherally towards the interlobular septa, where the canaliculi empty into terminal bile ducts. The bile contains the bile salts (sodium glycolate and sodium taurocholate) and bile pigment (Bilirubin).

**Destruction of RBC**- The Kuffer cells of the reticulo-endothelial system are responsible for breaking down the red blood corpuscles. The Kuffer cells also actively phagocytic and remove foreign particles from the blood stream.
**Carbohydrate metabolism**- The liver performs the specific functions like, storage of glycogen, conversion of galactose and fructose to glucose, gluconeogenesis and formation of many important chemical compounds.

**Fat metabolism**- Some specific functions of the liver in fat metabolism are, β-oxidation of fatty acids and formation of acetoacetic acid, formation of the lipoproteins, formation of large quantities of cholesterol and phospholipids, conversion of large quantities of carbohydrates and proteins to fat.

**Protein metabolism** - The most important functions are,- deamination of amino acids, formation of urea for removal of ammonia from the body fluids, formation of plasma proteins, interconversions among the different amino acids and other compounds important to the metabolic processes of the body.

**Miscellaneous functions of the liver**- Formation of heparin and prothrombin

**Detoxication function**- The indole, ketone, phenol etc. (Products of bacterial purification of some of the amino acids in the large intestine which are very toxic) are rendered less toxic or entirely harmless by the hepatic cells by forming conjugated compounds with sulphuric or glucuronic acid. Conjugation is due to esterification or peptide bond formation.

The bacterial toxins or proteins of similar complexity are also rendered harmless by the formation of antibodies (mostly globulin compounds) elaborated by the hepatic cells. Some of the bacterial and chemical toxins and also heavy metals are excreted into the bile.
Storage of iron- Iron is stored in the liver in the form of feritin. The hepatic cells contain large amount of protein called apoferitin, which is capable of combining with either small or large quantities of iron.

Relation of the liver to blood coagulation- The liver forms a large proportion of the blood substance utilized in the coagulation process. These are fibrinogen, prothrombin, accelerator globulin, factor VII and several other less important coagulation factors. Vitamin K is required by the metabolic processes of the liver for the formation of prothrombin and factors VII, IX, X. In the absence of vitamin K, the concentrations of these substances fall very low and almost prevent blood coagulation.

Storage of vitamins- The single vitamin stored to the greatest extent in the liver is vitamin A but, large quantities of vitamin D and vitamin B₁₂ are normally stored as well. Sufficient quantities of vitamin can be stored to prevent vitamin A deficiency for as long as one to two years and sufficient Vitamin D and Vitamin B₁₂ can be stored to prevent deficiency for as long as three to six months.

Drug metabolism- The metabolism of most of the drugs occurs in the liver by the action of microsomal and non-microsomal enzymes and also by conjugate formation with indigenous substance like glucuronic acid. After metabolism the drugs become less toxic more polar and easily excretable.

Alteration of hepatic blood flow- Hepatotoxins like carbon tetrachloride (CCl₄) can act directly on hepatic cells and would cause swelling resulting in mechanical obstruction of sinusoidal blood flow. Carbon tetrachloride induces a coagulate necrosis of hepatocytes that does not affect the sinusoid lining cells, permitting the retention of intact vascular pattern.
Hepatitis

Hepatitis is an inflammation of the liver. The characteristics of various types of hepatitis are -

**Acute anicteric hepatitis**- Inflammation of the liver marked by slight fever, loss of appetite, gastrointestinal upset without jaundice.

**Amoebic hepatitis**- Inflammation of the liver caused by the infection of *Entamoeba histolitica* as a complication of amebic dysentery.

**Cholangiolitic hepatitis**- Inflammation of the bile ducts of the liver associated with obstructive jaundice and there is pruritus and vomiting of bile.

**Fulminant hepatitis**- Hepatitis marked by sudden onset of nausea and vomiting, chills, high fever, severe jaundice, convulsions, coma and death usually occurs within 10 days.

**Viral hepatitis**- General inflammation of the liver caused by one of the five different viruses.

Hepatitis A is caused by hepatitis virus (HAV), which is single stranded RNA without envelope. It is transmitted through fecal-oral route by ingestion of contaminated food and water. Its incubation period is 2-6 weeks. The symptoms are mostly sub-clinical and in severe case fever, heads ache, malaise and jaundice.

Treatment- Inactivated vaccines. The immune globine provides temporary protection.
Hepatitis B is caused by hepatitis B virus that is double stranded DNA having envelope. It is transmitted through parenteral injection of contaminated blood or other body fluids and also by sexual contact. Its incubation period is 4 to 26 weeks. The symptoms are frequently sub-clinical, similar to HAV, but fever, no headache and more likely to progress to severe liver damage.

Treatment- Genetically engineered vaccine produced in yeasts. Persons with chronic HBV infections receive α-interferon (α-IFN).

Hepatitis C is caused by hepatitis C virus (HCV) that is single stranded RNA having envelope. It is transmitted through parenteral route. Its incubation period is 2-22 weeks. The symptoms are similar to HBV, but more likely to become chronic.

Treatment- None, but some chronic cases of hepatitis C respond to treatment with α-IFN.

Hepatitis D is caused by hepatitis D (HDV) virus that is single stranded RNA, envelope from HBV. It is transmitted through parenteral route, by the person co-infected with hepatitis B. Its incubation period is 6-26 weeks. The symptoms are severe liver damage having high mortality rate.

Treatment- HBV vaccine is protective because co-infection required.

Hepatitis E is caused by hepatitis E virus (HEV) that is single stranded RNA without envelope. It is transmitted through fecal or oral route. Its incubation period is 2-6 weeks. The symptoms are similar to HAV, but pregnant women may have high mortality rate.

Treatment- Under development.
Hepatoprotective studies

Though liver diseases are among the important diseases affecting mankind, no remedy is available to majority of them at present. However, number of medicinal preparations have been advocated in traditional systems of medicine, especially in Ayurveda for treating liver disorders. The search for the hepatoprotective agents started in medicinal plants is in progress after the discovery of sylimarin, a flavonolignan from *silybum marianum* a proven hepatoprotective drug.

The search was further facilitated by the description of *in vitro* technique involving evaluating test drugs against carbon tetrachloride induced toxicity in cultured hepatocyte by Hikino and Coworkers (1984) which enables the research workers to screen large number of test drugs by adopting this procedure as a primary screen. Hence, it was thought worthwhile to screen the plants for hepatoprotective activity.

In Indian Ayurveda system several plants and plant products are known to act as potentive hepatoprotective principles for healing infective hepatitis. The knowledge of Hindu physicians on medicinal plants was very vast, their vegetable materia was extensive. It is curious to note that they had picked up specific herb for a particular ailment (Chopra, 1965). In India a rapid progress has been noticed in the clinical study of hepatoprotective plants.

Kiso, *et al.*, (1983) have subjected the main sesquiterpenoid components of *Atractylodes rhizomes* against CCl₄ and galactosamine-induced cytotoxicity in primary cultured rat hepatocytes and found significant liver-protective effects.

Young, *et al.*, (1986) reported that the methanol extract of *Wedelia chiensis* possess a strong anti-hepatotoxic action against CCl₄ induced hepatitis.


Krishna (1996) worked on *Boerhaavia erecta, Boerhaavia rependa* and *Diospyrus cordifoila*. They comparatively evaluated the hepatoprotective effects of ethanol extract on *in vivo* roots (*Boerhaavia* spp.), stem bark (*Diospyrus cardifoila*) and their *in vitro* developed calli against CCl₄ induced toxic hepatitis.

Successive extraction of the aerial parts of *Trianthema portulacastrum* (Ficoidaceae) with petroleum ether, benzene, chloroform, alcohol and water were tested for the hepatoprotective properties against carbon tetrachloride (Mehta, et al., 1999).

Ethanolic extracts of the roots of *Vitex negundo* exhibited hepatoprotective activity against carbon tetrachloride induced hepatotoxicity (Srinivas, 2004).

Similarly hepatoprotective effects of the ethanolic extracts of the plants, *Carduus acanthoides, Carduus nutans*, (Asteraceae), *Cinchorium intybus* (Asteraceae), *Fumaria asepalae* (Fumariaceae), *Fumaria vailantii*, (Fumariaceae), *Gentiana olivieri* (Gentianaceae), *Plantago lanceolata*

The different extracts of *Apium graveolens* Linn (Apiaceae) and *Croton oblongifolius* Roxb. (Euphorbiaceae) were tested for their hepatoprotective activity against carbon tetrachloride induced hepatotoxicity in albino rats (Bahar Ahmed, 2002). Sethuraman, et al., (2003) have evaluated the ethyl extract of the stem of *Sacrostemma brevistigma* (Asclepidaceae) against carbon- tetrachloride induced hepatic damage in rats.

Mohideen, et al., (2003) have tested the aqueous extract of the seeds of *Nigella sativa* (Ranunculaceae) were tested for the hepatoprotective activity on male Wistar rats against carbon tetrachloride induced hepatotoxicity. Ethanol extract of *Piper longum* fruits and other fractions were screened for hepatoprotective activity in adult Wistar rats (Jalalpure, et al., 2003). The fruit pulp of *Balanites aegyptiaca* investigated for hepatoprotective activity against carbon tetra chloride induced liver damage in rats (Jaiprakash, et al., 2003).

Comparative study of the ethanol extracts of the leaves and bark of *Alianthus excelsa* Roxb. (Simaroubaceae), were investigated for hepatoprotective activity on experimentally induced liver injury with carbon tetrachloride (Hukkeri, et al., 2003).

The hepatoprotective activity of aerial parts of *Trianthema portulacastrum* was evaluated using paracetamol and rifampicin as liver toxicants in rats (Mehta, et al., 1999).
Suspensions of alcoholic extract, petroleum ether extract and aqueous extract of the leaves of *Wrightia tinctoria* in tween-80 were investigated for hepatoprotective activity against carbon tetrachloride induced liver damage (Chandrashekhar, *et al.*, 2004).

Venukumar and Latha (2004) have investigated the anti-hepatotoxic activity of methonalic extract of *Coscinium fenestratum* stem against carbon tetrachloride induced hepatotoxicity in rats.

Vidya, *et al.*, (2004) have evaluated the hepatoprotective activities of the seed kernel of *Entada pursaetha*. Ethanolic extract of has been reported to contain the significant hepatoprotective activity.

The comparative hepatoprotective effect of roots extracts *Boerhaavia rependa* was screened by Krishna and Shantamma (2004)

Many investigators were attempted to evaluate the hepatoprotective effect of the constituents isolated from the medicinal plants, but only a few reports were available.

Wagner, *et al.*, (1986) isolated wedelolactone and dimethyl wedelolactone from ethyl acetate soluble fractions of *Wedelia calendulacea*. They observed significant stimulatory effect on liver cell regeneration against CCl₄ cytotoxicity in rat hepatocytes.

Visen, et al., (1990) isolated flavonoid compound andrographolide from the leaves of *Andrographis paniculata*, which was evaluated to show hepatoprotective activity against paracetamol induced hepatic damage.

In D-galactosamine induced hepatitis in rats, a significant increase of lipid peroxidation and a decrease in liver anti-oxidant enzymes levels are observed pretreatment with the ethanol extract of *Picrorhiza kurroa* (Scrophulariaceae) prevented these alterations (Anandan and Devaki, 1999).

Sesquiterpene lactone extract from the leaves of *Vernonia amygdalina* was tested for their significant antihepatotoxic activity against CCl₄ induced hepatic damage in rats (Babalola, 2001).

Venkatesan, et al., (2003) studied the protective effects of the *Phyllanthus amarus* Linn (Euphorbiaceae), nirocil, phylanthin and silymarin against CCl₄ induced liver and brain toxicity.

From the seeds of *Foeniculum vulgare* (Umbeliferae) essential oil was extracted and tested for the hepatoprotective properties against carbon tetrachloride induced liver injury model in rats (Ozbek, et al., 2003).

Dagaonkar and Shankar (2002) have conducted a study on 150 patients with various liver disorders to test the efficacy of the drug Livosil B, a main constituent of which silymarin, extracted from the seeds and fruits of *Silybum marianum*. Significant hepatoprotective was observed.

Bioassy guided fractination of the ethanol extract of *Cnidium monnieri* (Apiaceae) furnished two hepatoprotective sesquiterpenes, torilin and torilolone, together with a new derivative, 1-hydroxytorilin. Both the
compounds showed hepatoprotective effects on tacrine-induced cytotoxicity in human liver-derived Hep G2 cells (Oh H, et al., 2002)

Nagaraja and Krishna (2002) isolated a flavonoid compound from the leaves of *Andrographis alata*, which was further evaluated for hepatoprotective activity against CCl₄ induced liver damage.

Mankani and Krishna (2004) isolated four triterpenes, ursolic acid, lupeol, betulin and betulinic acid from the petroleum ether and CCl₄ extract of *D. cardifolia* stem bark. All these four terpenoid compounds were screened for anti-hepatotoxic effect. Ursolic acid was most effective in controlling the liver damage against toxic hepatitis.

In the present investigation also an attempt was made to screen the alcohol soluble fractions of *Elephantopus scaber* and its isolated sesquiterpenoid compound deoxyelephantopin against CCl₄ induced toxic hepatitis.

**Inflammation**

Inflammation can be described as tissue response to an injury. The damage caused by microbial infection, physical agents such as heat, radiant energy, electricity or sharp objects, or chemical agents like acids, base and gases. The clinical manifestation of inflammation are, rubor (redness), calor (warmth), tumor (swelling) caused due to exudation, dolor (pain), due to stretching of nerve endings, change in tissue osmotic pressure and pH and functiolaesa (loss of local function) due to discomfort or destruction of the part involved.
Inflammation has the functions, to destroy the injurious agent, if possible, and to remove it and its by-products from the body. If destruction is not possible, to limit the effects on the body by confining or walling off the injurious agent and its by-products and to repair or replace tissue damaged by the injurious agent or its by-products.

During inflammation the local blood flow increases leading to the characteristic local heat (Calor) and redness (Rubor). There is slowing of the circulation accompanied by an increased permeability of capillaries, with exudation of protein rich fluid into the interstitium. Leucocytes marginate to the periphery of the vessel lumen and then emigrate into the interstitium. Cellular events are dominant in this stage and follow a chronological order. The platelets are the first cells to arrive at the site of inflammation. The neutrophils and red blood cells follow them. A fibrin network forms over the wound.

During inflammation, concentrations of some proteins change. These proteins, whose concentration changes markedly during inflammation, are called acute phase protein. Acute phase proteins include complement, the cytokines and several specialized proteins such as fibrinogen for clotting and kinins for vasodilation.

Inflammation and wound repairs proceed simultaneously with successive formation of granulation tissue, synthesis of wound collagen and ground substance. Wound contraction and finally scar formations are the final stages in wound healing.
The drugs used in inflammatory disorders are- paracetamol, phenacetin that are aniline derivatives. The commercially available drugs ibuprofen, naproxen of popionic derivatives and mainly salicylates and its derivatives like, aspirin, sodium salicylate, benorylate, aloxiprin etc. Pyrazolone derivatives like, phenylbutazone, oxyphenbutazone and indole derivatives like, indomethacin and sulindac etc. But, these drugs have certain unwanted side effects. After prolonged use it induces gastric or intestinal ulceration that may leads to anemia. Many reports are also indicated that over dose of paracetamol leads to jaundice. (Dwivedi, 1991). A variety of anti-inflammatory drugs are flooding the world market today but a very few are relatively non-toxic. Thus the drugs having low toxicity and better therapeutic index is required for the inflammation therapy.

In 1991, Udupa, et.al., studied the effect of the juice of *Aloe vera* (0.2ml/100 g-i.p.) for its anti-inflammatory action by observing percentage reduction in carrageenan induced rat paw volume at 3 hrs. and subcutaneously harvested granuloma tissue weight on 10th day. *Aloe vera* showed significant anti-inflammatory activity in acute inflammatory model without any significant effect on chronic inflammation. Significant increase in breaking strength (incision wound), enhanced wound contract in breaking strength of granulation tissue and biochemical parameters (dead space wound) were also observed. Mode of action of the drug by increasing the extent of cross-linking of collagen via lysyl oxidase as well as by enhancing the tensile strength by interaction with the ground substance has been suggested.

*Aloe vera* showed significant anti-inflammatory activity in acute inflammation model without any significant effect on chronic inflammation. Significant increase in breaking strength (skin granuloma tissue) enhanced wound contraction and decrease epithelization period was observed. An increased in lysyl oxidase activity and mucopolysaccharide content were also
seen. This drug could therefore increase tensile strength by increasing cross-linking in collagen and interaction with the ground substance (Udupa, et al., 1991).

In 1994, Udupa, et al., studied the root extracts of Moringa oleifera (Moringa) and Aegle marmelos (Bilva) for their anti-inflammatory and wound healing properties. Anti-inflammatory action was studied by observing percent reduction in carrageenan induced rat paw edema at 3 hrs. Moringa and Bilva showed significantly acute anti-inflammatory activity. However, only Bilva was able to suppress chronic inflammation significantly. A significant increase in the tensile strength as well as lysyl oxidase activity and hexosamine content were observed in the Moringa treated animals, indicating pro-healing action probably by better cross-linking of collagen. Bilva, on the other hand, was more effective as an anti-inflammatory agent.

The volatile oil extracted by the steam distillation of the wood of Cedrus deodara was examined for its oral anti-inflammatory and analgesic activity (Shinde, 1999).

The hydrosoluble fractions of Euphorbia royleana latex administered by gavage at doses of 50-200 mg/kg, showed dose dependent anti-inflammatory and arthritic effects in different acute and chronic test models in rats and mice (Bani, et al., 2000).

The possible anti-inflammatory activity of 90% ethanolic extract of Dalbergia sissoo leaves was studied in different models of inflammation in rats after different oral doses (Hajare, et al., 2001).

Cuellar, et al., (2001) studied the topical anti-inflammatory activity of extracts from Cassia angustifolia, Rheum palmatum, Coptis chinensis,
Phellodendron amurense and Scutellaria baicalensis, plants used in traditional East Asian medicine against different skin disorders.

Fractions of methanol, dichloromethane, water extracts and volatiles of Carthamus lanatus aerial parts given by oral route at a dose of 2 mg/kg showed significant anti-inflammatory activities in rats (Bocheva, et al., 2003).

Dried leaves extract from Bouchea fluminensis was assessed in anti-inflammatory (mouse paw edema) and analgesic models (Costa, et al., 2003).

Methanolic extract effects in topical administration were studied using carrageenan oedema and formalin test of Glaucium grandiflorum (Morteza Semanani, et al., 2004). Aqueous and alcoholic extracts of Adhatoda vasica and Berberis aristata on carrageenan induced paw edema in rats were studied (Rajput, et al., 2004).

The anti-inflammatory effect of Clerodendron trichotomum thumberg leaves was investigated on rats, mice and in raw 264.7 cells. 1 mg/kg solution of the 30 and 60% of methanol extracts were used and 1 mg/kg of indomethacin was used as a positive anti-inflammatory standards (Choi, et al., 2004).

The alcoholic and aqueous extracts of the bark of Machilus macrantha was investigated for anti-inflammatory activity in carrageenan induced rat paw edema (Tatiya and Hatapakki, 2004). Flavonoids and sesquiterpene lactone from Tanacetum microphyllum inhibits anti-inflammatory mediators in LPS stimulated mouse peritoneal macrophages (Abad, et al., 2004).

In the carrageenan induced paw edema in rats, (+)-pinitol (2.5-10 mg/kg i.p.) isolated from Abies pindrow leaves showed significant anti-inflammatory

A sesquiterpene lactone is purified from the alcoholic extract of *Arnica* and it has anti-inflammatory effect. Studies suggest molecular mechanism for the anti-inflammatory effect of sesquiterpene lactones, differs from anti-inflammatory drugs (Lyss, et al., 1997).

In the present study also, the anti-inflammatory affects the plant *Elephantopus scaber* has been evaluated.

*Elephantopus scaber* Linn.

A member of Asteraceae is a rather conspicuous herb growing among grasses, in the hotter parts of the India, particularly the mountain terrains (Fig. 1a) of the Western and Eastern Ghats especially in the forests of Belgaum, Chicmagalur, Coorg, Hassan, Mysore, North Kanara, Shumoga and South Kanara. The plant is erect, 15-38 cm high, rootstock giving off many stout fibrous roots, stem usually dichotomously branched, strigose with oppressed white hairs. Leaves mostly radical, 12.5 by 3.8-5.7 cm, forming a spreading rosette on the ground, obviate-oblong, rounded or sub acute, more or less hairy on both surfaces, base tapering into an obscure petiole, main nerves numerous, prominent beneath, with reticulate veins between, cauline leaves, smaller than the radical, sessile or nearly so. Heads numerous, sessile, closely packed, forming a large flat-topped terminal inflorescence nearly 2.5 cm across and surrounded at the base by 3 large bracts (Fig. 1b). Involucral bracts in 2 series enclosing 4 flowers, bracts of the outer row half as long as those of the inner, 1-nerved, bracts of the inner row usually 3 (rarely 5) nerved, scariosus, linear, cuspidate. Corolla purple exserted, tube long, slender. Limb deeply cleft on one side, causing the 5 linear lobes to
Fig. 1

a. *Elephantopus scaber* growing in the medicinal garden of Kuvempu University.

b. An inflorescence twig showing purple colored florets
present a palmate appearance. Style much exerted, the arms recurved. Pappus white, 1-seriate, consisting of 5 (rarely 4) rigid bristles dilated at the base. Achenes 5 mm. long truncate, finely 10 ribbed, slightly pubescent. The embryos sometimes germinate in the head.

Synonyms

English: Prickly-leaved Elephant’s Foot
Hindi: Gobhi
Sanskrit: Adhomukha, Anadujivha, Darvi, Darvika, Darvipatrika, Gojivha, Gojivhika, Hddhapushpi, Kharapatri, Kurasad, Satamulika
Tamil: Anashovadi
Telugu: Eddumalikechettu, Enugabira, and Hastikasaka.
Urdu: Gobhi.
Kannada: Hakkarike, Naayi nalige gida.


A survey of the Ayurvedic literature revealed that, the wound healing activity of *Elephantopus scaber* has been successfully used in number of ayurvedic formulations and found to be efficacious and cheap compared to synthetic drugs. The plant is used in diabetes, cough, wounds, fever, and skin disorders. Whole plant macerated with honey and applied on wound surface/bitten part of snake/venombite (Bapalal, 1999).
According to Chopra, et al., (1956) the Plant *Elephantopus scaber* is mucilaginous, astringent, cardiac tonic, alternative and febrifuge. A decoction of the roots and leaves is used as emollient and is given in dysuria, diarrhoea, dysentery and swellings or pains in the stomach. The root is given to arrest vomiting; powdered with pepper it is applied in toothache. Bruised leaves boiled in coconut oil are applied to ulcers and eczema.

According to Kirtikar and Basu (1991), The plant *Elephantopus scaber* has a sharp, pungent, bitter taste; vulnerary, astringent to the bowels, antipyretic, cures “kapha", biliousness; removes foul taste from the mouth; useful in all poisoning from the bites or from the nails of the animals; good in diseases of the blood and the heart, urinary discharges, bronchitis and small pox. The herb is tasteless with a flavour; tonic, laxative, analgesic, used in griping, inflammation, tonic to the brain; lessens sleep. The leaves are used in pains and piles. The juice is a good collyrium. The flowers are aphrodisiac, tonic expectorant; cure biliousness, liver troubles and coughs, good in syphilis. The plant is much used as a diuretic in Indo China, as a diuretic and febrifuge in Madagascar.

George and Pandalai (1949) have shown that, the alcoholic extract of the whole shoot of *Elephantopus scaber* have antibiotic activity against *Staphylococcus aureus* and *Escherichia coli*.

Mitsumasa Haruna (1985) has reported the anti-tumor activity of, nudaphantin, a new cytotoxic germacranolide and elephantopin from *Elephantopus nudatus*. Certain Elephantopus species are known to contain a number of novel sesquiterpene lactones. Examples: elaphantin and elephantopin from *Elephantopus elatus*, deoxyelephantopin from *Elephantopus scaber* and *Elephantopus carolinianus* and molephantin, molephantinin and
phantomolin from *Elephantopus mollis*. Further a novel cytotoxic anti-tumor agents are examined from *Elephantopus nudatus*

Chen, *et al.*, (1989) were carried out Preliminary anti-bacterial screening of local crude drugs using the carcinogenic bacterium, *Streptococcus mutans*. Out of 79 aqueous extracts, 6 crude drugs were shown to have significant anti bacterial activity with minimal inhibitory concentration equal to or lower than 7.8 mg/ml (expressed in terms of dry starting material). Of these effective crude drugs, *Morus australis, Ludwigia octovalvis* and *Thuja orientalis* were very effective in inhibiting the growth of serotypes c and d of *S. mutans* (MIC less than or equal to 2.0-7.8 mg/ml). *Elephantopus scaber, Artemisia vulgaris, Mosla chinensis* and *Orthosiphon aristatus* also exhibited considerable anti-bacterial activity (MIC = 7.8-23.4 mg/ml) against both serotypes. In the presence of 5% sucrose, the anti-bacterial potency of the majority of the extracts did not change for type c, while the potency decreased about one-half for type d.

Lin, *et al.*, (1995) has evaluated the hepatoprotective effects of Taiwan folk Medicine ‘Teng–Khia–u’ a folk medicine of Taiwan, derived from entire plants of *Elephantopus scaber, E. mollis* and *Pseudolephantopus spicatus*. The hepatoprotective effects of water extracts of these three plants against beta–D–galactosamine (D-GalN) and acetaminophen (APAP) induced acute hepatic damage were determined in rats. The results indicated that the serum glutamate oxalate transaminase (SGOT) and the serum glutamate pyruvate transaminase (SGPT) levels caused by D-GalN and APAP decreased after treatment with crude extracts of ‘Teng–Khia–u’.

Mohamed Suhaila, *et al.*, (1996) have screened anti-mycotic screening of 58 malaysian plants against plant pathogens. The ethonolic extract of the plant *Elephantopus scaber* has shown selective anti-fungal activity against
seven plant pathogens using the filter paper disc diffusion technique. (*Colletotrichum capsici, Fusarium pallidoroseu, Botryodiplodia theobromae, Alternaria alternata, Pencillium Citrinum, Phomopsis Caricae papyae and Aspergillus niger*).

Ali abdul Manaf, *et al.*, (1996) have screened anti-viral and cytotoxic activities of some plants in Malaysian indigenous medicine. Ethanolic extracts of 61 medicinal plants were screened for anti-viral and cytotoxic activities. Cytotoxic activity was present in the extracts from *Andrographis paniculata, Centella aciatica and Elephantopus scaber*.

Paul, *et al.*, 1997 isolated sesquiterpene lactones from *Elephantopus scaber*. The whole plant of *Elephantopus scaber* afforded to contain deoxyelephantopin, isodeoxyelephantopin and a new germacranolide sesquiterpene lactone scabertopin were determined.

Tsai-Chin-Chuan and Lin-Chun-Ching (1999) have tested the anti-inflammatory effects of Taiwan folk medicine ‘Teng-khia–u’ on carrageenan and adjuvant induced paw edema in rats ‘Teng–khia–u’ is a folk medicine from Taiwan, derived from entire plants of *Elephantopus scaber, E. mollis* and *Pseudolephantopus spicatus* (Compositae). To evaluate the anti-inflammatory activities and complete Freund’s adjuvant (CFA) induced chronic arthritis in rats were conducted. The results indicated that pretreatment with ‘Teng–khia–u’ significantly inhibited the carrageenan induced acute arthritis and chronic arthritis induced by CFA.

Rajesh and Latha (2001) have carried out the efficacy of the crude extracts of *Elephantopus scaber* to prevent CCl₄ induced chronic dysfunction in the rats. The results suggest the hepatoprotective effect of this plant.

Lin, et al., (1991) has determined the liver protective effects and pathological studies of the crude extracts of *Elephantopus scaber* ssp. *oblanceolata*, *E. mollis*. Improved hepatic fatty metamorphosis and necrosis of central lobule were observed by the crude extracts.

Recent work has revealed the importance of sesquiterpenoid lactones. Due to the presence of α-methylene lactone, they exhibit anti-tumor activity. The presence of sesquiterpene lactones in the plant *Elephantopus scaber* made several researches to undertake to characterize the chemotherapeutic agents that are responsible for anti-tumor activity.

In the view of the above, the present investigations was undertaken to derive protocols for *in vitro* regenerations of plantlets and comparative pharmacological evaluation of the crude extracts and the constituent against wound healing, hepatoprotective and anti-inflammatory models in rats.