# CHAPTER 1

INTRODUCTION

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MEDICINAL PLANTS CONTINUE TO PROVIDE HEALTH SECURITY TO MILLIONS OF RURAL PEOPLE ALL OVER THE WORLD. ACCORDING TO WHO’S ESTIMATES [1], OVER 80% OF PEOPLE IN DEVELOPING COUNTRIES DEPEND ON TRADITIONAL MEDICINES FOR THEIR PRIMARY HEALTH NEEDS. IN INDIA, MILLIONS OF RURAL HOUSEHOLDS USE MEDICINAL PLANTS IN A SELF-HELP MODE. Thus, traditional medicine is the main source of healthcare systems for more than 4-5 million people. They are supported by over one million traditional village based carriers of the herbal medicinal traditions through 8000 manufacturing units of traditional systems in India. The medicinal and aromatic plants have become critically important in supporting livelihood of millions of rural people who are fully or partially dependent on these plants.

The environment associated with human life having great influence on human evolution, culture and life style. The people are mainly dependant on the forest and forest resources for their survival. The primitive man gets much enthusiasm towards green plants and started to examine the properties using trial and error and obtained different beneficial properties. This valuable information has been preserved in tribal pockets as guarded secret without script. This vocal information has immense importance, which has been preserved gradually as family secrets. This undocumented folklore information is gradually depleting due to disintegration of their habitats, culture and traditions of adivasi tribes. This has been accelerated by severe biotic interference, deforestation, implementation of government policies to uplift the downtrodden people, etc. There is every need to document such valuable folklore information before depletion of tribal traditions due to modern civilization and culture.
Ethnobotany is the study of adivasi tribes and their dependence / interaction with their surrounding natural resources for food, shelter, medicine, etc. It is also to be referred as anthropogenic approach to botany and is essentially concerned with gathering information on plants and their local uses. Powers (1873-1874) [2] used the term Aboriginal botany - refers to a study of all forms of vegetable world, which the aborigines used for medicine, textile, fabrics, ornaments, etc. One of the most prominent contributions of Medicobotany to the society is natural medicine. In addition, Ethnomedicobotany is used for many beneficial things viz., food, shelter, fiber, dyes and non-wood forest etc.

Earlier people used plants as medicine, perhaps as early as Neanderthal man. Plants were believed to have healing properties and powers. In India knowledge pertaining to medicinal plants was well documented in Vedas viz., the healing properties of herbs were found in Rig-Veda, seems to be the earliest record of plants in medicine or surgery. Detailed account on medicinal properties with description was found in Chikista – Sthanam of Sushruta Samhita. There are several factors for the continued popularity of traditional drugs, and one is their ready availability and economic feasibility as modern medicine, besides adverse effects of synthetic drugs and the modern medicine. Allopathy which wanting rational origin in heritage is questioned and opposed by traditional medicine and Homeopathy [3]. World Health Organization estimated that about 80% of people still depend on traditional medicines of primary health care [4, 5]; while in developed countries the trend on the use of medicinal plants over the last century has not been significant [6]. Today 70% of the population has no access to manage their healthcare or medicines. So it is not about the prices only but access and availability. Pharmaceuticals form only 12-15% of the
cost of health care, the rest being prescription fee, hospitalization, etc, but yet the focus is only on western medicine and drug prices.

As evident from the present scenario the herbal care getting worldwide acceptance, thus emphasizing modern scientific evaluation of wild drug yielding plants, created new vistas in searching of new sources of alternative medicine. In this context many of new frontiers in the development of medicinal plants in search of new remedies, tested for pharmacologically active principles. Because of ill effects and costly affair of allopathic drugs, in recent past specialists shifted their interest towards plants and their derivatives emerged as Phytopharmaceuticals. There is a considerable observation among growing interest in the western world in medicinal plants and herbal drugs, infact increasing debate to bring the plant products under legislative control in line with synthetic drugs.

During last few decades’ medicinal plants have gained tremendous global importance, especially traditional herbal drugs, which are used in indigenous system of medicine. Everyday inspiring information is being added to enrich the folk information and development of drugs [7, 8].

The conservation of medicinal plants has key role on biodiversity components and ethnobotanical studies also resolving conservation and developmental issues. These studies even provide a significant framework for utilization of such traditional knowledge in deriving conservation strategies. During the past decade, a dramatic increase in export of medicinal plants attested worldwide interests as well as in traditional health systems. Most of the raw drugs being taken from the wild, hundreds of species are threatened with extinction because of over harvesting, destructive collection techniques, conversion of habitats into crop based agriculture and lack of data on availability of medicinal plants in abundance.
The report, Global Environment Outlook-3 (UNEP report on the degradation of global environment), predicts that by year 2032, more than 70% of the earth’s land surface is likely to be destroyed, fragmented or disturbed by cities and infrastructure like roads and mines. Large quantities of plants are collected and exported annually, although it’s harvesting is illegal in most of south Asian countries. Poor marketing techniques, indiscriminate collection and over exploitation are taken into urgent need of clarification and government should take out in marketing processes to protect from bio-piracy from developed countries. Introduction of certain drugs for cultivation offers best hope for conservation and reduction of pressure on forest resources, which also fulfill the present demand on the bench of international markets. The Ayurvedic medicine, an ancient Indian system of medicine, has always been aware of valuable plants for at least 2,500 years before west as awakened in respect of natural medicine. The demand for Ayurvedic or indigenous medicine has been recognised especially for ailments for which allopathy is not been very effective. The successful introduction of various drugs of plant origin by pharmaceutical industry gained maximum appreciation, which leads to the establishment of complementary and alternative medicine (CAM). The alternative approaches can be divided into five categories.

1. Acupuncture and oriental medicine.
2. Traditional indigenous systems (Ayurveda, Unani, Siddha, Kampo, Tibbi and Traditional medicine, etc.)
3. Unconventional western systems (Homeopathy, environmental medicine).
4. Orthomolecular and Prionic medicine.
5. Naturopathy.
In addition, biologically based therapies, manipulative and body based systems; bio-electromagnetic systems are used in complementary alternative system. Among them the biologically based therapy is most effective since this includes

a) Phytotherapy or herbalism (e.g. *Gingko biloba*, garlic, ginseng, turmeric, bee-pollen, mistle-toe, etc).

b) Diet therapy (e.g. vegetarian, natural hygiene, etc).

c) Pharmacological, biological and instrumental interventions (e.g. Coleys toxin, enzyme therapy, EDTA, Bio-resonance, apitherapy, etc.).

The integrated complementary alternative medicine may be considered as only system, in future, to satisfy the modern society.

Medicinal plants are being used in India either directly as folk remedies or medicaments of different ancient system of medicine like Ayurveda, Siddha and Unani. Out of about 40,000 plant species described in India, different medicinal uses have been attributed for about 7,500 species [9]. India hosting about 4,00,000 practitioners of herbal medicine, whose services could not be adequately utilized in the health care delivery systems. About 80% of raw materials for drugs used in the Indian systems of medicine and Homeopathy are based on plant products.

Nearly 80% of world’s population does not have access to modern medicine. Most of the money for healthcare in the developing world goes to the remaining 20% of the population. The health care expenses predicted to double in next 10 years. The complementary and alternative medicine with low-cost intervention such as life style changes, diet, nature therapy, etc., can be delivered as substitute for high cost drugs and technological intervention. The credibility of these systems of medicine, therefore, depends on the availability of authentic raw material in sufficient quantities.

Drugs derived from different sources in different ways. The earliest drugs were plant
extracts followed by pure natural compounds of known structures. The detection of biological active compound in extracts through bioassay directed fractionation. In addition, after identifying lead compound also attempted to study mechanism of action of biosynthetic pathway lead to drug discovery.

During the mid century, came the synthetic drugs, which are based on natural products and introduction of sulfa drugs in new era. Synthetic modification of already existing drug entities for the purpose of enhancing activity or reducing toxicity is also attracted modern phyto-pharmacologists. The semi synthetic drugs which have modified or intensified activity is encouraged because it has rational base as pure synthetic drugs wanting / lacking. The idea leads to new phase in pharmacology as pharmacological activity-drug design.

People becoming wise enough to understand the harmful effects of synthetic drugs, which lack rational background and also more cost effective. Disillusioned with the synthetic western medicine more people are now realizing that natural medicine is better and effective without side effects. The World Health Organization also stated that herbal medicine is non-replaceable with western techniques lead revival in interest in wild medicinal plants. Many higher plants produce economically important secondary metabolites that are commercially used as biologically active compounds viz., flavour, fragrances, bio-pesticides, pharmaceuticals, etc. However, only a few number of plant species were surveyed for extraction and characterization of biologically active compounds so far.

The deforestation at alarming rate and wanton destruction has brought 3-4 thousand species of Indian plants on the verge of extinction. If this current trend of destruction continues at its present rate phytochemists may have only few decades remaining to survey the chemical constituents of large part of plant kingdom for
potentially useful compounds. As the natural habitat for wild plants disappear due to environment and geographical instabilities make it difficult to acquire plant-derived chemicals. The disturbance also leads to loss of land races used in crop improvement programs through biotechnology and genetic engineering. Due to fast civilization and accelerated implementation of state and central government policies of tribal welfare, missionary activities, commercial interests, tourism activities of devoted individuals, etc., results in the rapid dissolution of relationship and dependence on forest. Further the tribal himself is being involved in local extinction of commercially important plants due to unscientific collection of required part of plant. These activities lead to modernization of culture and civilization replaced the traditional life style. This is necessary evil but the medicobotanical investigation aimed to salvage some of the native medico-botanical lore before it gets entombed with the culture that gave it birth.

Government of India established several premier institutions, such as Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow, Central Drug Research Institute (CDRI), Lucknow, Tropical Botanical Garden and Research Institute (TBGRI), Tiruvananthapuram and many local universities have put considerable efforts to gather information on medicinal uses of plants from different forest inhabitants. A few institutes taking the tasks of isolating the lead compounds from potential crude drugs based on traditional data / information.

India’s traditional medicine as part of honoured time-tested culture that still intrigues people today in developing countries. There are several advantages to the traditional remedies because of ready availability, easily transportable, easy to store, minimum side effects and cheaper to synthetic drugs. There should be continuous effort on documentation from each class of people in India, who hide the novel
medicinal properties from their surrounding environments. Even an average Indian grandma, housewife, rural people, witch doctors and tribal heads are well familiar with curing ailments at urgency.

About 15% of total geographical area of India is endowed with 550 tribal communities of 227 ethnic groups contribute 95% of total population, inhabited in 5000 forested villages. There are about 106 different languages and 227 subsidiary dialects spoken by tribals of India (Ministry of welfare, Govt. of India, 1992). These tribals have been associated with their traditions, ancient history of rituals and performances, which were related to the plant world through ages.

1.1 Study area

Chittoor district, the southern most region of Andhra Pradesh, falls under the South Eastern Ghats of Peninsular India. It lies between $12^0\ 37'$ and $14^0\ 8'$ of North latitude and between $78^0\ 30'$ and $79^0\ 55'$ East longitude. The district spreads over an area of 15,152 sq. kms with the total population of 37.35 lakhs, of which 29.25 lakhs people are living in rural areas and 8.10 lakhs are in urban areas and the density of population is 247 per sq. km. while the forest area comprises of 4,513.40 sq. kms (Fig 1).

Physiography

Based on its physical shape, Chittoor district has been categorized into three regions viz., Hilly, Plateau and Plains. The district can be divided into two main divisions viz Chittoor East with seven sectors (Bhakrapeta, Tirupathi, Srikalahasti, Satyavedu, Puttur, Karvetinagaram and Chittoor) and Chittoor west division with five sectors (Bangarupalem, Palamaner, Kuppam, Madanapalli and Punganur).
Soil types

There are 3 types of soils in which 57 per cent of the land consists of red soils, 34 per cent consists of red gravel soils and 9 per cent of sand is made up of black cotton and gummy red soils. Laterite soils are also found in some parts of Srikalahasti, Satyavedu, Nagalapurum and Puttur in the east division.

Climate

Usually the entire district has a dry climate. The western part of the district is comparatively cooler than the eastern part.

Rainfall

Vegetation of this area is influenced by both the monsoons. The Southwest monsoon (June-September) accounts the major proportion of rainfall in the district, whereas the eastern part is mostly affected by the Northeast monsoon (October-December). However, the average rainfall is gradually decreases from the East towards West.

Temperature

The temperature ranges from 25\(^0\)C-42\(^0\)C in the eastern mandals and the temperature soars from March to May (up to 47\(^0\)C).

Drainage system

There are no perennial rivers or multipurpose projects in the district. The entire irrigation depends upon small water sources of reservoirs, projects, tanks, ponds and wells.

Humidity and Wind

The relative humidity is 65-85% in the morning and nearly 55-60% in the afternoons during June-December. From March-June the relative humidity in the afternoons is 20-42% on an average. The light wind blows South-West and North-West during April-September.
Fig 1: Study area
1.2 Ethnology

Tribal population

Tribal’s, a distinct ethnic group usually confined to definite geographical areas. About 250 million ethnic people scattered all over the world except the European continent. The largest concentration can be found in the African continent and the second largest concentration is recorded in India. In India ethnic population is about 9.55 per cent of country’s total population (Ministry of Welfare, Govt. of India, 2002) belonging to 550 tribal communities of 227 ethnic groups as per the classification made by anthropologists on linguistic basis. The adivasi communities inhabit about 5000-forested villages across the nation [10]. Predominant tribal areas cover about 15 per cent of the total geographical area of the country. There are about 106 different languages and 227 subsidiary dialects spoken by tribals in India. In India the tribal peoples are living mostly in the forests, valleys, open forests and isolated zones.

Andhra Pradesh with 33 tribes and 60 other small tribes has a total population of 4.75 million, which constitutes 7.15% of the state’s total population of 66.35 million. Thus Andhra Pradesh form a very large component of ST’s in South India. Of all the recognized tribes in Andhra Pradesh eight are predominant. This state has been divided into three geographical regions namely Andhra (Coastal), Telangana and Rayalaseema.

The present study area comes under Rayalaseema, which comprises of Anantapur, Kadapa, Chittoor and Kurnool districts; possess thick population and diversified groups of tribals. The main tribal communities of the area are Chenchu, Sugali, Yanadi and Yerukala (Plate 1) and most of them are scattered all over the region except Chenchus. The Chenchus are restricted to the Nallamalais of Kadapa
and Kurnool districts only. The percentage of tribal population in about 10.84
(Anantapur 3.54, Chittoor 3.32, Kadapa 2.09 and Kurnool 1.89). Anantapur district
has the highest tribal population in the region. The chittoor district has distinct tribal
habitations mostly belonging to yanadi, yerukala and sugali communities.

Habitat of Tribes

Normally forests are the natural and traditional habitat of ethnic people. These
tribes differ from one another in race, language, culture, beliefs and striking diversity.
The diversity is caused by various social characteristics, traditions, linguistic trades,
physical features, etc. Tribals of this region belong to the Proto-australoid racial stock
and speak dialects of the Dravidian family. A brief ethnographic account of each tribe
is given below.

Sugalis

The Sugali is one of the main tribes of Andhra Pradesh. The sugalis have the
rich heritage and culture and are subjected to severe exploitation due to their socio
economic backwardness and illiteracy. The sugalis are predominantly concentrated in
Chittoor, Anantapur, Kurnool, Prakasam, Guntur and Mahaboobnagar, Warangal,
Adilabad, Khammam and Nalgonda districts.

The sugalis are known variously in different parts of the country as Lambadi,
Brinjari, Banjari, and Boipari, etc. The sugali tribes live near the small hills in
detached clusters of huts called ‘Thandas’ in close proximity to the forests. Sugali
tribe mostly depends on the agriculture works. They speak in language called
‘Lambadi’. This language concept related to the Urdu and Hindi languages. But this
language has no script of its own. In general sugalis are of dark reddish brown and
women are tall and of good looking while the men are robust.
Sugali men wear the brown colored cloth and mass of brass collars around the neck. Sugali women hands are covered with bracelets up to the elbow and also wear the kadayams. The dress of the women is striking and consists of a kind of patchwork of very bright colours. A kind of stomacher, with the holes for the arms, and tied at bottom to cover their upper part of the body and has some strings behind dangling at their backs. They wear wide earrings, necklace, rings on the fingers and toes. They pay little attention to the maintainance of hygiene, good health including clothing and other living styles.

Generally sugali people use ‘Naiks’ at the end of their names. Each thanda has a headman called ‘Nayakan’. The nayakan’s statement is law. He is considered the thanda priest. Nayakan is incharge of all cultural activities like scarifies and religious responsibilities of the thanda. They worship Hindu Gods.

Due to poorness, illiteracy and lack of technical skills, they took to crimes like robbery, cattle lifting and kidnapping children until the middle of last century [11]. Now, sugalis have new opportunities to work for their socioeconomic betterment. Most of them have taken agriculture and various types of labour. They are cultivating crops like red gram, groundnut, castor, sorghum, rice, etc. Their staple food is a coarse cake made of wheat or maize. Their women collect forest produce and sell firewood out of sheer economic necessity. Both males and females are addicted to heavy drinking.

The wealth of knowledge on medicinal plants among the tribals appears to have been developed their age-old trial and error methods and transmitted orally from generation to generation.
**Yanadis**

The Yanadis are more primitive aboriginal and concentrated mainly in Chittoor, Kadapa, Nellore, Ongole and Guntur districts of Andhra Pradesh. The tribes are set to be direct descendants of Paleolithic people. Chenchus and Yanadis both are from one parental stock and are believed to be originated in Nallamalai hill tracts [12]. Yanadis speak only Telugu language with a characteristic dialect and accent. They don’t have any special functions while ceremonies or celebrations are particular to them. They are integrated with Hindu social system and practice.

The Yanadi lead a carefree, life with contentment and unbridled merriment. Their diet chiefly consists of vegetable food and animals, wild fowls and other birds of food value. They even dig rat holes and use them in menu. However, the best satiating food for them is fish. Honey gathering in forests and plains is also a common practice among them.

Two sub–tribes are recognized with in Yanadis, based on their occupation, Manchi yanadi, the superior type and the challa yanadis are inferior type and carry different names including garapa yanadis, chettu yanadis, kappa yanadis, based on their habitation and the food taken. The yanadis are short statuned with dark skin colour, platyrrhine nose, long head, distinct chin, bulged lips and thin hair on head. They reside in huts usually construct adjacent to a water source. Yanadis living in and around forests keep themselves busy in collecting and selling minor products.

**Yerukalas**

The Yerukalas originally a Tamil tribe speaks ‘Yerula’ but which has no script of their own to data. The Yerukalas are the medium stature with well – built bodies, black in colour with small hair and brown eyes. They are chiefly basket and roap makers. They prepare a wide variety of baskets with plant materials. They also rear
pigs and some people wander from place to gain aliving. The women of this tribe are noted for their sooth saying.

The Yerukalas are said to have existed since the time of the Mahabharatha and consider themselves as the descendents of Ekalavya, who excelled in the art of archery. Thurston [11] wrote that Korava or Yerukalas are a vagrant tribe found out the state. Etymologically, the word yerukala is derived from the Telugu word ‘Eruka’ which means foresight or disclosing the facts about the future, present and past of one’s life. The women of this tribe get their livelihood by telling ‘Eruka’. This was probably the reason why these people are called Yerukala [12].

The Yerukalas are medium statured with well built bodies, dark brown to black skin, coarse, straight and black or dark brown hair and dark brown eyes. Yerukala men wear shirt (Angi) and dhoti while women wear the saree and a simple ravika. They construct houses with stones and bricks and roof covered by palm leaves or grass. Yerukala problems are solved in ‘Kula panchayat’. The members of this panchayat belong to yerukala society. The head of kulapanchayat is to decide all the judgements. He is the supreme, he settle all the disputes in the community as per the horms to their society. They worship Hindu Gods.
PLATE-1: General features of Tribes

a. Yerukolas

b. Sugalis

c. Yanadis
1.3 Phytochemistry

Phytochemistry or plant chemistry is concerned with the examination of plants to find the chemical constituents responsible for their biological activity. It is concerned with the structural elucidation and characterization of different natural substances, synthesized and accumulated by plants.

Phytochemistry plays a significant role in giving the solutions to systematic problems on one hand (chemotaxonomy) and in the search for additional resources of raw materials for pharmaceutical industry on the other hand. Plants synthesize a wide variety of chemical compounds numbering well into the hundreds of thousands, perhaps even millions. These compounds can be classified into two major groups based on their biosynthetic origin and functional groups i.e. primary metabolites and secondary metabolites. Primary metabolites consists of compounds such as carbohydrates, lipids, chlorophylls and nucleic acid, which make up the physical integrity of the plant cell and are involved in the primary metabolic process of building and maintaining living cells. Secondary metabolites have been defined as naturally occurring substances that do not seem to be vital to the immediate survival of the organism that produces them and are not an essential part of the process of building and maintaining living cells.

It is necessary to isolate secondary metabolites from traditionally used medicinal plants, because of the following features:

1. Provides a scientific complement to traditional approaches.
2. To understand functional similarities among different drugs.
3. Provides better comprehension of toxicology.
4. Establishes correlation between scientific approach and traditional herbal practice.
5. Provides tools to communicate with researchers and other practitioners.

6. Provides tools for understanding scientific literature.

1.4 Antimicrobial activity

Microorganisms are ubiquitous, i.e., they can be found in any environment that will support biological activity. They are found in soil, water, air, and particularly in association with plants, human beings and other animals. The indigenous flora of the human body is by far the most important source of microorganisms that cause disease in humans. They are normally found in harmless close association with the human body surfaces and are often beneficial since they compete with potential pathogens for attachment sites and nutrients. However, under uncontrolled circumstances, they can cause infectious disorders. Microorganisms can be divided into five groups, such as bacteria, yeast, helminthes, protozoa and viruses [13, 14].

Diseases have been man’s heritage from the beginning of his very existence. Human beings must have searched from early times for substances that would relieve their suffering and cure their loved ones. Since, illness thought to be caused by mystical agents underlying the natural world, cures for mental and physical diseases were sought among plants and animals. A perilous process of trial and error must have discovered the curative agents. Medical knowledge accumulated slowly as it was painstakingly passed on from generation to generation. Since communication between tribes was poor, remedies were probably discovered independently several times.

Reports revealed that the world’s oldest therapeutic or pharmacological writings came from India and China. A scholarly description of the legacy of Charak in contemporary idiom, best attempted with notable observations from modern medicine and science point of view, explains some glimpses of ancient culture and wisdom. Indian healthcare consists of medical pluralism and still remains dominant
therapies compared to modern medicine, particularly in case of chronic diseases. India has about 45,000 plant species most of them possess medicinal properties have been assigned to several thousands and about 2000 are found in the literature. Indigenous systems commonly employ about 500-700 plant species. Currently, with over 4,00,000 registered Ayurvedic practitioners, the Government of India have no formal rules to regulate quality, safety, efficacy and practice of herbal medicine [15].

World wide, infectious disease is the number one cause of death accounting for approximately one-half of all deaths in tropical countries. Death from infectious disease is ranked 5th in 1981, has become the 3rd leading cause of death in 1992 with an increase of 58%. Conventional and modern allopathic medicine is not able to solve the catastrophic increase of dreadful diseases such as cancer, diabetes, AIDS, SARS, Ebola and others yet to be understood completely. Many of these ailments are declared as incurable. But the practitioners of traditional medicine do have successful treatment for these so-called incurable diseases by their age old, time tested herbal drugs.

Plants constitute one of the major raw materials of drugs for treating various human diseases. The modern society has been interested in drugs of natural origin due to their harmonious nature with our biological system. It is reported that 41% prescriptions in USA and 50% in Europe contain constituents from natural products, which shows that the trend of using natural products is getting increased. Scientific research on wild medicinal plants relies on identification of the active principles, scientific validation of folk remedies, which lead to standardization, and quality control of products to ensure human safety. The enumerated drug samples can be approved for use in the primary health care. Such research activities could also help in the development of new drugs [4].
Phytochemical tests have been performed in about 5,000 species and nearly 1,100 species are extensively exploited in Ayurvedic, Unani and Allopathic medicines. In fact active plant extracts screening programs continue to end always with new drug discoveries.

In order to find new sources of plant drugs, numbers of plants have been screened for wide range of biological activity in various research institutions. In India about 3,000 plant parts from 2,764 plant species have been screened for their pharmaceutical and chemotherapeutic properties. The Central Drug Research Institute (CDRI), Lucknow (India) alone has screened over 3,800 plants for a wide range of biological activities in the past 25 years. A vast wealth of medicinal plant resources is still under utilized for curing a number of diseases.

Plant based antimicrobials represent a vast untapped source for medicines by possessing enormous therapeutic potential. They are effective in healing of infectious diseases while simultaneously mitigating many of the side effects that are often linked with synthetic medicines. Even though, ample numbers of antibiotics are widely used in medicine, the search for antimicrobial substances from plants is getting alarming need to develop better and safer drugs to combat bacterial and fungal infections. Because they are biodegradable in nature and being relatively safer for human beings and non-target organisms in the environment. Extensive survey of the flora has been undertaken to search for potential plant extracts, which could be used in the management of agriculture and household pests. Moreover, investigations on the insecticidal properties of plant extracts have been given an impetus because of imposition of restrictions on the use of chemicals for insect control. Plant extracts are widely used as pesticides and in folk medicine in tropical and subtropical areas. In order to study possible applications of extracts or compounds derived from extracts,
methods to screen for biological activities and separation techniques to isolate the active principles have to be established.

1.5 Antioxidant activity

The term antioxidant was used to refer specially to a chemical that prevented the consumption of oxygen. Oxygen, which is considered as essential to life, is also reported to be toxic. When oxygen is metabolized it creates free radicals, which seals electrons from other molecules. The oxidative stress, defined as the imbalance between oxidants and antioxidants in favor of the oxidants potentially leading to damage has been suggested to be the cause of aging and various diseases in humans. Free radicals are species with very short half-life; unstable molecules that play a role in illness and such species may be either oxygen derived (ROS) or nitrogen derived (RNS). The most common reactive oxygen species include Superoxide anion (O$_2^-$), Hydrogen peroxide (H$_2$O$_2$), Peroxy radicals (ROO$^\cdot$) and Reactive hydroxyl radicals (OH$^\cdot$). The nitrogen-derived free radicals are nitric oxide (NO), Peroxynitrite anion (ONOO$^-$), nitrogen dioxide (NO$_2$) and dinitrogen trioxide (N$_2$O$_3$). High levels of free radicals in the body develop from oxidative stress. Oxidation involves the loss of an electron from an atom or molecule. All these are capable of reacting with membrane lipids, nucleic acids, proteins and enzymes and other small molecules, resulting in cellular damage. In living organisms various reactive oxygen species can be formed in different ways, including normal aerobic respiration. Endogenous sources of free radicals are stimulated polymorphonuclear leucocytes, macrophages and peroxisomes. Exogenous sources for the production of free radicals include tobacco smoke, radiation, certain pollutants, organic solvents and pesticides causing hazards. Free radicals may be defined as chemical species associated with an odd or unpaired electron and finally achieve stable configuration. They are capable of attacking the
healthy cells of the body, causing them to lose their structure and function. Cell damage caused by free radicals are responsible for ageing and degenerative diseases such as cancer, cardiovascular disease, immune system decline, liver diseases, diabetes mellitus, inflammation, renal failure, brain dysfunction and stress etc. To protect the cells and organ systems of the body against reactive oxygen species, humans developed a highly sophisticated and complex antioxidant protective system that performs well protection to neutralize free radicals. Thus antioxidants help in stabilizing or deactivating free radicals before they degenerate cells. Antioxidants are absolutely critical for maintaining optimal cellular and systemic health and well being.

An antioxidant is a molecule, which is capable of slowing or preventing the oxidation of other biological molecules. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent. Oxidation reactions involved in the production of free radicals, which start chain reactions by eliminating free radical intermediates and inhibit other oxidation reactions by being oxidized themselves. As a result, antioxidants are often reducing agents such as thiols, ascorbic acid or polyphenols. Till recently, extensive study was devoted to the uses of antioxidants in important industrial processes like the prevention of metal corrosion, the vulcanization of rubber, and the polymerization of fuels in the fouling of internal combustion engines.

Oxidative stress plays a significant pathological role in many types of chronic diseases such as diabetes, heart disease and cancer. Oxidative stress result due to formation of excessive free radicals increases [16]. In oxidative stress, the balance between the amount of antioxidants and reactive oxygen species is destroyed.
Oxidative stress causes damage to cell components, such as proteins, lipids and nucleic acids [17] and ultimately leads to cell death [18, 19].

1.6 Anthelmintic activity

People living in poverty in developing countries often suffer from helminth infections, which more often physically impair their hosts than kill them. Although the majority of infections due to worms are generally limited to tropical regions, they can occur to travellers who have visited those areas and some of them can develop in temperate climates [20]. Bioactive substances that is present in ayurvedic medicinal plants used for the development of new helminthic drug [21].

Helminth infections are the most common infections in man, affecting a large proportion of the world’s population. In developing countries they pose a large threat to public health and contribute to the prevalence of malnutrition, anaemia, eosinophilia and pneumonia. Although the majority of infections due to worms are generally limited to tropical regions, they can occur to travelers who have visited those areas and some of them can develop in temperate climates [22]. Helminthiasis is a disease in which a part of the body is infested with worms such as pinworm, roundworm or tapeworm. Typically, the worms reside in the gastrointestinal tract but may also burrow into the liver and other organs; infected people excrete helminth eggs in their feces, which then contaminate the soil in areas with inadequate sanitation [23]. Other people can then be infected by ingesting eggs or larvae in contaminated food, or through penetration of the skin by infective larvae in the soil (hookworms). Parasitic diseases cause severe morbidity, including lymphatic filariasis (a cause of elephantiasis), onchocerciasis (river blindness), and schistosomiasis [24]. WHO estimates only synthetic drugs are used in the treatment of helminth infestations
though causes lot of side effects, however, synthetic drugs are out of reach of millions of people living in developing countries.

1.7 Antitumor activity

Cancer is one of the most life threatening diseases and creating serious public health problems in both developed and developing countries. It is a group of diseases characterized by the irregular proliferation of cancerous cells that invade and disrupt surrounding tissues [25]. Due to the toxic and adverse side effects by synthetic drugs resulting failures in attaining final results and satisfaction. For these consequences herbal medicine has made a comeback to improve the fulfillment of future health needs [26].

Crown gall is a neoplastic disease of plants caused by Agrobacterium tumefaciens [27, 28], which occurs in more than 60 families of dicotyledons and many gymnosperms [29]. The Ti-plasmid causes the plant’s cells to multiply rapidly without going through apoptosis, resulting in tumor formation similar in nucleic acid content and histology to human and animal cancers [30, 31]. The potato disc assay demonstrates the inhibition of tumor formation on potato discs; materials (e.g. plant extracts) that inhibit these plant tumors have a high predictability of showing activity against the P388 (3PS) leukemia in mice [32]. Development of a simple antitumor prescreen using a convenient and inexpensive plant tumor assay systems can offer numerous advantages as alternatives to extensive animal testing in the search for new anticancer drugs.

1.8 Diabetes Mellitus

Diabetes mellitus is a major endocrine disorder characterized by elevated blood glucose levels resulting from absence of inadequate pancreatic insulin secretion with or without concurrent impairment of insulin action. Infact, diabetes nowadays a
global problem affecting nearly 10% of population all over the world, comes to 150 million people [33]. According to WHO report the number of cases of diabetes mellitus was 171 million in 2000, which may increase to 360 million by 2030. As the number of diabetic patients multiplies worldwide, the entire healthcare system fails which ultimately leads to disturb the world’s health care budget.

The first widely accepted classification of diabetes mellitus was published by WHO in 1980 [34] and in modified form in 1985 [35]. The main classes of diabetes are Type 1 or insulin-dependent diabetes mellitus (IDDM), Type 2 or non insulin-dependent diabetes mellitus (NIDDM), Malnutrition related diabetes mellitus (MRDM), and Gestational diabetes mellitus (GDM). Type 1 diabetes mellitus, also known as insulin-dependent diabetes mellitus (IDDM), usually begins in childhood and is thought to be a result of autoimmune destruction of the pancreatic β-cells which results in a complete or almost complete loss of insulin production thereby necessitating insulin injection to maintain blood sugar control. Thus patients with Type 1 diabetes mellitus are characterized by a deficiency of endogenous insulin. From literature review it has been revealed that 15-20% of diabetic patients are suffering from Type 1 diabetes. Type 2 diabetes, also known as non-insulin dependent diabetes mellitus (NIDDM), is usually diagnosed after 40 years of age. NIDDM is the most common form of diabetes mellitus. It is frequently associated with insulin resistance and normal or even elevated levels of insulin, although subnormal insulin levels are also seen in some Type 2 diabetes. The epidemic of Type 2 diabetes is complicated by the fact that it is a multi-factorial disease, frequently associated with a cluster of pathogenesis including obesity, hyperglyceridemia, impaired glucose tolerance and insulin resistance, collectively referred as the metabolic syndrome. About 85 per cent of all people with diabetes have NIDDM. According to the WHO
(WHO, 2006) more than 176 million patients are affected by this disease in the world. Treatment of Type 2 diabetes is complicated by several factors inherent to the disease process, typically insulin resistance, hyperinsulinemia, impaired insulin secretion, and reduced insulin mediated glucose uptake and utilization [36]. Malnutrition related diabetes mellitus could be caused by malnutrition or protein deficiency. Gestational diabetes is characterized by hyperglycemia during pregnancy and usually disappears after the child is delivered. Even though gestational diabetes may be relatively short lived; it can affect the health of both mother and fetus. Gestational diabetes mellitus is usually asymptomatic and not life threatening to the mother. The condition is associated with an increased incidence of neonatal morbidity, neonatal hypoglycemia, macrosomia and jaundice.

According to a recent estimate, 171 million people worldwide suffer from diabetes [37] almost five times more than the estimates were recorded earlier. Reports from the WHO indicate that diabetes mellitus is one of the major killers of our time, with people in southeast Africa and Western pacific being most at risk [38]. India is home to about 20 per cent of the world’s diabetes population with 79.4 million only in 2010, which is due to rapid economic, demographic and life style habitats [39].

Several causative factors such as heredity, race, lifestyle, nutritional status, stress, infection, altered metabolic/physiological status, drugs and hormones have been found to be involved in the etiology of the disorder. Epidemiological data from different parts of the India show a rising prevalence of diabetes in the urban areas. There is a wide difference between urban-rural populations in the prevalence of diabetes including a major role for urbanization in the causation and of the disease. 30 per cent of diabetes in urban India is below the age of forty. A national study in 2000 AD showed that the prevalence in urban adult aged ≥ 20 years was 12.2 per cent. The
study on prevalence of diabetes in India showed significant regional differences, Western and Southern India showed the highest prevalence while East and Central India showed the lowest, with the north in between. These regional differences were further correlated to industrialization and physical exercise [40]. Prevalence of the complications is higher in low socio-economic groups due to lack of good control of glycemia and hypertension and also due to lack of good control of glycemia and hypertension and also due to behavioral factors.

1.9 Significance of Lamiaceae

Lamiaceae (syn. Labiatae), one of the largest and economically important flowering plant families consists of more than 250 genera and 7000 species [41], which occupies eighth position in Indian flora [42], and consists of cosmopolitan members [43]. They have traditionally been considered closely related to Verbenaceae [44]. The family has been reported as most prominent medicinal plant group with potential therapeutic properties that are common in Mediterranean region [45]. The Lamiaceae plants are generally aromatic in all parts including a number of widely used culinary herbs, such as sage, thyme, rosemary, oregano, basil, mint lavender, marjoram, savory, and perilla [46, 47]. Some of them are shrubs, and a very few are vines or trees. The aromatic essential oils are contained in leaves, which emerge oppositely with each pair positioned at right angles to the previous one (called decussate) and stem is mostly quadrangular. The flowers are symmetrical with united sepals and united petals (5 each), such plants are mostly bisexual and verticillate (a flower cluster that looks like a whorl of flowers but actually consists of two crowded clusters) in native [48, 49].

Lamiaceous species are used as culinary spices and folklore medicine. For example oregano, rosemary, sage and thyme are typical seasonings in the
Mediterranean region, and especially oregano is consumed in larger quantities all around the world as part of pizza seasoning mix [50, 51]. As the plants possess toxic components the crude drugs are used in culinary and essential oil industries [52, 53, 54, 55]. The herbs like oregano, rosemary, sage and thyme are often included in generally recommended as safe (GRAS) list as provided by the U.S. Food and Drug Administration. Essential oils recovered from them have been used against different diseases like intestinal disorders and bronchitis [56].

Many members of Lamiaceae are used in the Ayurveda, Unani and Homeopathic systems of medicine [57]. In Lamiaceae 40 per cent of the genera are aromatic, owing to essential oils that are located in highly specialized secretory structures known as glandular trichomes, present primarily on the leaves and calyces [58]. The most ancient books on medicines of India, namely 'Charaka Samhita' and 'Sushruta Samhita' describe the wonderful curative properties of members of Lamiaceae, especially Ocimum. L., which are attributed to their chemical principles. More over the medicinal and aromatic qualities of Indian Lamiaceae members are very well described in 'Materia Indica.'

Economically many members of Lamiaceae are of outstanding importance since their volatile oils form indispensable ingredients of perfumery, flavour, fragrance and pharmaceutical industries [59]. The family is of great ethnobotanical value, being employed in indigenous medical systems [60]. In this family, tannins, iridoids and saponins are common and alkaloids are present in a few genera [61]. The discovery of biologically active compounds in the Lamiaceae, such as diterpenes, opens up a new realm of medical investigation [62]. In addition, some members are successfully employed in aromatherapy, a branch of herbal medicine, which exploits the therapeutic properties of herbs and herbal oils to cure many ailments [63, 64].
Mentha species are commonly used in commercial spice mixtures for many processed foods as well as in herbal teas [65, 66]. Moreover, the essential oils from Mentha species are generally employed to flavour liquors, breads, salads, soups and cheese, as well as an ingredient of cosmetics [67]. Locally Salvia species are used as traditional medicine to treat a variety of diseases such as wounds, malaria, microbial infections and cancer [68]. Origanum plants are extensively used for the flavoring of alcoholic beverages, food products and in perfumery due to their spicy fragrance [69]. Some Lamium plants have been used in folk medicine worldwide as remedy in the treatment of several disorders, such as trauma, fractures, paralysis, hypertension, menorrhagia and uterine hemorrhage [70, 71].

Traditionally, Ocimum species have been extensively utilized in food and perfumery industries [72]. Fresh leaves of basil plant are used as an ingredient in various dishes and food preparations. The aerial parts of the plants are considered as antispasmodic, stomachic and carminative in native medicine [73]. In native medicine, flowering parts and leaves of Thymus species widely used as herbal tea, tonic, carminative, antitussive and antiseptic [74, 75, 76, 77, 78].

1.9 Genus Leonotis

Leonotis is a small genus, which belongs to the subfamily Lamioideae under the family Lamiaceae [79]. Its generic name is derived from the Greek words “Leon” and “otis”, i.e. “lions ear”. This name is given to the genus because the morphology of hair-fringed upper corolla lip in its entire species resembles lions ear [80]. The number of known species included in this genus is about 12 [81] and they have been reported to occur only in the tropical parts of the world. Leonotis is an herbaceous genus with annuals and perennials. All but one species, Leonotis nepetifolia (native
to both tropical Africa and southern India), are native to southern Africa, which is well naturalized in south India especially Rayalaseema region in Andhra Pradesh.

It is taxonomically characterized by spiny calyx and weakly developed lower corolla lip, which withers soon after anthesis. *Leonotis* (Pers.) R. Br., with flowering stems bearing dense verticels with orange or infrequently yellowish cream flowers, is a well defined and a striking genus of the family Lamiaceae, densely pubescent on veins; secondary veins 4-5 pairs; petioles 4-10 cm long. Inflorescence 1-3 verticels per branch, with 6-10 cm.

*Leonotis* flowers with the floral characters such as orange scarlet colour, lack of odour, concealed nectar, absence of nectar guides characteristic of insect pollinated flowers and nectar with low calorific value confirm to ornithophilous pollination syndrome. Further, the poorly developed lower lip, which withers shortly after anthesis easily facilitates access to the floral reward by birds, which usually approach the flowers from below. The weak protandry in *Leonotis* species facilitates self-pollination to a large degree. Cross-pollination is exclusively a function of pollinator activity. *L. nepetifolia* is primarily self-pollinating and also cross-pollinated when visited by sunbirds [82].

The decoction of roots or leaves of *Leonotis* species mainly used for toothache, snake bites, skin disease, muscular cramps, haemorrhoids, influenza, coughs, colds, indigestion, high blood pressure, bronchitis (twigs) and also smoked as a narcotic in place of *Cannabis sativa* [83, 84]. Almost most of the species are ornamentals. The flowers with their scarlet orange color being used in aesthetic value.

*Leonotis* species possesses many organic compounds grouped into tannins, quinones, saponins, alkaloids, resins and terpenoids [85, 86]. Some of these have been isolated and chemically identified as marrubiin and premarrubiin during extraction [87]. Other terpenoid lactones including Leonotin have been found in *Leonotis*
ocymifolia [88]. All this research has shown that Leonotis species is very rich in terpenoids essentially in diterpenoid lactones, however L. nepetiifolia received less attention and hence, the present study gains importance.

1.11 *Leonotis nepetiifolia* (L.) R. Br.

**Synonym:** *Phlomis nepetiifolia*

**Common names**

Hejurchei (Hindi); Kaaduthumbagida (Kanada); Granthi, Granthika and Granthiparni (Sanskrit); Beri, Hanumantabira, Ranaberi (Telugu).

**Description**

Annual erect herb, loosely branched, grow up to 8 ft (2.4m) tall in its single growing season. Stems angled (square in cross section) and leaves in pairs opposite to each other; leaves smooth with coarsely toothed margins, triangular in shape and 2-5 in (5.1-12.7cm) long; flowers borne in rounded, spiny clusters, 2-4 in (5.1-10.2cm) across that encircles the stems (**Plate 2**), so that stems looks like growing right through the middle of the clusters, stem elongate, new flower clusters continue to develop above the older ones; tubular flowers that peek out of the spiny heads, orange and furry like a lions ear. Calyx tubular, mouth oblique, 8-10 toothed, valvate, coriaceous, spinescent; corolla tubular, bilipped, tube with five annular rings with upper lip hooked, lowerlip 3-lobed; stamens four, didynamous hooded by the upper lip, excerted; filaments minutely beared, disc copular; ovary bicarpellary, tetralocular, ovule one per locule; basal style gynobasic, stigma bifid, capitate; fruit schizocarpic; nutlets four, oblong, trigonous and seeds oblong (**Plate 2**).

**Distribution**

It is originally native to tropical and subtropical Africa, however, now naturalized all over the world in appropriate climates, where it grows along roadsides, waste places and in distributed areas. Annual lion’s ear occurs throughout Florida and
much of American south. It is listed as an invasive garden plant in Australia and a pest plant in Hawaii. This is well naturalized along the roadsides, wastelands in southern Andhra Pradesh.

**Culture**

Annual lion’s ear grows rapidly and vigorously with regular watering, but still hangs on during drought. It is easy to grow from seed, and under favorable conditions will self sow.

**Taxonomy**

- **Domain**: Eukaryota
- **Kingdom**: Plantae
- **Phylum**: Tracheophyta
- **Subphylum**: Euphyllophytina
- **Infraphylum**: Angiospermae
- **Class**: Magnoliopsida
- **Subclass**: Asteridae
- **Superorder**: Laminae
- **Order**: Lamiales
- **Family**: Lamiaceae
- **Subfamily**: Lamioideae
- **Genus**: Leonotis
- **Tribe**: Lamieae
- **Species**: nepetiifolia
Plate 2: Leonotis nepetifolia (L.) R. Br.

2a. Habitat

d. Lf- Adaxial  e. Lf- Abaxial  f. Fl- Adaxial  g. Fl- Abaxial
**Chemical constituents**

*Leonotis nepetiifolia* (L.) R. Br. is rich in alkaloids (leonurine and stachydrine), iridoid glycosides (leonuride, leonurin and leonuridine), diterpenoids (leocardin), flavonoids (rutin, quercetin, hyperoside, apigenin), volatile oil, tannins, vitamin A, etc.

The root contains n-octacosanol, n-octacosanoic acid, quercetin and coumarin like 4,6,7-trimethoxy-5-methylchromene-2-one, campesterol and beta-sitosterol-beta-D-glucopyranoside. The seed oil contains oleic, linoleic, palmitic and stearic acids. The fatty oil, extracted from the seeds, is similar to olive oil. The leaves contain neptaefolin, neptaefuran, neptaefuranol, neptaefolinol, leonitin, neptaefolinin and 6-octadecadienoic acids.

Phytochemical screening has revealed that *L. nepetiifolia* contains, amongst many constituents, labdanic acid [89], diterpene methoxynepetaefolin, the terpenic alcohols- nepetaefolinol and leonotinine and a coumarin, characterized as 4,6,7-trimethoxy-5-methylchromen-2-one [90]. Laballenic acid, a new allenic acid is present in seed oil.

**Therapeutic uses**

The plant is used in traditional medicine in therapy of bronchial asthma, diarrhoea, fever, malaria and as an analgesic agent in menstrual pains; also to treat common cold and to alleviate cough [91, 92, 93]. In India, the flowers are used in case of hardly healing wounds, scars and burns. To burn healing, the seeds are used as well [94, 95]. The leaves are used traditionally in the management of type-2 diabetes mellitus, pain, arthritis, coughs, indigestion, warm infestation, nasal-disorders, skin infections, malaria and flowers are used in burns, scalds, itches and skin diseases. In the Carribean region plant was found to be used in treatment of asthma. The plant is
also medicinally useful to treat rheumatism, rickets, headaches, wounds, ringworm, laxative, bitter, narcotic, fever and convulsions.

The pharmacological actions of the crude hydro alcoholic extract and stems of tea extracts obtained from *Leonotis nepetiifolia* may be purported for anti-asthmatic and anti-diarrheal properties [96]. The plant has been evaluated for its hypotensive potential, anti-inflammatory, antiplasmodial and antibacterial activities. It has relaxing effect on rat and guinea pig smooth muscle and rat cardiac muscle. Aerial parts of methanol extracts shown significant active in brine shrimp lethality test.

*Leonotis nepetiifolia* is one of the important Ayurvedic herbal drugs known as Grantiparani in Sanskrit. Roots have been used in Brahat, Guduchi, Tailaand, Mrtsanjivani and Sura in Ayurvedic formulations and also used in indications of swasa (Asthma and bronchitis), kandu (Fever) and visa (poisonous conditions). Phytochemical examination of various plant parts yielded different diterpenoids of labdane type. This plant exhibited various biological activities viz. antifungal, antimalarial and anti-cancer. The essential oil is mostly used in skin infections as it process efficient activity on dermatophytes even with secondary antibacterial principles.

The plant is reported to be useful in skin infections and also as a laxative and narcotic. A decoction of the leaves is used as tonic and to cure burns. The seeds possess feeble anti-malarial activity. The seed extract exhibited toxicity against Gram +ve and Gram -ve bacteria[97]. Flower ashes are used against burns (Wealth of India, 1962). The medicinal uses of *Leonotis nepetiifolia* are enumerated (Table1).
Table 1: Medicinal uses of *Leonotis nepetifolia*

<table>
<thead>
<tr>
<th>Activities and uses</th>
<th>Plant parts</th>
<th>Authority</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>To cure ringworm</td>
<td>Flower</td>
<td>Dymock <em>et al.</em>, [98]</td>
<td>1980</td>
</tr>
<tr>
<td>As an antipyretic; in malaria</td>
<td>Flower</td>
<td>Roigy Mesa [99]</td>
<td>1945</td>
</tr>
<tr>
<td>To cure burns, scalds &amp; ringworm</td>
<td>Flower</td>
<td>Chopra <em>et al.</em>, [100]</td>
<td>1956</td>
</tr>
<tr>
<td>Used against breast swellings</td>
<td>Root</td>
<td>Chopra <em>et al.</em>, [100]</td>
<td>1956</td>
</tr>
<tr>
<td>To cure skin diseases</td>
<td>Leaf</td>
<td>CSIR [103]</td>
<td>1986</td>
</tr>
<tr>
<td>To cure malarial fever</td>
<td>Leaf and Flower</td>
<td>Barua &amp; Sharma <em>et al.</em>, [104]</td>
<td>1987</td>
</tr>
<tr>
<td>For ringworm and skin diseases; For rheumatism</td>
<td>Leaf and Flower</td>
<td>Jain <em>et al.</em>, [105]</td>
<td>1989</td>
</tr>
<tr>
<td>For treating asthma; as an antitussive</td>
<td>Leaf</td>
<td>Dhetchuvi &amp; Lejody <em>et al.</em>, [106]</td>
<td>1990</td>
</tr>
<tr>
<td>To treat dengue fever, cold, urinary problems; in womb prolapse as cholagogues &amp; abortifacients.</td>
<td>Leaf</td>
<td>Heinrich <em>et al.</em>, [107]</td>
<td>1992</td>
</tr>
<tr>
<td>As a tonic and fabrifuge</td>
<td>Leaf</td>
<td>Dymock <em>et al.</em>, [98]</td>
<td>1980</td>
</tr>
</tbody>
</table>