CHAPTER 1

Introduction
## CHAPTER 1

### Chapter 1: Introduction

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1. INTRODUCTION

1.1. Backdrop on Herbal Medicines

The vigorous products derived from biological resources like plants, animals, microorganisms and minerals from the natural settings have been the very basis for management of various human ailments and diseases. In the current scenario, it is been envisaged that, majority of the population in the globe are depending on herbal medicine system for their primary health care. The popularity of herbal medicines has been increasing progressively. Therefore, study has been focused explicitly on richness of the Indian biodiversity from there, various medicinal plants are being used for treating several ailments traditionally\(^1\).\(^2\). In the ancient civilization, the practical evidences are available relating to the inventiveness of practicing medicinal plants for treating various ailments and diseases in a broader prospection. Subsequently, in the middle of 19\(^{th}\) century, certain group of people have involved in processing of plants and their different parts to prepare desired drugs with dynamic ingredients of different plant components in order to combat against some life threatening ailments. This has created an accurate path for discovery of novel drugs with energetic molecules which can lead crucial role in the biological system\(^3\).\(^4\).\(^5\).

In the later phases, some developed countries have involved actively in isolation of energetic components from natural resources to develop suitable drugs against various ailments and the target specificity was also analyzed in the newly designed drug for their side effects if any\(^6\).\(^7\). Therefore, clinical trials were made with conventional protocols to assess the different pharmacological properties in order to ascertain the parameters like, quality, efficacy and safety of these herbal fractions against the ailments\(^8\).\(^9\). Further, active fractions of different herbal medicines were subjected for clinical trials based on the significant outcome\(^10\), correspondingly the driving force of antibiotics and anticancer agents derived from these path breaking discoveries were recommended for clinical use\(^11\).\(^12\). These were instigated the systematic approaches for both pharmacological and phyto-chemical evaluations in the various indigenous medicinal plants towards development of novel active drugs\(^13\)-\(^15\).

The medicinal plant drugs and their formulations have been screened for biological activities in search of new fangled herbal drugs against some serious ailments. Likewise, the indigenous medicinal plants which are practiced by the healers in the
traditional medicine system have been subjected for bio-prospecting for new potent drugs through analyzing their mechanism of action. Inauspiciously, the outcome of such preliminary investigations from the concerned industry does not necessarily reach the public domain and the details are kept in locked built-up files \textsuperscript{16,17}. Therefore, the real need of new clinical drugs was not been accomplished appropriately due to lack of memorandum on delivery of novel drugs along with regulatory strategies.

There is an urgent need to develop new clinical drugs for numerous diseases including the breakdown of the central nervous system (CNS), for instance, Alzheimer’s and Parkinson’s disease, epilepsy, migraine, pain, schizophrenia, sleeping disorders etc. The drugs from natural products have a demonstrated track record for CNS activities such as caffeine, codeine, morphine, nicotine, reserpine etc. which are obtained still from the natural resources \textsuperscript{18,19}. The extraction of these natural products has altered the existing mode of treatment by herbal extracts with single chemical element. There is a basic hypothesis that any plant possessing clinical effectiveness must contain an active principle which can completely replace the plant crude extract \textsuperscript{20}. These findings enfold the clinical implication of plant based drug which has not been accomplished earlier.

Further, an approach was made on ‘dragon blood’ extracted from bark of Croton species that include polymeric anthocyanidins as a chief component which is proposed for the treatment of wound and related problems. Additionally, the sap of red wood was used to coat a wound as a protective layer which avoids microbial infection in association with phenolic constituents that in turn exercise anti-inflammatory effects; hence the plant based medicine has become most popular because of no side effects \textsuperscript{21}. The practices of herbal medicines in the traditional medicine system have contributed many therapeutic protocols towards management of human health from different ailments and diseases through appropriate remedial approaches. At present, considerable amount of pharmaceutical recommendations that contain active ingredient based on single plant. In the recent trend nearly 125 pharmaceutical products and their formulations are validated based on the traditional knowledge obtained from different sources \textsuperscript{22,23}. 
1.2. Herbal Medicines and Health care system

In the health care system, plant based effective drugs which are traditionally practiced against life threatening ailments and their formulations are well known to the herbal practitioners followed by rural communities. The medicinal plants are being used in particular for preventive, promotional and curative applications by large number of practitioners exist only in the traditional medicinal system. It is known that, the traditional knowledge of medicinal plants has been transferred in the course of many centuries based on distinct medicinal systems such as Ayurveda, Unani and Siddha. The indigenous traditional healers are treating the people for their primary health care regularly with different fractions herbal formulations which are pre-established by them. Likewise, the interest on these traditional medicine systems has been increased in different parts of the globe which is noticed during the last few decades. However, documentation of the indigenous knowledge and possible exploration for the active molecules via ethno-pharmacological studies is most imperative assignment accepted towards conservation, utilization and reestablishment of biological resources, respectively.

According to the reliable sources, the local herbal medicine practitioners may have possible way of income generation regularly treating the people through their practice of traditional medicine system. The main cause for enforcement in the people for going herbal medicine system for their common ailments which are mainly due to less communication means, poverty, ignorance and unavailability of modern health facilities. The usage of traditional medicine knowledge for herbal treatment has been still in practice at all levels of the society. Besides, more than 25% of the people from developed countries are still practicing the plant based medical drugs and their derivatives are being used positively for some specific ailments. Since from the beginning, the ingredients, dosages and mode of treatment for all primary health care are subjected for refining in its formulations time to time to achieve better management of the ailments. The practice of traditional medicines not only helping the common people who are suffering from different ailments; but, also influencing community medicine which in turn helps the health care system with new fangled drug development. At present, the use of medicinal plants in traditional healing by either tribal people or indigenous folk medicine men is of great importance in the country because, most of the serious diseases are being treated by their
traditional healers when it is not possible by allopathic treatment. Apart from the traditional healers, many other forest dwellers and rural people also possess unique traditional knowledge about plants and their practices against different fatal diseases.

On the other side, the interest on traditional knowledge has been declining in the present scenario, that is because, lack of interest in the younger generation who has developed the tendency to move towards urban area for profitable occupations. Therefore, systematic approaches in ethno-botanical survey for documentation of medicinal plants and their practices by traditional healers for different ailments are also lacking in the present condition. Hence, an ethno-pharmacological study with systematic informations relating to possible exploration of medicinal plants along with their sound knowledge has been accomplished by the local healers. Likewise, the traditional knowledge will transfer from original traditional healers to their own generation through oral communication or written formats in the coded approaches. But, the documentation study on the traditional knowledge should be transferred steadily to the younger generations irrespective of any cast and creed. Hence, the studies on ethno-medicinal practices are found to be very important, as a result, some studies are emphasizing on conducting interactions with local traditional practitioners to document their knowledge on medicinal plants practiced for various ailments with respects to their taxonomy, part used, preparation of drugs, usage and the types of diseases treated along with dosage and duration etc.

The documented wealth of traditional knowledge will be subjected for both in vitro and in vivo analysis to isolate active principles keeping in view of the type of ailments, effect and frequency of the diseases will be taken into consideration. Further, based on the effectual concentrations of the prepared drug will be accomplished for its efficacy, safe and effective management of the particular ailments. The drug established on the basis of plants will be considerably competitive as compared to western medicine system. Therefore, the modifications with periodical alterations in the traditional medicines are also referred as evolutionary medicines in parallel which has been a part of evolution of man on the earth system. In the present scenario, the traditional medicines have got unique position in the pharmaceutical industry for its exceptional and distinctive characteristic features in the different herbal formula which include active principle, purified fractions, new fangled
constituents and lead molecule with respect to various ailments. This will facilitate the better management of the herbal drugs in the traditional health care system.

1.3. Wound and Healing Process

Wound healing is an important biological process involving tissue repair and regeneration for instance, after the disturbances occur in the skin or body tissue system, the restoration of the tissues will takes place that influences the wound contraction. In the normal condition, both epidermis and dermis will acts as protective stratum against any diverse situation of the environment. An appropriate conception of wound is that a split of discontinuity of the skin tissues due to any unexpected aggression for which, the contraction or restoration of tissue system will be facilitated to attain normal conditions under controlled settings. There are three major organizations in wound healing based on the type and severity of wound and its healing process. In the first arrangement, the boundaries of the wound are efficiently closed without any mark/scratches and disfiguration.

Similarly, in the second organization, the granulation of tissues will takes place that facilitate filling up of wound gap through tissues to normalize the surface of the skin by leaving a little scars or marks. Consequently, in the third organization, if the wound is left open habitually for few days, in which the granulation tissue bed falls down negatively prior to treatment which leads to formation of scars and marks with austerity. Hence, the different phases of wound healing will have conceptual stages like, from the state of injury followed by coagulation that admits inflammation in 24 to 48 h. Further, this will facilitate proliferation in 72 h which leads to remodeling through contraction in subsequent weeks to few months (Fig.1.1).

The complex and convoluted process in Wound healing will return to normal condition in response to injury through restoration of tissue system. The restoration of tissues in any wound will comprising specific course of action, that is between cell to cell, interactions in cell matrix which allows the overlying of segments i.e., coagulation, inflammation, proliferation in cells followed by remodeling.
The veracity in the vascular tissues at the injured area will be disintegrated that results in extravasations of blood and its circulations in the adjacent tissue system followed by plasma. Further, the thrashing of blood by unusual aggregation of platelets due to coagulation and inflammation leads to formation of thrombus. Then, the neutrophils will appear to eliminate the contamination and infection causing organisms after the sixth day of injury through debridement stage. The injured or damaged tissue system will be repaired by endothelial budding via capillaries that formed close to blood vessels which further go into the injured tissues for possible nourishment. On the tenth day to subsequent months, that is in maturation phase, the capillaries formed by budding will turn down which facilitate the wound from pink to white. On the contrary, certain factors like, bacterial or fungal infection, nutritional deficiency, matchless drugs, sterility, over fatness, extension of wound limits, wound site and diseases due to assassination will have their own contributions to delay of
wound healing processes\textsuperscript{43,44}. On account of all these problems, quite a few drugs particularly, antibiotics are established for better management of wound and related ailments. The most popular drugs are Penicillin and Streptomycin is employed in the wounds of both man and animals which can fight against the infectious entities even after post operational conditions\textsuperscript{45}. The preference of antibiotics will be made on the severity of wound and the depth of infection caused by pathogenic microorganisms\textsuperscript{46}. In addition, the antibiotics will be accomplished based on their ability to devastate or suppress the multiplication infectious microorganisms where the tissues will be safe and sound. The concentrations of the drug will be employed till vanishing of the signs and noxious symptoms\textsuperscript{47,48}.

The exploration of medicinal plants and their formulations in the folklore medicinal system have significant track record in successful accomplishments of wound healing process\textsuperscript{49}. This is because of presence of active principles and lead molecules in the plant drugs. The active principle constituents will have ability to diminish the activity of pathogenic microorganisms followed by fulfilling the nutritional deficiencies\textsuperscript{50}. Therefore all the biological activities will be influenced by active constituents or secondary metabolites present in the plant drugs\textsuperscript{51}.

1.4. Wound healing and folklore medicines

Since prehistoric period, wound has been the major ailment and it would be a critical issue, if it is not treated on time. This is because the wound will be connected with integrity of skin and epithelial tissue system, so breaking of cellular functionality in the active tissues will deviate the normal conditions of the body system. According to Wound Healing Society (WHS), the physical injuries or damages to the tissue system will destruct the normal functions in the skin followed by changes in anatomical compositions.
The natural way of managing wound healing process can have most significant approaches in repairing and remodeling the wound area in to normal conditions without affecting any non target regions of the body system. Hence, the plants are leading a very crucial role in wound healing process for attaining the success of natural therapy which still exists in folkloric as well as traditional medicine system. Thus, considerable investigations are being attempted in this area for better management of wounds through plant based medicinal system\textsuperscript{52}.

The proper dressings of the wounds facilitate healing processes in an effectual manner with respect to stipulated period of duration. During which, anatomically disrupted cells and tissue system would be restored and the functional status of the skin will be normalized\textsuperscript{53}. The intricate and complex process of healing will makes the possibility of integrity of damaged tissues in the wound\textsuperscript{54,55}. The wound healing necessitates the collaborative attempt in scores of different tissues and derivations of cell in appropriate overlapping phases\textsuperscript{56-58}. These phases include, aggregation of platelets, clotting of blood, fibrin formation in response to the wounds with inflammation further, the ground matters will be altered that facilitates angiogenesis and re-epithelialization (Fig.1.2). The process of wound healing will be absolutely completed through interweaving of collagen in the disrupted surface of the wound\textsuperscript{59}. In the wound healing, the reduction in tissue damage, perfusion of adequate tissue followed...

\textbf{Fig.1.2. Showing wound dressing and healing approaches in Ancient times}

(Introduction to the History of Medicine-By Ambrose Pare, 16th Century)
by oxygenation with proper nutrition and healing of wound by wet condition are the major objectives to make possible of restoration in wound via stability and function of exaggerated part. The following are the ciphers and symptoms often accompany wounds (Fig.1.3).

a. Blood loss from the wound, b. Ruddiness or red impression
b. Distension or Inflammation, d. Ache, soreness and softness
c. Warmness or heat, f. Infectivity and fever
d. Loss of Mobility and h. Secretion of pus in infected wounds with tainted smell

![Fig.1.3. Different signs and symptoms](image)

(Wound images taken from the patients at authorized hospital)

In addition to the above symptoms of wounds, due to some specific causes like, accidents and injuries are the extreme basis for wounds, they are as follows.

a. During surgical treatment
b. Due to excess heat or skin destruction due to chemicals
c. Due to burning incidents
d. Due to extreme temperature and frost bite
e. Due to exposure with Radiation
f. Skin Cuts and Cells/Tissue damage

1.5. Therapeutic approaches to different wound types

The drugs derived from indigenous medicinal system are much older and it is a great deal with respect to the complexity of existing biomedical structure. There are two major categories of wound incidence, namely acute and chronic type of wounds. The wound with chronic symptoms is of major concern because the chronic wounds will
affect the quality of patients at large (Fig.1.3). There will be statistics on prevalence of both acute and chronic wound types and at present, substantial amount of drugs are recommended for wound and related ailments. In these set of drugs, ample of herbal medicines are in the forefront for the treatment of various ailments.\textsuperscript{62-64} Comprehensively, the resources and database on wound healing is not adequate both in developing and developed countries. Therefore, the research is on to fulfill the gap in order to help the people who suffer particularly from chronic wound ailments.

In addition, the valuable information’s were accessed from traditional medicine knowledge for possible exploration of desired drugs for the treatment of wounds of any kind followed by wound due to burns. In the data base of traditional medicine knowledge, the unknown plant drugs which are already in practice were also subjected for proper authentication.\textsuperscript{65} The derivation of preferred drugs from ethnomedicinal plants, animal source, minerals etc. are explored from traditional medicine system that are described in ‘Vranaropaka’ of ayurvedic system. The medicinal classification such as folk remedial system, traditional and tribal medicine systems are employed list of plants, animal sources towards skin cuts, wounds and burns therapeutics. Even though, the different plants are validated scientifically and subjected for screening especially for wound related ailments, but, the pharmacology and lead constituents from the active principle are not yet fairly explored.

1.6. Course of action in Wound healing

The injuries in wound due to varied rationale, the anatomical structure will be disrupted which makes the invading of foreign entities into the affected part of the wound. The microbial spores will facilitate growth of hyphae that in turn cover up entire tissue system. Then, hemostasis and coagulation will takes place that leads to obliteration of the components like, fibroblast, macrophage, blood vessels followed by destruction of entire dermis region further, that cause early inflammation. On appropriate therapeutic approaches, the inflammation will be healed that results in proliferation and migration of components in the dermal region which facilitate re-epithelialization (Fig.1.4). Finally, the healing stage will be concluded by assessing remodeling stage where, both epidermis and dermis layer will be freshly accomplished.\textsuperscript{60}
The progression in wound contraction comprises re-epithelialization of destructed tissue system are associated with series of biological events\textsuperscript{66}. The exciting mechanism of action by the drugs in the wound system along with better management is considerably inadequate even though there is a rapid advancement in the pharmaceutical industry\textsuperscript{67-69}. The drug from pharmaceutical industry will have surplus side effects apart from managing the chronic wound and the cost effectiveness of the wound treatment is also of great concern\textsuperscript{70,71}. The effective monitoring of chronic wound and its healing process involves the cytoprotective enzymatic group which has an ability to scavenge free radicals from cells and tissues of the wound\textsuperscript{72,73}. The pathogenesis of wound needs removal of free radicals by introducing appropriate antioxidant drugs at the crucial stage.
This maintains the right phase of wound healing through topical application of the drug which facilitates the course of action in scavenging of free radicals to attain remodeling stage in the process of healing (Fig.1.4 and Fig.1.5). This will improve the healing process and defend the tissue system from oxidative damage in the wound area. Currently, only the herbal drugs are challenging the severity of wounds in the human system and no allopathic treatment is justified even after the proper diagnosis of the chronic wounds. Hence, till today plant based drugs are being used for the wounds with chronic conditions which are due to presence of active constituents. Additionally, naturally occurring minerals, metals, ores followed by animal sources and marine products are employed in effective management of wounds and related ailments.

The wound caused due to mechanical, physical, chemical and biological factors are viewed in both traditional and modern medicinal approaches, for their effectual management. The different responses in wound healing start from humors to the appearance of clinical features in traditional way of treatment whereas, in case of modern way of medicine, the response starts from obliteration in the blood vessel and its actual flow to the stage of tissue damage due to inflammation. Hence, the efficacious factors of herbal drug treatment relating to etiopathology of wound have been put in the leading edge of the existing medicinal system.
1.7. Ethno-pharmacological approaches/leads to wound healing

The natural way of treatment with herbal medicines are well described in the classical manuscripts emphasizing on Devonian period where hanuman (a follower of Sree Rama in Ramayana epic) went to Himalaya region in search of life saving herbal drug as per the instructions of a great saint. Then, he lift up the huge mountain called ‘Sanjeevini parvatha’ due to unavoidable circumstances and carried the same to southern county (SriLanka) along with life saving plant for treating Sree Lakshmana.
to reinstate his potency when he mortally wounded by enemies in the Lanka battlefield. Since then, the ethno-medicine has its own stand with respect to its efficacy in treating the life saving wounds as compared to other way of medicinal systems. In addition, Alexander the king who was famous for that period as battle winner, during his war era, he accomplished a drug with Aloe vera as a post battle care to the wounded soldiers. Hence, the information’s with extensive data base are gradually transformed into folkloric medicinal system with fractional knowledge. Later, the wounds are classified into different categories like, skin cuts, skin infection, tissue damage, gangrene due to microbial infection, wound due to burns and accidents etc. in order to manage these wounds through appropriate herbal treatment procedures.

Fig.1.7. Inflammatory phases in the Wound

The plants oriented therapies are considerably safe, cheaper and target specific which facilitates remodeling of the wounds through multiple mechanisms. Thus, the lead molecules are to be explored from the active fractions of plant drugs with respect to the type of plants, parts used, formulations, mode of treatment, dosage and duration of the treatments towards better management of wounds. Therefore, surplus amount of active constituents are being established for the treatment of wounds in the current medicinal system. The traditional herbs are well employed in healing of wounds
formed due to various reasons, by way of increasing in tensile strength, DNA content which eventually facilitate re-epithelialization\textsuperscript{79,80}. Besides, the inflammation in the wound will be remarkably reduced by owing of wound healing effect by the ethno-medicines (Fig.1.7). Similarly, the isolated lead constituents from the active fractions of plants are known to have effectual wound healing properties which are functionally efficient against sores, crevices in lips and other parts of the body with chapped skin. These active principles with lead molecules have justified in managing wounds through clinical trials using animal models and support the worth of plant based drugs\textsuperscript{81,82}.

Furthermore, the poly herbal fractions are also emphasized on wounds of different categories. The activity of poly herbal extracts particularly combating with microbial infections due to both gram negative and gram positive types. There are some considerable reports stating that, the active fractions of different herbs will facilitate re-epithelialization through developing tensile strength absolutely which promote wound contraction by myo-fibroblasts positively\textsuperscript{83,84}.

In developing countries, the people particularly from rural areas suffers from wound related issues which are caused in the agricultural fields, burns from cooking process and wound due to quarrel followed by any traffic accidents. Consequently, people frequently seeking medical care for their ailments caused due to any reasons. Since the traditional way of treatment has no data base in the WHO, the appropriate method of research is most requisite to accomplish various formulations of plant drugs. The herbal formulations and their uses by traditional healers is gaining much attention because, the efficacy and mode of treatment is very much linked with managing of chronic wounds followed by most advanced stage of wound and infection in the human system\textsuperscript{85-88}. Hence, the plants which have listed for treating various ailments and diseases that have very basis of wound healing properties. Incidentally, the plants available in the research data are providing traditional basis for their therapeutic applications in one or the other way of combating with ailments\textsuperscript{89-95}. In the existing reports, most of the plant drugs are validated with respect to their specified formulations by the traditional healers\textsuperscript{95-106}.

Subsequently, the active constituents especially secondary metabolites explored from various medicinal plants are well established through ethno-pharmacological studies\textsuperscript{107-112}. These secondary metabolites and lead molecules are the key
components in dealing with wounds and associated ailments which have been justified through \textit{in vivo} studies\textsuperscript{113-120}.

\textbf{1.8. Herbal drug becomes the better substitute for Modern drug}

There are several ambiguities with respect to the mechanism of active principle which are responsible for wound healing so, still most of the concepts are unknown to the traditional system of medicinal in the existing scenario. Several formulations are not yet claimed in the traditional medicine system as most of the herbal practitioners are not ready to reveal the respective herbal drug formulas. Therefore, majority of the traditional claims are not subjected for scientific validation to justify the practice of particular herbal drugs. Even though, the plants are being used for wound treatment, but, the procedural approaches are very imperative with respect to type of advocacy and mode of administering the drugs. For instance, the herbal decoction will have direct impact at internal parts of the body whereas; topical application the drug with pastes with hot or cold is most preferable as compared to the drug derived through organic solvents. As a result, the assessment of the new-fangled active principle in these extracts is more multifarious as they are bracket together in a comprehensive manner. The administration of the herbal drug in crude state is correlated with the natural mode of practices being executed by the herbal medicine men. The drug derived from the leaves in paste form has been enforced particularly for wounds and associated ailments which are then followed by the preferential application of root and bark parts, flower and reproductive components of the plant system\textsuperscript{121-126}.

The bioassay guided fractionation has implemented certain course of action for conducting \textit{in vitro} bioassays to improve the existing protocols and also to authenticate some specific experiments by substituting animal models during experimentation\textsuperscript{127, 128}. There are some deficiencies in appraising the lead molecules derived from the manifold herbal active principles. In addition, the status of diseases might be quite complex and the etiology of the some ailments are still unknown, for this the drug with target specific action in their active fractions are of central importance. Therefore, through \textit{in vitro} analysis, the extrapolation of the results has some restrictions to provide substantiation for medical efficiency and in due course the usage of animals in clinical trials are found to indispensable to justify the drugs and their mechanism action against the ailments is concerned\textsuperscript{129}. 
As wound healing has multiplicity in its processes which starts from inflammation caused due to microbial infection to contraction through formation of collagen created with lattice. The herbal fractionated drug can have an effect on wound inflammation and free radicals to carry the wound to normal condition which was already in cutting edge in the traditional medicine system before assessing the drug has technical rationalization\cite{87,126}.

The pharmacological rationale of some herbal drugs in wound healing is not known yet. This is because; most of the researchers are attaining the positive outcomes in the preliminary screening of plant drugs for wound healing in the early phase of infection. Whereas, the severity of wounds with chronic conditions have not been analyzed for its exact mechanism and its lattice of complexity. This is based on the specificity of factors like, defense mechanism by antioxidants followed by biochemical changes that further leads to re-epithelialization\cite{130}. In this line, many pharmacists are still exploring the base of right component of herbal drug for the exact form of wound which is already practiced in the traditional medicine system. The explored herbal constituents through pharmacological approaches have drawn the global attention to manage the wound healing with most desired plant based drugs which are of Indian origin\cite{131}. Now, the synergistic effects of herbal drug formulations in wound healing is in progress which facilitate the development of most efficacious, safer, cheaper and eco-friendly drugs with global acceptance. The progression in the multiple mechanisms of poly herbal fractions along with a notion of synergism can act as a most potent drug which further can be a most appropriate and alternate of modern wound healing drugs. Hence, the drugs derived from herbal fractions are projecting in the international drug market as substitute to the drugs which are available in the present market\cite{132}.

1.9. Ethno-medicinal Plant drugs used for Cancer treatment

The plant drugs and their formulations are well practiced by the herbal practitioners in the traditional medicine system explicitly for cancer and malignant tumor cells and related ailments. On the other side, the research is on to isolate vigorous constituents from the active fractions of the plant drugs identified specifically for the cancerous ailments. In the preliminary stage, it was confirmed that, the energetic complex extracted from the botanicals are able to exterminate the carcinogenic cells in the human system. The management of cancerous tumor cells with chemotherapy has
serious side effects on the non target organs in the human system. Therefore, finding alternative therapies for chemotherapy is a right choice with plant based drugs as a substitute to the allopathic medicines. The findings of some research studies also indicating that, the specific fractions of the herbal drugs acquired anticancer properties which prevents the human system from the risk of varied forms of cancer ailments. The lead constituents of herbal fractions are explored to treat cancer tumor with a specific protocol at particular stage of disease symptoms and the crumbling of tumor or apses are made possible by the vigorous active chief component. In addition, the active fractions of individual plant drugs and synergistic action of poly herbal drug formulations also confirm that, the potentiality of inhibiting the cancerous cells. Hence, the accomplishments of these anticancer herbal drugs have gained importance with global acceptance.

The mammarian cancer or breast cancer is one of the leading ailments among women compared to other cancer types. There are no efficacious drugs are available to combat this particular cancer ailment and the existing medicines are recommended only at the metastatic development of primary stage of cell tumors. In the traditional medicine system, some most effective plant drugs are accomplished by the traditional healers especially for breast cancer treatment. In order to develop new drugs, different plants are being selected randomly or based on ethno-botanic and ethno-pharmacologic knowledge. The extracts obtained from these plants are then evaluated using different in vitro assays as well as their effects on normal or tumor cells. Then, the potential extracts are purified in order to obtain their potential fractions or molecules to be tested by in vitro and in vivo assays again, followed by analysis of their potential for new drugs.

The competent herbal drug with greater idea is ought to be developed by emphasizing on bio-chemical nature in the active fractions of plant drugs. By taking into consideration of plant drugs with a superior notion, tribal medicine formulation with a wide range of active chemicals has been subjected for its anti-tumor and anti-proliferative properties and tested on mammarian cancer cells along the lines of antioxidant activities. Thus, it is very important to establish newfangled bioactive lead molecule which can be recommended to treat cancer cells and associated ailments. Consequently, the same fraction of drug can be employed to confiscate free radicals in the tissue system apart from its anti-cancer efficiency.
1.10. Anti-proliferative properties in Herbal Medicines

The accretion of different genetic and epigenetic actions at cellular level leads to development of cancer in the human system\textsuperscript{138,139}. Further, anomalous net accumulation distinctive cells arise from excess proliferation, insufficient apoptosis or amalgamation of both in the system\textsuperscript{140,141}. Since ancient times, the herbal drugs with a broader perspective are used for treating cancerous and associated ailments in the traditional medicine system which also brings the considerable changes in the newfangled synthetic drugs. The development of natural drugs with prospective actions for confronting the ailments relating to cancer and associated problems in a rational approach to accomplish the derivative of secondary metabolites for clinical relevance\textsuperscript{143}.

Globally, the application of traditional medicine with broad range of actions for cancer is still in front line as compared to other forms of medicines. Moreover, the very basis of several modern drugs is plants only and basically are originated from the nature. In spite of diversified chemical drugs, the synthesis and quantification of all these chemical drugs with molecular modeling are sourced naturally specifically from medicinal plants\textsuperscript{144}.

1.11. Mammarian Cancer (MCF-7 Human Breast Cancer)

There are two major evil diseases distressing human population at present namely Prostate and Mammarian or Breast cancer types are the dreadful and frequent malignancies affecting fatally both male and female communities respectively. The mortality of these two cancerous types is mainly due to the surplus metastatic growth of cell tumors at primary level\textsuperscript{136}. These cancerous ailments are unable to cure competently with allopathic drugs. Nevertheless, many instances with cancerous ailments particularly at last stages are exceptionally challenged by the herbal practitioners and also treated positively by plant based drug formulations as a source of newfangled drugs in their traditional systems\textsuperscript{145-148}. In some recent studies, plant based traditional herbal formula which has been used for lung and liver cancer treatments. In addition, some specific herbal formulas from oriental medicines in India, China and Korea were found to show anti-cancer activities such as anti-angiogenesis and apoptosis. In India, many herbal formulas have been used as complementary medicine without any proven evidence of their effectiveness.
The mechanism of mamary cancer affecting the biological system is of very intricate a process which is because of inconsistency in line with the production of reactive oxygen species and incidence of pro-oxidants that leads to oxidative stress which in turn causes patho-physiological manifestations. The free radicals produced during oxidative stress which is not stable in nature and these reactive oxygen species will search for electron pairing through stability with macromolecules such as proteins, lipids and DNA in the healthy human system. As a consequence, these macromolecules will be damaged under oxidative stress conditions which lead to lipid peroxidation, ageing, inflammation followed by cancerous indications\textsuperscript{149, 150}. Hence, it may be worthwhile to investigate further on anti-metastasis and other anticancer activities together with studying novel plant based chemical compounds responsible for the activities against breast cancer. The fractions of any plant based drug will be administered to model cell lines called HeLa cells which they have ability to grow in controlled conditions at laboratory. Therefore, the proliferation in the cells is possible as these cells are remarkably forceful and prolific in nature\textsuperscript{151, 152}.

1.12. Anti-snake venom effects by herbal medicines

The World Health Organization ascribes that, the snake bite has been avowed as one of the derelicted topical diseases. Consequently, this has been measured as universal health concern by emphasizing on both urban and rural population. The frequent envenomation occurs due to most common snake species are \textit{Naja naja} and \textit{Naja nigricolis} which belongs to class Elapidae. In India, there are three common snake types namely, cobra, viper and krait which are affecting the population with high mortality particularly at rural areas. The biting of these snakes will leads to hypersensitive reactions in the human system which include, hemorrhage induced by venom, necrosis followed by neurotoxicity and nephrotoxicity. Generally, antiserum will give utmost protection to these hypersensitive reactions as vigorous therapeutic agents but, the venom induced disorders will not be under the control of hypersensitive reactions\textsuperscript{153-156}.

Tribes of southern India have several claims of effective use of ethno-medicinal plant drugs in treatment of poisonous snake bites including bites due to \textit{Naja naja} and \textit{nigricolis} sp., respectively. The plant based treatments are very popular especially for prophylaxis of snake bites during winter and rainy seasons when the incidence of snake bites are usually more. The practice of ethno-medicinal plants for snake bites is
not only important in remote areas but, it is also very important in both rural and urban areas where the accessibility to hospitals and availability of anti-venom drugs are not established properly which is still common especially in developing countries like, India. Since many years, a lot of attempts on plant drugs and their active formulations have been made for the progress of venom antagonists predominantly by the researchers based on the notion of traditional medicine system. The use of ethno-medicines against snakes bite and their post bite effects of have been extensively documented and more scientific attention has also been given to develop most effectual anti-snake drug\textsuperscript{157}.

1.13. Snake venom and its chemical composition

Snake venom, which is formed in a salivary gland of the venomous snakes known as venom gland, which contains diversified proteins of both enzymatic and non-enzymatic components and toxins responsible for imparting toxicity in victim’s post-envenomation. The activity and number of enzymes present in snake venom vary from venom to venom. The venoms of elapidae group are rich in phospholipases, phospho-diesterase, nucleotidase, ATPase and cholinesterase 2,4 whereas, Russell’s viper and pit viper venoms contain proteases, coagulant, kinin-releasing and argininester hydrolyzing enzymes. The several non-enzymatic toxins such as neurotoxin, cardiotoxin, myotoxin and three-finger family of proteins present in snake venom are playing crucial role in induction of venom toxicity\textsuperscript{158}.

The chemical constituents of snake venoms are extremely complicated and the highest percentage of proteins is present in the venoms and in turn most of the proteins in venoms are enzymes. The enzymes in the venom are digestive hydrolases which include proteolytic enzymes and phospholipases A\textsubscript{2} followed by polypeptide toxins and other factors respectively. These in turn increase permeability resulting in local inflammation which can also destroy cell membranes and tissues. In addition, damage in nerve endings, initially releasing acetylcholine transmitter, by the pre-synaptic neurotoxins of Elapidae are of Phospholipases A\textsubscript{2}s that subsequently intrusive with the release of acetylcholine. Further, post-synaptic neurotoxins are polypeptides that contended with acetylcholine for receptors in the neuromuscular intersection and lead to curare-like paralysis. Additionally, the other type of components such as carbohydrates, lipids, nucleoside followed by metal groups like magnesium, calcium and zinc respectively are the prevalent metal assemblage are also part of venom
composition. Besides, copper metal has also been noticed in some specific venom types which are playing critical role in inducing the lethal factors in the venom.\textsuperscript{159, 160}

The comprehensive symptoms are nausea, vomiting, malaise, abdominal pain, chest pain, weakness, drowsiness, paraesthesiae, haemoglobinuria, abnormalities of taste and smell, “heavy” eyelids, external ophthalmoplegia, paralysis of facial muscles and other muscles of the human system. Apart from these, snake venoms are known to contain a number of enzymes and the complex series of pathological alterations are attributed to both enzymatic and non-enzymatic factors present in the venoms. Among the enzymatic factors, Phospholipase A\textsubscript{2} has been identified as an important group of enzymes with multitude pharmacological effects.\textsuperscript{161, 162}

1.1.4. Phospholipase A\textsubscript{2} (PLA\textsubscript{2})

The chief sources of snake venom comprise inflammatory enzymes endowed with lethal or venomous functions are perhaps phospholipases A\textsubscript{2}. They exhibit lipolytic actions apart from secreting the diversified toxicities.\textsuperscript{163, 164} The majority of the noxious effects of snake venom PLA\textsubscript{2} appear to result from their promotion of membrane dysfunction by hydrolyzing phospholipids of cellular membranes and leads to generation of phospholipid hydrolysis breakdown products, namely lysophospholipids and free fatty acids, which are themselves becomes lytic and cause substantial injure to the membrane.\textsuperscript{165, 166}

1.1.5. Pharmacological effects of snake venom PLA\textsubscript{2}

The PLA\textsubscript{2} can have pharmacological properties in most of the instances without having any association of other components. Whereas in exceptional cases, the PLA\textsubscript{2} can have complete pharmacological efficiency as they involved in formation complex with other protein factors. For instance, the interaction between two proteins derived from two different biological sources \textit{i.e.}, snake venom and plant drug which can be assessed during mechanism of action of drug over venom during neutralization effect.

The formation of complex with other factors like will be protein detained through covalent bond while, non-covalent bondage will also be possible for other type of interactions.\textsuperscript{167, 168} The synergistic effects protein complexes of the venom will have considerable early symptoms and in later stages, the symptoms are different such as damage of tissues will leads to dysfunction of brain, lungs, kidney, heart, liver etc respectively. The plant based drugs are being practiced since several years by the
herbal healers for snake envenomations of different types in the traditional medicine system. The preparation of herbal drugs for snake envenomations is very complex with respect to their active formulations, dosage and duration of the treatments. Interestingly, the out-come of some studies proposed a hypothesis relating to therapeutic applications of some specific components snake venom against cancerous ailments followed by production of recombinant neurotoxins\textsuperscript{169, 170}.

1.16. Poly herbal remedies for Snake bite

Many Indian medicinal plants are recommended for the treatment of snakebite through their indigenous practices. Some of the active fractions plant drugs have revealed antivenom properties against various snakes and their effectual concentrations have been assessed along with mechanism of action of drug\textsuperscript{171}. Hence, venom snake bite is a medicinal emergency needs immediate attention. Most bites of the venomous snakes occur in the fields most of the agricultural labors. Therefore the agriculture workers immediately look for antidote in the surrounding environment. Most often available depends on the effect of known plants (roots, leaves and seeds) as antidote. In surroundings several plants are using as a source medicine for venomous snake bite. They are \textit{Datura metel}, \textit{Rubia chordifolia}, \textit{Emblia rabes}, \textit{Glyceria glabra}, \textit{Albizia lebbeck}, \textit{Aristolochia} species, \textit{Andrographis paniculata} etc. ‘\textit{Nothapodytes nimmoniana}’ is one among these medicinal plants\textsuperscript{172}.

Some investigations have explored the possibility of neutralizing effect on snake venom by assessing interaction of proteins between plant drug and venom. The studies relating to active fractions of herbal drugs which are tested with folk medicines, and neutralization of venom with herbal protein have been experimented with mice. On the contrary, the mixtures of crude extracts were not significant with respect to possible envenomation effect. This necessitates the search for potential and active constituents of the plant drugs which can have supportive effect in antivenom and most rational approach would be proposed to treat some of the symptoms or responses\textsuperscript{173}.

In recent years, the ethnomedicinal plants used to treat snakebite has attracted the attention of several researchers and reviewers. This attention has served to highlight the need of scientific information relating to chemistry, lead molecules, action specificity and efficacy of the plant drugs\textsuperscript{174}. Similar kind of practices in treating of
many serious ailments has been noticed which are being performed by traditional or tribal medicine men which stays at Biligirirangana Hills of Chamarajanagara district, Karnataka. Hence, the proposed study has been undertaken to achieve the proposed objectives at the aforesaid area where, the traditional medicinal practices are undergoing. The descriptions about the study area are as follows.

1.17. STUDY AREA

1.17A. Biligirirangana Hills: A Religious Hillock

The Biligirirangana Hills in general ‘B R Hills’ which is a mountain formed due to vast range of numerous hills located at south-eastern parts of (Chamarajanagar district) Karnataka state. The areas of manifold hillocks are in close vicinity and edging with Tamil Nadu state of Southern India. The locale is also entitled as Biligiriranga swamy Temple Wildlife Sanctuary or in short, BRT Wildlife Sanctuary. The sanctuary is meant for exclusive eco-systems in which the habitats are unique to both the mountain ranges. This is because of convergence between Western Ghats and the Eastern Ghats (Fig.1.8).

Fig.1.8. A view of Biligirirangana Hills (Study area)

The B.R. hills are adjoining with the forest range of Satyamangalam of Erode district of Tamil Nadu, India. The hills area is present in the range of 90 km away from Mysuru and 220 km away from Bangalore. The B.R.Hills gain its name as Biligiri which is drawn from the pasty white rock face that composes the main hill headdress with the holy place, temple of Lord ‘Biligiri-Rangaswamy’ or from the fairy white
mist and the silvery clouds that cover up these supercilious hills for a larger part of the year (Fig.1.8).

1.17B. Tribals and their Practices

In India, the entire population of tribes comprises more than seven percent and the tribes are exists in diversified categories. This distribution of various tribes at different geographical locations is based on their habitat, variety, complexity of their traditional beliefs and their religious practices, respectively.

The north-east part of Karnataka comprises more than 30% of tribal communities such as Toda, Beda, Soliga, Hakki-Pikki, Konda Kapu, Koraga, Bhils, Chenchu, Gonds, Maleru, Badaga, hasala, Meda, Iruliga, Jenu kuruba, Erava and Siddis are distributed in diversified manner with respect to varied religious beliefs and practice of many rituals. Additionally, the past histories of tribes along with beliefs and myths are frequently being represented orally through their traditional epics and folk like songs175,176. Correspondingly, traditional knowledge on plants and their practices against different ailments and diseases is a celestial gift to the tribal community. Since several years, the practice of ethno-medicinal plants by the tribal healers has been transmitted generation to generation through their own community members177-180. Today, tribals are also depending on ethno-medicinal plants and their traditional practices for their livelihood (Fig.1.9 and Fig. 5.3A, B, C, D).

1.17C. Soliga tribals and their traditional medicine Knowledge

The tribal, ‘Soligas’ are the major indigenous tribes of BR Hills and they have a rich and deep traditional indigenous information’s or data base on ethno-medicinal plants which gets transformed from one generation to the next generation of their community members (Fig.5.3A, B, C, D). The Soliga’s share their knowledge about different aspects of practicing of tribal medicines amongst their own group of people relating to drug formulation, mode and duration of treatment against different ailments/diseases starting form cold, cough, fever and to serious diseases like, cancer, wound healing, snake bite and respiratory disorders181.
The Soliga tribes dwelling in this range are regularly worshipping of the nature by chanting (mantra) in their local language before starting their daily works (Fig. 1.9). The Soligas have affluent and profound traditional medicine knowledge on practice of ethno-medicinal plants for different ailments which is being transformed from the elders of tribal healers to their own subsequent generation. The tribals share their knowledge about different aspects of practicing of tribal medicines, drug formulation, mode and duration of treatment against different ailments/diseases starting form cold, cough, fever etc. and to serious diseases like, cancer, wound healing, snake bite and respiratory disorders respectively 182.

‘Tribal Formulation’ is a mixture of different parts of plant/herbal components that are used to treat various abnormalities. The biochemical activity of formulation will not be known to the tribals but their action will be known because of the practice since many years 182.

By taking into consideration of above base line informations on ethno-medicinal practices, the present study has been proposed explicitly on one of the tribal medicine formulations which are being practiced for wound healing and related ailments. In this association, the obtained herbal formula was aimed to evaluate the bioactivity against wound healing, antioxidants, antimicrobials, anti-proliferative \textit{i.e}, breast cancer
followed by anti-snake venoms and neutralization aspects of snake venom using tribal medicine formula (Fig. 5.3E, F).

1.17D. Medicine Formulations and ailments

Formulation is a mixture of the tribal medicinal components of various parts of plants that are used to treat various abnormalities. The parts used for the mixture can be leaves, roots, stem, twigs, fruits, seeds and flowers. The formulation is usually prepared by mixing the components in various amounts and pasting it using cold or warm water. They are rarely prepared in any other solvents. It can be directly applied on to the exterior parts of the body or given for the intake depending on the abnormality being treated. These formulations are the indigenous knowledge of Tribal people in India. Based on the practices of traditional medicine systems, the natural ingredients used in their formulations have to be validated scientifically. Then, the validated formula of herbal drug should be subjected for analysis both in phyto-chemically and pharmacologically.

The pharmacological screening of ethno-medicinal plants and their formulations are aimed explicitly to accomplish the most efficacious and desired herbal drug with active and target specific drug against the ailment is concerned. Apart from these, the drug derived from herbal fractions and developed with exact chemical classification can be synthesized further and the combination of lead molecules will facilitate new fangled drug with respect to the type of ailment in the pharmaceutical industry. Therefore, the preliminary screening of herbal drugs and their active formulations will give gross picture about pharmacognistic status of the drug which is based on the active constituents like secondary metabolites. Besides, biochemical activity of formulation will not be known to the tribals but their action will be known because of the practice since many years. The components react with each other and show the suitable activity on the patient. Hence, in order to characterize the formulation, the other ingredients of the tribal formulation are enunciated here under.

The traditional practice of the ploy herbal extracts will give exact path to carry the herbal decoction or active fractions for phyto-chemical screening processes. The progress on accomplishment of phyto-chemicals in the active principle of herbal extracts will make possible of achieving a new chemical constituent with considerable biological activities. India holds a goldmine of great deal of well known
medicinal plants practiced traditionally for use of herbal medicine. It is generally estimated that over 6000 plants in India are in use in traditional, folk and herbal, medicine representing about 75% of the medicinal needs of the third world countries. The similar attempt has been made with less known ethno-medicinal plant drugs along with herbal formulations being used in tribal/traditional medicine system for the ailments like, antimicrobial, anti-inflammatory and wound healing ailments respectively.  

Hence, in view of the above scenario, a search is on for looking for most potential and efficacious drug i.e., traditional medicine against the ailments relating to wound and associated problems followed by cancerous and snake bite complaints/diseases. Therefore, the present study was undertaken to evaluate the selected ethno-medicinal plants drugs and formulations explicitly for wound related problems which are being practiced by tribal healers at ‘Biligirirangana Hills’ followed by the herbal healers of surrounding area. The background details comprising classification, ethno-medical uses against various ailments of the selected ethno-medicinal drugs are as follows.

1.18. Ethno-medicinal Plant drugs and formulations preferred for the study

1.18A. *Andrographis serphyllifolia* (Vahl.) Wight

*Andrographis serphyllifolia* is a common small shrub belongs to Family: Acanthaceae. In the indigenous practices, the extract leaves, shoot and root parts of the plant is used to cure infection, fever, Jaundice, wounds and associated ailments including gangrene. This plant was reported to possess Serphyllin, apiginin7, 4-dimethyl ether and tectochrysin and acylated flavone glycosides and andrographidine (Fig.5.2A).

**Taxonomical information:**

- **Common name** - Gayada soppu
- **Vernacular Name** - Kasina sara.
- **Botanical name** - *Andrographis serphyllifolia* Vahl.
- **Family** - *Acanthaceae*

*Andrographis serphyllifolia*, a folk, traditional and ethno-medicinal plant is being used in the traditional medicine system by the herbal healers at the study area. The plant is mainly used to treat wound infection caused due to cancerous ailment.
followed by gangrene which was due to snake envenomation. The leaves of *A. serphyllifolia* were chiefly used to prepare crude decoction as well as pastes in order to treat the patients suffering from wound and related problems followed by the tumor with cancerous growth. The plant contains a wide range of phenolic composites that can demonstrate an outstanding antioxidant and antimicrobial activities. Consequently, this ethno-medicinal plant and its efficacy can be proposed as a superior herbal drug for further development for its exact pathways of antioxidant remedies which in turn connected to other serious ailments.

**1.18B. Dioscorea hispida Dennst.**

*Dioscorea hispida* Dennst an ethno-medicinal plant commonly called Yams which is grown mainly for its tuber importance as well as a valid source of carbohydrates. In India so far twenty-six species of *Dioscorea* have been reported. At present thirteen *Dioscorea* species are available in Orissa (**Fig.5.2B**). The stem of yam is rope like structure and of different shapes depending upon the species specificity. The stems grow several meters before any branching occurs and appendages on the stem, like wing, spine, hairs etc., apparently prevent the stem from slipping from its support (**Fig.5.2CD**).

**Taxonomical information:**

- **Common name** - Intoxicating yam.
- **Vernacular Name** - Karukandu, Noolana humbug.
- **Synonym** - Palidumpa, Pashpoli (Ind.); Gado(e) ng; Maranpash(Ind.).
- **Botanical name** - *Dioscorea hispida* Dennst.
- **Family** - *Dioscoreaceae*

The tubers of *Dioscorea hispida* are practiced by the local herbal healers in connection with various serious ailments as chief component of the herbal formulations. Besides, the tubers are also used to prepare poisons on certain occasions. The major use of the plant is tubers which is subjected for pounding and are used in confined medicine for the treatment of open wounds. It has been suggested that the residue left after starch extraction could be used as an insecticide.
1.18C. *Glycosmis mauritiana* (LAM.) Tanaka

*Glycosmis mauritiana* Tanaka, is an ethno-medicinal plant commonly known as Orange berry, which is found all through the Western Ghats followed by South East Asia and South China. The plant, *Glycosmis* is a genus of small trees of forty species belongs to the family, Rutaceae. The species were used in preparations of some important traditional medicines for the treatment of various diseases such as infection, wound due to cancerous growth on any part of the human system. Besides, the crude decoction will be used for the other ailments namely, allergy, cold, indigestion, chest pain diarrhea and hernia pain etc. (Fig.5.2E).

**Taxonomical information:**

- **Common name** - Orangeberry, Ash sheora, Rum Berry, Gin Berry.
- **Vernacular Name** - Guroda gida, Guruvaade, Jangama, Kumana paanu, Maanikya beeja, Synonym - Limonia mauritiana, Glycosmis pentaphylla, Limonia pentaphylla.
- **Botanical name** - *Glycosmis mauritiana* Tanaka.
- **Family** - Rutaceae

The literature describes, about chemistry, synthesis, applications and various pharmacological actions of acridone- an alkaloid used as one of the main components for Anticancer, Anti-herpes, Anti-malarial, Anti-leishmanial, Nuclease activity etc. It has also antibacterial and anti-psoriatic activity. Besides, acridone derivatives are also found in natural plant sources, which are proving worthwhile in various disorders.

1.18D. *Nothapodytes nimmoniana*, Graham

*Nothapodytes nimmoniana* is less known ethno-medicinal plant belongs to the family, Icacinaceae and the plant is already at the verge of extinction. The plant is commonly known as Amruta is found in India particularly at the biodiversity areas namely, Maharashtra, Goa, Kerala, Assam, Jammu and Kashmir as well as Tamilnadu apart from the biodiversity of Karnataka.
Taxonomical information:

- Common name: Orangeberry, Ash sheora, Rum Berry, Gin Berry.
- Vernacular Name: Ghanera, Durvasane mara, Kal kurinji.
- Synonym: Premna nimmoniana J. Graham; Mappia foetida (Wt.) Miers
- Botanical name: Nothapodytes nimmoniana (Graham) Mabberley
- Family: Icacinaceae

It is an important medicinal plant, the major source of a potent alkaloid, namely camptothecin, of a wide spectrum of pharmacological activities like anti-cancer, anti-HIV, anti-malarial, antibacterial, wound infection, antioxidant, anti-inflammatory, anti-fungal and also applied in the treatment of anemia and associated ailments (Fig.5.2F).

1.18E. Rauwolfia densiflora Benth & Hook

(Wall) Benth & Hook is a less known ethno-medicinal plant which has an erect herb with a smooth stem. The plant is an imperative therapeutic plant used to prepare decoction from the fresh leaves and flowers to treat rheumatic complaints and the paste will be used for wound healing and other related infectious problems. (Fig.5.2G, H).

Taxonomical information:

- Common name: Sarpa gandha
- Vernacular Name: Paarisirunila
- Synonym: Sarpa gandha
- Botanical name: Rauwolfia densiflora
- Family: Apocynaceae

Since, there were no reports available on therapeutic applications of the plant, R. densiflora, the traditional practice of the herbal fractions against the ailments of snake bite and wound caused by the infection followed by the effect of post snake envenomation will be the basis for the detailed studies with respect to pharmacological parameters.

1.19. Current scenario on ethno-medicinal plant drugs and need for the research

The ethno-medicinal plants have infinite and unexploited prosperity of chemical compounds with far above the ground potentials of the drug which are used as
nutraceuticals, food supplements, folk medicines, pharmaceuticals, agrochemicals, flavors, fragrances, colours, bio-pesticides, food additives, and chemical entities for synthetic drugs. In India, herbal drugs are of great importance and used extensively for various ailments particularly concentrating of rural areas\textsuperscript{191}. Now, the traditional medicines are also transformed to the urban area since they have considerable effects on some specific ailments which are connected to regular health management. Therefore, the herbal medicines are being prepared in large quantities in order to bridge the gap between human health and existing medicinal system. Correspondingly, the global market for medicinal plant materials and herbal medicines is estimated to be worth several billion dollars a year. India exports 32,600 tonnes annually\textsuperscript{192}.

The rich sources of both medicinal and aromatic plants are concentrated in India compared to the other parts of the globe. The efficacious drug can be developed on the rich chemical diversities which were derived from multi-herbal formulations. Hence, the active principles prepared based on the poly-herbal formulations will have multi-facet remedies against multiple ailments\textsuperscript{193, 194}.

Although in traditional/tribal medicine system, the practice of ethno-medicinal plant drugs and their formulations against serious ailments apart from inflammatory issues is well known. However, after justifying the practices of traditional medicine system, scientific validation of tribal/traditional drugs and their biological evaluation still encourage the interest of investigators for development of new fangled drug by taking into consideration of some serious ailments such as, anti-microbial, anti-inflammatory, wound and associated problems, cancerous tumor problems followed by snake bite and venom neutralization aspects. On account of literature survey, comparatively there was no much information relating to detailed analytical studies (phyto-chemical and pharmacological profile) on wide-ranging herbal formulations for the particular ailments are concerned. Hence, the present investigation was overviewed to explore the possible outcome on phyto-chemical and pharmacological profile of traditional medicine formulation in order to justify the practice of valued ethno-medicinal plant drugs by the traditional/tribal healers. The main aims and objectives of study have been discussed thoroughly in the next chapter.