



# ETHNOPHARMACOLOGY and BIODIVERSITY of MEDICINAL PLANTS

Jayanta Kumar Patra | Gitishree Das  
Sanjeet Kumar | Hrudayanath Thatoi  
*Editors*

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**ETHNOPHARMACOLOGY  
AND BIODIVERSITY OF  
MEDICINAL PLANTS**



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# **ETHNOPHARMACOLOGY AND BIODIVERSITY OF MEDICINAL PLANTS**

*Edited by*

**Jayanta Kumar Patra, PhD, PDF**

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**Hrudayanath Thatoi, PhD**

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# Abbreviations

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2AA	2-amino-anthracene
ABR	Agasthyamala Biosphere Reserve
AGB	above ground biomass
AICRPE	All India Coordinated Research Project on Ethnobiology
AMR	antimicrobial resistance
AMR	Antimicrobial resistance
BF	Bhitarkanika mangrove forest
CBD	convention on biological diversity
CF	colonization frequency
CNH	Central National Herbarium
CP	cyclophosphamide
CR	colonization rates
DBH	diameter at breast height
DHFR	dihydrofolate reductase
DOE	Department of Energy
DPPH	2,2-diphenyl-1-picrylhydrazyl
ECDC	European Centre for Disease Prevention and Control
EIA	Environmental Impact Assessment
ENNG	Ethyl-N-nitro-N-nitrosoguanidine
FDA	Food and Drug Administration
GRAS	generally recognized as safe
HAL	Hindustan Aeronautics Limited
HELA	human cervical epithelioid carcinoma
IMTECH	Institute of Microbial Technology
IPNI	International Plant Naming Index
IR	isolation rates
ISE	International Society of Ethnobiology
IUCN	International Union for Conservation of Nature and Natural Resources
MAPs	medicinal and aromatic plants
MIC	minimum inhibitory concentrations
MNNG	Methyl-N' nitro-N-nitrosoguanidine
MNP	marine natural products
MOEFCC	Ministry of the Environment, Forest and Climate Change

MSSRF	M.S. Swaminathan Research Foundation
NAD	Naval Armament Depot
NFP	National Forest Policy
NPs	nanoparticles
NRSA	National Remote Sensing Agency
NRSC	National Remote Sensing Center
PDA	potato dextrose agar
PDF	passport data form
QSAR	quantitative structure-activity relationships
RF	relative frequency
SBR	Similipal Biosphere Reserve
SF	Sundarban mangrove forest
TB	tuberculosis
TM	traditional medicinal
USGS	United States Geological Survey
WHO	World Health Organization

# Preface

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The traditional therapeutic systems and biodiversity of the world are under varying degrees of threats due to rapid modernization and urbanization. During the last two decades, there has been a greater consciousness about the need for the conservation of biodiversity and ethnobotanical practices. It is widely recognized that the loss of bioresources and traditional practices have great health impacts on rural and tribal areas as well as in the formulation of new drugs as ethnobotany is the base of pharmacological industries. It is needless to mention here that the forested tribal areas rich with ethnobotanical knowledge which offers the broadest array of options for sustainable health care activities for human welfare and for adapting contemporary changes. Considering the pivotal importance of the great diverse practices and diversity of medicinal plants, there is an urgent need to document and study the ethnobotanical agents from our bioresources for the formulation of new drugs to fight against diseases and disorders as well as contemporary clinical and biodiversity issues. The other exigency steps are the implementation of appropriate conservation strategies for the protection of the traditional therapeutic skills and medicinal bioresources of the country where about 8,000 plants species are reported having potent medicinal and pharmacological values.

The present book, *Ethnopharmacology and Biodiversity of Medicinal Plants*, highlights the importance of medicinal plant wealth to the formulation of new drugs and brings attention towards the conservation of our bioresources along with traditional therapeutic values. Also the present documentation provides transparent and informative ideas covering a wide array of topics like biodiversity bioprospecting, importance of mangroves wealth, urban biodiversity and their floral wealth with uses, medicinal microflora, role of protected areas in the conservation of medicinal plants and traditional therapeutic skills, and role of common nutraceutical in our day-to-day life. The information pertaining to the topics of the documentation is based on fieldwork and literature survey made by the different esteemed researchers of diverse landscapes of India. It is hoped that this edited book will not only provide the knowledge on ethnobotany and biodiversity of medicinal plants but also will give a glimpse on rich traditional therapeutic systems and biodiversity of India from Kanyakumari to Arunachal Pradesh

and biodiversity hotspot from Indo-Burma to Western and Eastern Ghats of India. This edited book will be useful particularly for the healthcare sector, and it will also provide a baseline data for the study of ethnopharmacology and reverse pharmacology.

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# Foreword

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At this time of resource crunch, sustainable development is the buzzword for the whole world. This is the only solution for the effective and efficient use of all natural resources. Proper information about the quality and quantity of these resources is a must for ensuring sustainable usage and conservation.

The present edited volume, titled *Ethnopharmacology and Biodiversity of Medicinal Plants* by Dr. Jayanta Kumar Patra, Dr. Gitishree Das, Dr. Sanjeet Kumar, and Prof. H. N. Thatoi is an important addition to the knowledge repository in this direction.

The papers in the volume are selected carefully covering varied aspects of the titled subject, providing the reader with an overview and in-depth knowledge on some of the specific aspects, such as bioprospecting, value-added biomolecules of Indian mangroves, and ethnobotanical studies of major medicinal plants.

I congratulate the authors and editors for this fruitful effort and hope that the book will be useful to the scientific community and the entire humanity.

—**Padma Mahanti, IFS**

*Director*

*Department of Environment and Climate Change  
Government of Kerala*



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**PART I**  
**Biodiversity and Conservation**



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## CHAPTER 1

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# Biodiversity Bioprospection with Respect to Medicinal Plants

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### ABSTRACT

Medicinal plants have been in use for the treatment of a range of diseases from the beginning of civilization. Around 65–80% of the world population living in developing countries believes in traditional herbal medicines for their primary health care. Even in the modern allopathic system, medicinal plants are playing a key role in public health care. According to an estimate, approximately 25% of currently used medications are obtained from different higher plants. In addition to this, the interest in plant products has increased exponentially especially the phytotherapeutic supplements (nutraceuticals) and cosmetics over the past decade. Apart from direct clinical use, these plants and their products are also utilized for agriculture in pest control in biodiversity-rich countries like India, China, Sri Lanka, Brazil, and Africa. Every nation has a sovereign right over its biodiversity which is frequently violated by the act of biopiracy or gene robbing. There are many examples of exploitation of traditionally used medicinal plants by the biotechnologically rich but biodiversity poor countries. *Pentadiplandra brazzeana* from tropical Africa, *Vinca rosea* from Madagascar, *Curcuma longa*, *Azadirachta indica*, and *Withania somnifera* from India are some classical examples of biopiracy. Hence, bioprospection would help the native countries in legal exploitation of the bioresources by preventing the act of biopiracy. Hence,

bioprospection is a burning issue for biodiversity-rich countries like India, China, and tropical African nations to document their bioresources as well as to identify their useful plants, related phytochemicals and genes controlling them.

## 1.1 INTRODUCTION

Bioprospecting refers to the process of exploring natural resources for commercialization of new products without perturbation of natural pathways. Traditional bioprospecting includes the huge utilization of birch polypore, *Piptoporus betulinus* fruiting body for recovery of intestinal ailments in Iceman. From pre-historic times, the healing properties of different medicinal plants were recognized and utilized by old world people and other primates. Different animals like monkey, ape, gorilla, and chimpanzee have selected and consumed a particular type of plants for management of their disease, injury and other health problems (Baker, 1996; Glander, 1994). A similar type of style has also been used by humans. The use of traditional therapeutic plants as folk medicines for large-scale production of phytoactive constituents for curative and psychotherapeutic purposes has required a long journey (UNESCO, 1994). Some archeological evidence also indicates the use of medicinal plants from ancient times. The use of medicinal plants for herbal drug preparation was first documented from Sumerian clay slab of Nagpur, India (5000 years old) (Kelly, 2009). The oldest Chinese herbal book “Pen T’Sao” written by Emperor Shen Nung circa (2500 BC), had mentioned about 365 plant products for recovery of different humans ailments (Petrovska, 2012). The Illiad and Odysseys, the great epic of Homer at circa 800 BC, had described 63 plant species for therapeutic purposes (Toplak Galle, 2005). In ‘Vedas’ the holy mythological books of India, use of various spices like nutmeg, pepper, and clove by Arya Monk had been listed for their health care promises (Agarwal, 2013). More than 500 plants with their therapeutic uses had been classified by Theophrastus (371–287 BC) and were further renowned by an eminent medical writer Celsus (25–50 AD) (Pelagic, 1970). Dioscorides, a military physician, also studied different medicinal plants and their medication during travel with the Roman army. Several important domestic plants *viz.* garlic, nettle, sage, coriander, parsley, sea onion, and chamomile were also described by them (Thorwald, 1991; Katic, 1967). During the 17<sup>th</sup> century and Middle Ages, physician monks treated health problems by using commonly growing medicinal plants in their monastery. Early in the 18<sup>th</sup> century “Species Plantarum” by Linnaeus had developed a

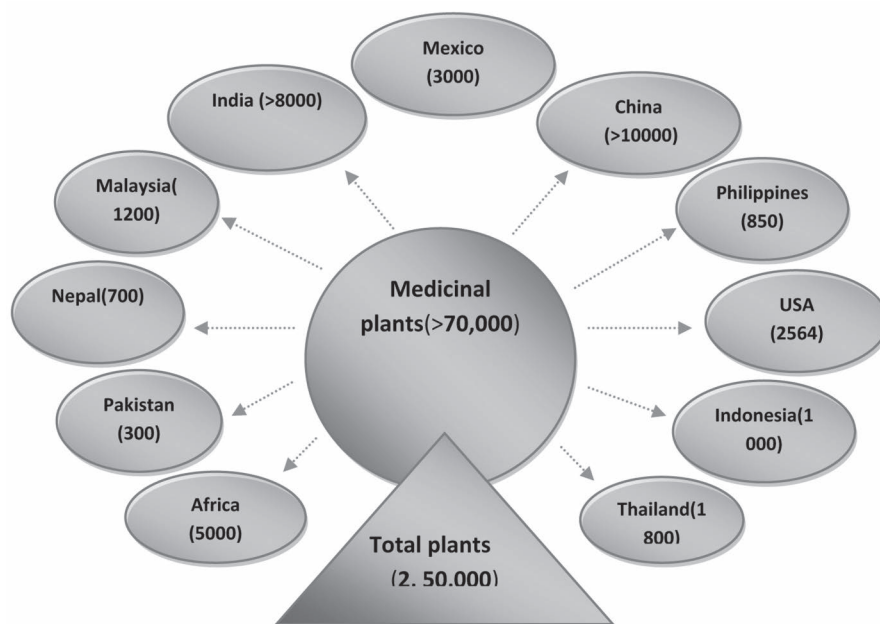
solid pillar of botanical nomenclature and also supported the proper plant identification and isolation followed by upgrading methods for extraction of secondary metabolites such as saponins, essential oils, hormones and vitamins for the prevention of different diseases (Frodin, 2004). In the 20<sup>th</sup> century, herbal medication was in great danger due to some poisonous impact of medicinal plants and dose-dependent mode of action (Saad et al., 2006). Over the past years, people are moving towards the allopathic and other surgical treatments for their quick response to human health. However, in modern days, due to the inexpensive price and less chance of side effects, most pharmacopeias of the world focused on isolation and characterization of active plant constituents for real drug development. Recently, different active plant constituent is being encapsulated by different coating materials in order to synthesize nanomedicine with major emphasis on targeted action. The combination of modern technical systems with traditional herbal knowledge could upgrade the old preparatory procedures and help in the discovery of new drugs.

## **1.2 BIODIVERSITY OF MEDICINAL PLANTS**

Since a long time, medicinal plants have served and provided health security to human beings and other life forms. The demand of medicinal plants for health purpose is increasing in developing as well as developed countries. This problem can be resolved by looking into the worldwide diversity of medicinal plants so as to harness as much as resources and knowledge to secure health needs of present generation (Balick et al., 1996). According to an estimate, around 1/10<sup>th</sup> of the world's plant species have been used for the medicinal purpose (Chen et al., 2016). However, their distribution is not uniform over the globe, like China and India have a higher diversity of medicinal plants than others.

The botanical survey has estimated more than 2.5 lakhs plant species on earth, among which more than 70,000s were identified to possess medicinal properties used in folk medicine throughout the world (Alamgir, 2017; Farnsworth and Soejarto, 1991). It has been estimated that about 25% of the drugs prescribed worldwide for the disease treatment are derived from plants (Sahoo et al., 2010). Currently, 17 countries have been identified as a mega-biodiversity center, which are home to the bulk of the world's species including medicinal plants. A few years ago WHO has also made an attempt to identify medicinal plants existing in the world.

The total number of species on earth is unknown, and only a small number have been screened for medicinal properties. However, data available from different countries on medicinal plants is inspiring. India, which is known for one of the most diverse mega biodiversity regions in the world and cultural traditions, uses herbal medicines based on more than 7,000 plants species (Lange, 2002). In China, total numbers of plant species used for the medicinal purpose were around 10,000 (He 1998). In Africa, over 5,000 plant species are used for medicinal purpose (Luyt et al., 1999) followed by USA, Thailand (Phumthum et al., 2018), Mexico (Alonso-Castro et al., 2017) Malaysia, Indonesia (Caniago and Stephen, 1998), Philippines, Nepal and Pakistan (Rajeswara et al., 2012) (Figure 1.1).



**FIGURE 1.1** Schematic status of medicinal plants in some major countries.

These plants bear a diverse array of specific metabolites having one or more therapeutic importance. In the USA, most of the top prescribed drugs and 50% of the drugs all over the world have at least one compound derived from the plant source. Today, many chronic diseases are possible to treat with the help of these herbal remedies. In upcoming few decades, medicinal plants surely will become a new era of the medical system for the management of diseases and exploration of diversity may open up huge

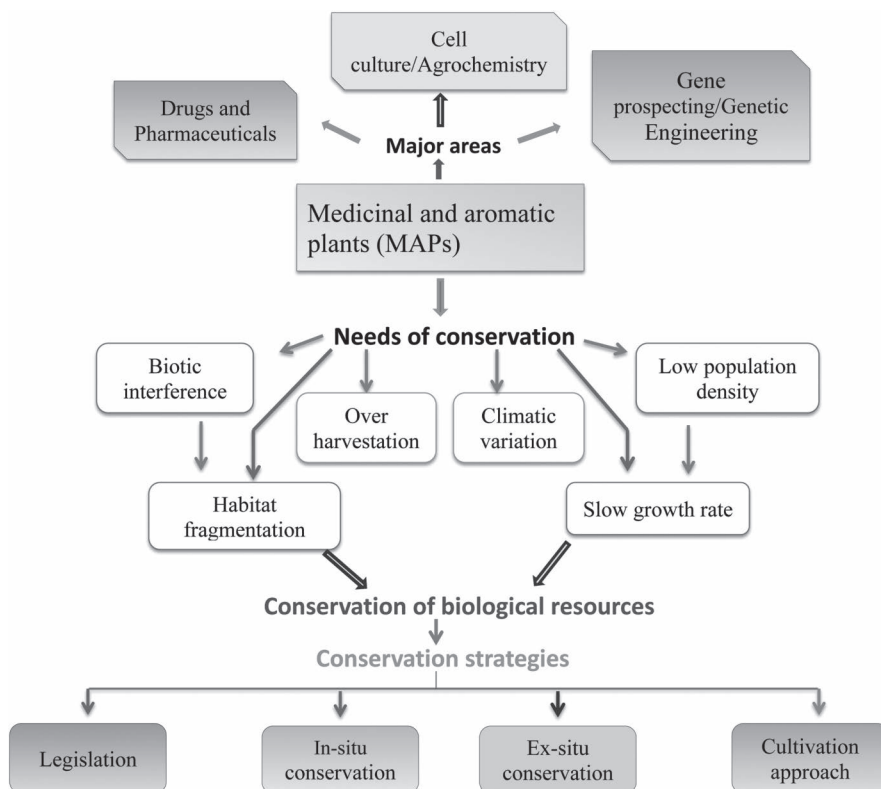
opportunities for overcoming such difficult tasks and thus appears promising for exploration of new drugs (Shakya, 2016).

### 1.3 CONSERVATION OF GENETIC AND CHEMICAL DIVERSITY OF MEDICINAL AND AROMATIC PLANTS

The biological resources of medicinal and aromatic plants (MAPs) of different countries represent a progressive contribution to natural biodiversity, local economies and cultural integrity around the world. Before the development of pharmaceuticals, local mankind of many places used their traditional knowledge and skills to prepare different plant-based formulations to diagnose and treat health associated problems (Traffic International, 2015; WHO, 2013). Aromatic plants have a characteristic fragrance and are known to act as a reservoir of diverse secondary metabolites to protect themselves from natural predators (King, 1996). These metabolites or bioactive constituents have potent therapeutic properties and are being used in novel drug synthesis (Harvey, 2008). In contrast to modern medicine, the traditionally used plant medicines have a holistic approach and less chance of side effects. About 85% of herbal medicines are derived from different medicinal plants based on their habitat, climatic and varied geographical distribution (Farnsworth, 1988; Prasad and Bhattacharya, 2003; Phondani et al., 2014). Although some natural compounds obtained from plant species are not pharmacologically active in their original form while they act as a precursor of several bioactive compounds (Atanasov et al., 2015). Aromatic medicinal plants especially include traditional herbs and spices for their delicious flavor and fragrance. US-FDA recognized spices of key medicinal significance due to the presence of significant amount of flavoring principles (Kaefer and Milner, 2008). Some aromatic plants of Apiaceae have chemoprotective and therapeutic potential up to a certain doses. The leaves of *Melaleuca alternifolia* and *Eucalyptus globulus* were traditionally used for the treatment of chest infection, and decongestion of coughs (Vail and Vail, 2006). India has contributed a major role in Ayurveda using medicinal and aromatic plants. Hamilton (2004) reported that 44% of Indian flora is being used medicinally throughout the world. Due to the enormous natural distribution of different plant species, India is considered as “Herbarium of World” and one of the 12 megadiversity countries. Today, medicinal plants and their bioactive compounds are increasingly recognized not only for its local therapeutic use but also for improvement in the economy of the nations. Iqbal (1993) has estimated that about 4,000–6,000 botanicals are of

commercial importance throughout the world. The increasing demand for plant-based medicine has resulted in overexploitation of several high-value medicinal plant populations. Robbins (2000) reported that 29% of total US plant species are facing a major threat due to excessive land use operation and overexploitation. If the ruthless and unscientific collection of medicinal plants from Himalayan regions continues, it will lead to the documented extinction of 19 plants species in the wild, 41 species suspected to become extinct in the recent future, 152 species in great danger of extinction, movement of 102 species towards the higher category of rarity and 251 plant species at greater risk and localized to a particular area with limited access (Walter and Gillett, 1998). Medicinal sector of IUCN has moved towards the identification of threatened plant species due to non-sustainable exploitation or other reasons. Walter and Gillett (1998) have reported about 34,000 out of 49,000 species to be globally threatened with extinction. Some of the medicinal plant species have slow growth rate, localized distribution and low population density which make them more prone to extinction (Kala, 2005; Nautiyal et al., 2002; Jablonski, 2004). Moreover, increasing biotic interference, habitat fragmentation and changing climatic conditions also lead to low regeneration potential of medicinal plants in the natural habitat (Kala, 2005). The weakening of legal, customary rules has resulted in increased exploitation of medicinal plant species (Kala et al., 2006). Destructive harvesting from temperate and alpine zones of Himalaya, India has caused alarming scarcity of genetic stocks of many high-value medicinal species. Ministry of the Environment, Forest and Climate Change (MOEFCC), India has recognized 29 plant species such as *Rauwolfia serpentina*, *Pterocarpus santalinus*, *Picrorhiza kurroa*, *Swertia chirata*, and *Nardostachys jatamansi* which are localized to a particular habitat and banned for export of these plants (Nishteswar, 2014). International Union for Conservation of Nature and Natural Resources (IUCN) has listed 121 plant species in red data book from the Himalayan regions, among these 17 are medicinal plants (Nayar and Sastry, 1987).

Currently, one of the major difficulties to study the traded and commercial details of medicinal plant products is due to its fragmentary reports on a national and international level. Therefore, different plant species with marked medicinal properties are being harvested at a local and regional scale for supply in international markets (Schippmann et al., 2002). Now, scientists are moving toward cultivation approach for the supply of excessive products at the commercial level, but active component/secondary metabolites are often very low in the monoculture conditions due to certain controlled conditions of cultivations (Palevitch, 1991; Uniyal et al., 2000).



**FIGURE 1.2** (See color insert.) An overview of the need for different conservation strategies of MAPs.

### 1.3.1 CONSERVATION STRATEGIES FOR MEDICINAL AND AROMATIC PLANTS

The progressive increase of developmental activities, gathering, and overexploitation as well as changing environmental situation has caused an alarming decline of medicinal plant wealth throughout the world. Therefore, conservation strategies have envisaged with primary goals of preservation of species, genetic diversity and sustainable use of plant products for human welfare (Chandra, 2016). Basically, there are four scientific techniques applied for the preservation of the diversity of medicinal plants. They are described under as

- a) **Legislation:** Rules of IUCN, CBD (Convention on Biodiversity) and environmental laws have been formulated by different countries

to protect the herbal flora by implementing forest act (1927), wild-life amendment act (1972), environment protection act (1986), and national biodiversity act (2002).

- b) ***In-situ* conservation:** It includes the conservation of specific biogeographic zones with intra- and inter specific genetic variation. National park, biosphere reserves, sacred sites, sacred groves, and wildlife sanctuary are principle policy decision process for in-situ conservation of biological and genetic diversity of medicinal plants at the national, international and global level. MOEFCC (India) has recognized 14 biosphere reserves, 91 national parks and 448 wildlife sanctuary including world heritage site, coral reefs, mangroves and Ramsar convention (for wetlands conservation) for ethnobiological preservation in their respective habitats (Chandra, 2016).
- c) ***Ex-situ* conservation:** It includes conservation of medicinal plants outside the natural habitats for long-term preservation such as seed bank, pollen bank and DNA libraries. Seed conservation is an important ex-situ approach, also called as an insurance policy against extinction of medicinal plants and cost has been estimated as little as 1% of in-situ conservation (Hawkes et al., 2012).
- d) **Cultivation:** It is an important approach to conserve threatened medicinal plant species to support the ever-increasing market demands. The strategy will be successful only with the immense help of public domestication programmes. There are many threatened plant species such as *Garcinia afzelii*, *Panax quinquefolius*, *Saussurea costus*, and *Warburgia salutaris* that can be marketed at a high price due to its cultivation approaches (Cunningham, 1994). However, domestication will also achieve conservation of threatened plant's diversity for selected plant species. Sometimes, cultivated plants have been found qualitatively inferior than wild plants. Chinese people prefer wild ginseng roots instead of cultivated ones because the cultivated plants did not possess the characteristic features as collected from the wild (Cunningham, 1994).

#### 1.4 MEDICINAL BIOPROSPECTING

The development of infectious diseases and the evolution of multi-drug resistance during the long course of human history has compelled the scientist

of the current generation to search the new medicines for disease treatment. In this scenario, medicinal bioprospecting provides a boom in the field of medicine and pharmacognosy (McClatchey, 2005). In general sense, at any time if a person is searching for food or other biological value in their environment, they are bioprospecting. Searching substances for medicines in the natural milieu are known as medicinal bioprospecting, which is a multidisciplinary venture involving various researchers and logical subjects (Juan, 2017). Medicinal bioprospecting may provide new leads against pharmacological targets such as cancer, HIV-AIDS, Alzheimer's disease, malaria, etc. Currently, there is a need for broad revise of natural products derived from plants (herbal remedies) (Tyler, 1999; Cardellina, 2002), which needs further refinement and research on medicines approved by Food and Drug Administration (FDA).

A current literature survey has shown that 60% of the drugs used for oncotherapy and more than 70% for the management of anti-infectious diseases recommended up to 2002 are from natural sources (Newman et al., 2003). Plant-derived drug molecules help in identifying the association between drugs and their target site and enhances the chances to develop more effective drugs by laboratory synthesis.

In modern medicine based disease therapy too, plants contribute significantly in novel drug discovery and development. Some of the important lead bioactive molecules of plant origin having a major development in medical science are under thorough clinical investigations as well as recommended by Food and Drug Administration (FDA) are listed in Table 1.1.

These compounds obtained from different parts of the plants like seeds of *Mucuna pruriens* are an important source of L-dopa which helps in the treatment of most important neuro-degenerative Parkinson's disease. Similarly, the bark of a yew tree (*Taxus brevifolia*), leaf of *Catharanthus roseus* and stem/bark of *Camptotheca acuminata* bears important photochemical compound having antitumor potential. Furthermore, some plants like *Galanthus woronowii* and *Gingko biloba* bear compound having anticholinesterase activity and helps in the treatment of the so called neuro-degenerative disorder, Alzheimer's disease.

Considering these facts, there is a need for bioprospection in order to provide the available natural source for treatment of health threats. In many instances, it has been found that the compounds isolated from the medicinal plants may not serve as the final drug, but they can comprise lead compounds for the development of potential drugs.

TABLE 1.1 Some Important Lead Compounds Obtained from Plants As a Source of Medicine

S. No.	Compounds	Medicinal plant	Treatment	References
1.	L-Dopa	<i>Mucuna pruriens</i>	Parkinson's disease	Cotzias (1969)
2.	Taxol	<i>Taxus brevifolia</i>	Cancer	Wani et al. (1971)
3.	Vinblastine & Vincristine	<i>Catharanthus roseus</i>	Cancer	Cragg and Newman (2005)
4.	Camptothecin	<i>Camptotheca acuminata</i>	Cancer	Dancey and Eisenhauer (1996)
5.	Combretastatin	<i>Combretum cafrum</i>	Cancer	Dark et al. (1997)
6.	Podophyllotoxin	<i>Podophyllum peltatum</i>	Antitumor	Canel et al. (2000)
7.	Galantamine	<i>Galanthus woronowii</i>	Alzheimer's disease	Sahoo et al. (2017)
8.	Ginkgolides	<i>Ginkgo biloba</i>	Alzheimer's disease	Yoo and Park (2012)
9.	Artemisinin	<i>Artemisia annua</i>	Malaria	Klayman (1985)
10.	Tiotropium	<i>Atropa belladonna</i>	Pulmonary disease	Van Noord et al. (2000)
11.	Reserpine	<i>Rauwolfia serpentina</i>	Antipsychotic, and antihypertensive	Singh (1955)

### 1.4.1 ECOLOGY AND BIOPROSPECTING OF MEDICINAL PLANTS

Over the course of evolution through thousands of years, the plants have developed an array of phytochemicals that had managed their survivability by fighting against, infectious diseases, predator attack, and facilitated food availability. Most of the today's pharmaceuticals constitute these plant-derived chemicals. The World Conservation Union (IUCN) in a recent survey found that 72,000 species of higher plants are used for extraction of medicines worldwide, constituting 17% of the higher plants of the world. The World Health Organization (WHO) has reported earlier that 80% of the world's population relies on traditional medicines for their fundamental health care and the scenario remains the same even today (IUCN, 2006). And for this, the pharmaceutical, agricultural and cosmetic industries depend on plant biodiversity thriving in the wild for their raw materials. *Cinchona officinalis* (the Cinchona tree) from South America is the source of vital quinine and quinidine which are the milestones in the herbal drug industry for their effectiveness against malaria and cardiac arrhythmias, respectively (Efferth et al., 2007). Digitalis has provided the synthetic drugs digoxin and digitoxin which has proved high efficacy against cardiovascular disorders such as atrial fibrillation and even heart failure (Ahmed et al., 2006). Willow tree provides aspirin which is still the most commonly used remedy for pain and inflammation, all around the world (Vlachojannis et al., 2011). There are ample examples of plant metabolites that have been searched for beneficial bioactivity for the welfare of human beings and society.

Progress in biotechnological and molecular biology research has revolutionized the natural product research by the introduction of the concept of 'Bioprospection.' Bioprospection deals with the search for novel biological resources through exploration of biodiversity which may impart some social and economic value. The pharmaceutical industry, agriculture sector, engineering, manufacturing, and many other industries are the basic stakeholders of bioprospection (Beattie et al., 2005).

Ecological studies on medicinal plants deal with the aspects of floristic composition, forest stand structure, distribution of species (Raunkier's frequency classes), species diversity, soil physicochemical properties, etc. (Szafer, 2013). The studies on species ecology hold much importance as they provide new hints/leads for novel drug research as well as the management and conservation of source plant species. There has been increasing attention of the scientific community for the ecological studies on medicinal plants for resource management worldwide.

The Rio de Janeiro Earth Summit on 5th June 1992 presented the Convention on Biological Diversity (CBD) with major emphasis on sustainable development, biodiversity conservation and equal benefit sharing resulting from utilization of biological resources (Dutfield and Suthersanen, 2008). A number of pharmacological projects are undertaken, and several phytochemical studies are performed every year to investigate the potential medicinal value of plant species. However, very few of them actually resulted in the development of novel drugs. Literally, the bioprospection initiatives are rightly phrased to be ‘in their infancy.’ Bioprospecting is widely broadcasted as a way to discover new phytochemicals to serve mankind; however, the shortcomings of the approach have largely made it farther from its goal (Buenz et al., 2004).

The major causes for such failure may be the methodology related to experimental flaws, the absence of repetition of experiments, non-replicable results, findings based on superficial studies, etc. The technologies utilized during the process are advanced and reliable, but the efforts for drug discovery projects are more or less confined in one direction only. The need is to coordinate multiple disciplines in the same direction to have some vital and significant outcomes (Siqueira et al., 2012). The ecological studies relating the medicinal plants can greatly increase the probability of success in such large bioprospection projects which can save money, time and labor. They provide new clues to predict the potential medicinal properties of certain plants (Albuquerque, 2010).

Chemical ecology is one of the very recent approaches in this context which has been utilized to predict the secondary metabolite allocation in higher plants. Such predictions are based on the widely accepted ecological theories of plant defense. The defense mechanism developed amongst plants against herbivores during the course of evolution led to the formation of a big pool of secondary plant bioactives (Donaldson and Cates, 2004). The trends and patterns related to the habitat of the plant can boost bioprospection efforts (Coley et al., 2003) which can be described as

- i) High molecular weight metabolites such as polyphenols get allocated in plants of dry forest (Ecogeographical pattern). For example, Caatinga plants dwelling in semi-arid regions are metabolically rich in phenolic compounds.
- ii) Medicinal plant species of humidity rich areas such as Atlantic forest allocate a higher amount of toxic compounds such as alkaloids.
- iii) Young leaves contain more active secondary metabolites than mature leaves. Even, they harbor several unique bioactive molecules.

- iv) The mature leaves of slow growing plants dwelling in the shade are proposed to have a greater level of chemical and physical defense in comparison to the mature leaves of fast growing plants of light conditions.
- v) 'Metabolic specialization' has been reported to be highest in ecotones (The transition zone between two different ecosystems).

The allocation of secondary metabolites has also been interpreted from the phylogenetic patterns (Leonti et al., 2013). The basal angiosperms *viz.* Magnoliids and Chloranthales have been reported to show more activity than the more evolved Asterids and Rosids. On the other hand, Monocots have been demonstrated to harbor a lesser amount of bioactives. The probable cause for such pattern has been attributed to the development of parallel leaf venation in monocots permitting lesser attack by herbivores and thus, fewer chances of the synthesis of secondary metabolites for chemical defense (Coley et al., 2003).

#### **1.4.2 BIOPROSPECTION OF PLANT ESSENTIAL OILS FOR MEDICINAL USES**

Diseases are considered as one of the major cause of mortality throughout the globe. Several laboratory studies have validated the diverse role of traditionally used plants and their parts for the treatment of human diseases. The disease curing ability is attributed to the presence of different phytochemicals including alkaloids, flavonoids, and terpenoids. Traditionally used medicinal plants are one of the chief sources of disease treatment among poor people who are unable to afford the cost of modern drugs. Traditional knowledge offers the source of new drugs from plants. Efficacy of traditional medicinal plants has very much influenced to pharmaceutical industries leading to theft of traditional knowledge for their economic benefit which is known as biopiracy. Global climate change and overexploitation are the major factors affecting the existence of numerous traditional medicinal plants used for therapeutic purposes. Under such conditions, searching novel sources of bioactive molecules from the very diverse pool of plant diversity, e.g., bioprospection, can relieve the pressure of overexploitation. Bioprospection is more important for developing countries because it not only increases the economy but also conserves biodiversity. The importance of traditional medicinal plants, few cases of biopiracy along with the need of bioprospection to fill the increasing demand of drugs is addressed briefly

From the early ages of civilization, people are using essential oils for food preservation, fragrance, taste, and disease treatment. Use of medicinal plant-based essential oils by many traditional systems of disease prevention such as Siddha, Unani, Ayurveda, and Chinese are known. Essential oils are defined as low molecular weight, a volatile and complex mixture of various compounds which possess several properties including antimicrobial and antioxidant potential (Ribeiro-Santos et al., 2017). They can be extracted from the whole plant or different plant parts like root, stem, leaf, flower, seed, and bark. The amount of extracted essential oil depends significantly on the type of plant material, the methodology used (Nakatsu et al., 2000), and geographical location. The chief constituents of essential oil can be grouped as terpenes and terpenoids while minor fractions are contributed by aliphatic and aromatic components (Bakkali et al., 2008). Due to their natural origin, and inclusion under generally recognized as safe (GRAS) category by Food and Drug Administration (FDA) (FDA, 2016), there is growing significantly in the application of EOs in food as well as pharmaceutical industry.

Indiscriminate utilization of synthetic antimicrobials by current generation has given rise to drug-resistant bacteria and fungi (Reichling et al., 2009). In order to alleviate the chances of resistance development in microbes, medicinal plants should be investigated for novel bioactive principles. Medicinal plants have been recognized as an important source of drug molecule for the treatment of many diseases. Many plants have found their place in traditional medicine like Ayurveda, Siddha, and Unani because of their disease-curing properties. Enormous evidences are available indicating the significance of plant extract in disease curing. Thus, bioprospecting medicinal plants would be helpful in chemical synthesis and commercial utilization of natural bioactive compounds. Some of the important activities of the essential oils are described below.

#### 1.4.2.1 ANTI-INFLAMMATORY POTENTIAL OF ESSENTIAL OILS

Essential oils obtained from cones of gymnosperm plants have been reported to possess the anti-inflammatory activities (Tumen et al., 2011). Wound repairing activity was assessed by linear incision and circular excision followed by histopathology. Anti-inflammatory actions of essential oils were determined against capillary permeability provoked through acetic acid. Essential oils extracted from *Abies cilicica* subsp. *Cilicica* and *Cedrus libani* were found good in wound models. The activities were suggested to be due to synergistic actions of individual bioactive molecules.

Essential oils from rest of the selected plant did not exhibit good potential. Öztürk and Özbek (2015) have described the anti-inflammatory actions of *Eugenia caryophylla* essential oil. The activity was comparable to that of etodolac (0.025–0.10 mL/Kg) and endomethacin (0.05–0.2 mL/Kg). The major components responsible for observed activities were identified as  $\beta$ -caryophyllen (44.70%) and eugenol (44.20%). The *Eugenia caryophylla* EO should be analyzed and tested further for large scale application. Anti-inflammatory, as well as antioxidant potentials of *Mentha piperata* essential oil, was evaluated against croton oil-induced edema in the mouse. The activities associated with essential oils were found to be due to the presence of major components like methyl acetate, menthone and menthol (Sun et al., 2014). The anti-inflammatory property of *Citrus aurantium* L. essential oil has been described by Khodabakhsh et al. (2015). The chronic and acute anti-inflammatory effects were the result of essential oil components linalool, linalyl acetate, nerolidol, *E,E*-farnesol,  $\alpha$ -terpineol, and limonene. The essential oil at 40 mg/kg dose demonstrated anti-inflammatory activity, which was comparable to sodium diclofenac (50 mg/kg). The observed effect supports the ethnomedicinal value of *Citrus aurantium* L. essential oil.

#### 1.4.2.2 ANTIMUTAGENIC POTENTIAL OF ESSENTIAL OILS

Perturbations in metabolic pathways are associated with the development of cancer and health-threatening diseases (De Flora et al., 1996). Use of plant-based products in the human diet as long practiced in Indian food system may be considered as one of the most effective approaches to avoid cancer. Essential oil of ginger (GEO) has been reported to possess potent antimutagenic activity (Jeena et al., 2014). Essential oil inhibited the mutation induced by sodium azide, extract of tobacco and 4-nitro-*o*-phenylenediamine in a dose-dependent manner. The study established the stimulatory action of GEO over phase II carcinogen-metabolizing enzymes and suggested its use in chemoprevention. The antimutagenic potential of essential oils from *Citrus sinensis* and *Citrus latifolia* was determined against mutation induced by Methyl-N<sup>1</sup>-nitro-N-nitrosoguanidine (MNNG) and Ethyl-N-nitro-N-nitrosoguanidine (ENNG) in *Salmonella typhimurium* TA100 (Toscano-Garibay et al., 2017). Essential oil from both species represented antimutagenic potential against MNNG as well as 2-amino-anthracene (2AA). However, antimutagenic effect against ENNG was shown by *Citrus latifolia* only. The observed antimutagenic activity was attributed to the presence of components like  $\beta$ -thujene,  $\alpha$ -myrcene, R-(+)-limonene,

and  $\gamma$ -terpinene. Antimutagenic efficacy of *Foeniculum vulgare* essential oil against cyclophosphamide (CP) induced genotoxicity in mice was documented by Tripathi et al. (2013). *Foeniculum vulgare* essential oil was effective in ameliorating the changes induced by CP such as decreased activities of enzymes like superoxide dismutase and catalase. Pretreatment with essential oil resulted in reduced chromosomal abnormality in bone marrow cells suggesting the antimutagenic activity.

#### 1.4.2.3 ANTIDIABETIC POTENTIAL OF ESSENTIAL OILS

Diabetes has long been recognized as disabling disease resulting mainly due to genetic and environmental factors as well as oxidative stress (Akram et al., 2011). Antidiabetic activity of essential oil obtained from *Syzygium aromaticum* and *Cuminum cyminum* has been presented by Tahir et al. (2016). The bioactivity assay of selected essential oil was based on its inhibitory action over the alpha-amylase enzyme. Concentrations of EO used for antidiabetic activity were taken in the range of 1 to 100 ppm. Highest antidiabetic activity was recorded at the highest dose. Five different emulsions of each essential oil were formulated by mixing in tween 80, ethanol and water. One of the emulsion preparations from *Syzygium aromaticum* (A5) and another from *Cuminum cyminum* (B5) demonstrated the highest alpha-amylase inhibitory activity as 95.30 and 83.09%, respectively. The antidiabetic responses were expected to be due to the presence of eugenol (main compound of *Syzygium aromaticum*) and  $\alpha$ -pinene (the main component of *Cuminum cyminum*). Antidiabetic activity of essential oils from *Citrus* peels based on inhibition of  $\alpha$ -glucosidase activity was demonstrated by Dang et al. (2016). Among six selected *Citrus* essential oils, Buddha's hand citrus essential oil showed remarkable inhibitory action on alpha-glucosidase with  $IC_{50}$  value 412.2 ppm. The major components of essential oil were identified as limonene and  $\gamma$ -terpinene. The synergistic action of this essential oil with antidiabetic drug acarbose enhanced the overall efficacy suggesting the use of plant-based essential oil for the treatment of diabetes. Essential oils from two species of *Acacia*, e.g., *Acacia mollissima* and *Acacia cyclops* have been assessed for their antidiabetic potency by determining the  $\alpha$ -glucosidase inhibitory activity (Jelassi et al., 2017). The  $IC_{50}$  value was found around 89 ppm which is equivalent to acarbose, the commonly used antidiabetic drug. A major component of *A. mollissima* was reported as (E, E)- $\alpha$ -Farnesene (51.5%) and (E)-cinnamyl alcohol (10.7%) whereas the active principle of *A. cyclops* was nonadecane (29.6%) and caryophyllene oxide (15.9%). Adefegha et

al. (2017) have illustrated the antidiabetic efficiency of essential oil from *Aframomum melegueta* and *Aframomum danielli*. The selected essential oils significantly minimized the activity of  $\alpha$ -amylase and  $\alpha$ -glucosidase.  $EC_{50}$  value of *A. melegueta* essential oil recorded for  $\alpha$ -amylase and  $\alpha$ -glucosidase was found to be 139  $\mu$ l/ml and 91.83  $\mu$ l/ml, respectively which were better as compared to *A. danielli*.

#### 1.4.2.4 ANTICANCER ACTIVITY OF ESSENTIAL OILS

Cancer is recognized as a group of many diseases. This life-threatening disease has emerged as the first reason for large mortality worldwide. Cancer cells are characterized by uncontrolled cell growth and invasion to newer locations through metastasis (Hanahan and Weinberg, 2011). Therefore, disease treatment should be based upon the inhibition of cell division. Essential oil from *Elsholtzia ciliata* has been reported to possess anticancer activity (Pudziuelyte et al., 2017). The main components of essential oil obtained through hydro-distillation were dehydroelsholtzia ketone (78.28%) and elsholtzia ketone (14.58%). Anticancer assay of essential oil was performed against human glioblastoma (U87), breast and pancreatic (Panc-1) cancer cell lines.  $EC_{50}$  value recorded for selected EO ranged from 0.017–0.021%. Viability test indicated considerably higher survivability of normal human fibroblast in comparison to cancer cell lines at the same essential oil concentration. Yang et al. (2017) have elucidated the anticancer properties of citrus by MTT assay. The essential oil exhibited a pronounced inhibitory effect against the proliferation of lung (A549) and prostate (22RV-1) cancer cell lines. Limonene (74.60%) was the major component of essential oil as determined by GC-MS analysis. The effectiveness of seed essential oil obtained from *Foeniculum vulgare* has been reported to possess anticancer activities against human cervical epithelioid carcinoma (HELA) and breast cancer (MDA-Mb) cell lines as revealed by MTT assay (Akhbari et al., 2018). Essential oil showed remarkable activity against both cell lines with  $IC_{50}$  value corresponding to less than 10 ppm. The major active components of essential oil responsible for anticancer activity were identified as Trans-Anethole (80.63%), followed by L-Fenchone (11.57%), Estragole (3.67%) and Limonene (2.68%) through GC-MS analysis. Recently, Han and Parker (2017) have reported the anticancer properties of commercially available essential oil derived from *Foeniculum vulgare*. The essential oil displayed anti-proliferative behavior against dermal fibroblasts.

### 1.4.3 CONSERVATION THROUGH BIOPROSPECTION AND ECONOMIC BENEFITS

The recent surge in the consumer preference for fascination towards herbal products has resulted in increased demands for plant-based consumables across the world which has definitely elevated the threat for their over-exploitation. In this context, statistical data/reports of habitat destruction and unsustainable collection are piling up day by day. Nearly, 150 plant species have got extinct in the wild due to the prevalent illegal trade and destructive harvesting in a situation where 90% species of plants utilized in the herbal industries are collected from the wild (Lange, 2002). Nearly, 3.5% of medicinal plant species of the Indian Himalayas have been categorized under different categories of threats as a result of the unethical collection, habitat loss and ecosystem disruption (Kala, 2005).

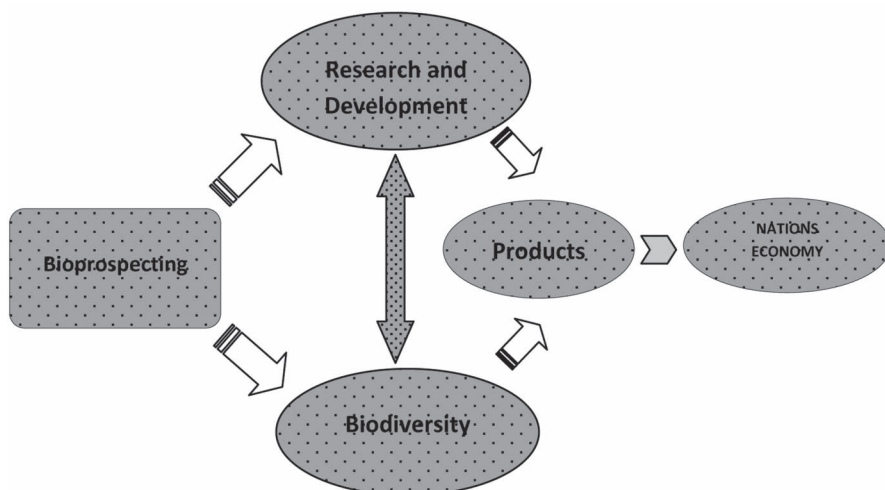


FIGURE 1.3 Graphical relationships between bioprospection and conservation.

### 1.4.4 BIOPROSPECTING AS GREEN DEVELOPMENTALISM

Bioprospecting natural resources have frequently been cited as a sustainable use of biodiversity, which can serve as a global reserve with anticipated fitting into rational property systems and world markets. Numerous research groups have presented the importance of biodiversity in global

development (Gari, 1999). Biological diversity and the ‘green’ World Bank, follow attempts to normalize global flows of ‘natural capital’ by means of so-called approach ‘*green developmentalism*’ which comprises the combination of conservation, development and equal benefit sharing. According to this hypothesis, nature is constructed as world cash (McAfee, 1999). Green developmentalism abstracts nature from its spatial and social contexts and strengthens the claims of global leaders to the greatest share of the earth’s biomass and all it possesses. Across the range of countries and institutions, there is now a prevalent approval that the ways to protect the environment is to value nature’s services, assign property rights, and trade these services within a global market (Liverman, 2004). Green developmentalism provides apparent insights into the current as well as emerging challenges of environmental sustainability, social and financial progress and looms to nature management that proposes to endorse a notable revolution to twist an ecologically caustic market into eco-savior.

#### **1.4.5 NEGATIVE ASPECTS OF BIOPROSPECTING**

Bioprospection includes the search for traditional knowledge or screening of biological diversity or indigenous information about plants, with an objective to develop commercial products which are beneficial for our society. The information collected through bioprospecting process is also called “bio-discovery,” with the aim to report natural products that can be utilized for beneficial results.

The developing countries don’t have much-developed techniques in comparison to developed countries, which can be used in the identification of valuable chemicals from plants. Thus, in order to bioprospect the chemical compound, bioprospector requires from developed countries. This way, bioprospecting is fruitful for our society, but this may lead to patent some biomaterials by multinational companies; as there are no guidelines available to reward the contribution of local people whose knowledge has now become the platform of drug designing and discovery. The illegal collection or patent of indigenous plant chemical compounds by the multinational companies for their own profit comes under biopiracy. From the 90s onwards there has been raised in cases related to biopiracy with patents and trademarks being used to acquire domination rights over native resources without simultaneous benefit sharing. Some examples of biopiracy are mentioned in Table 1.2.

**TABLE 1.2** List of Some Plant Resources Patented by Different Countries and Their Biopiracy Status

S. No.	Native country	Native resource	Biopirate country	Patent numbers	References
1.	China	<i>Momordica charantia</i>	USA	US Patent No. 5484889	Chang et al. (1996)
2.	China	<i>Camptotheca lowreyana</i>	USA	US Patent No. PP11959	
3.	India	<i>Basmati Rice</i>	USA	US Patent No. 6274183 and 5663484	Sahai et al. (2007)
4.	Philippines	<i>Cananga odorata</i>	France	N/A but used by several perfumeries in France	
5.	Philippines	<i>Lagerstroemia spp.</i>	Japan & USA	US Patent No. 5980904	
6.	India	<i>Curcuma longa</i>	USA	US Patent 5,401,504	Avantika et al. (2015)
7.	India	<i>Azadirachta Indica</i>	USA	US Patents Nos. 5420318, 5391779 and 5371254	Adhikari (2005)
8.	India	<i>Commiphora mukul</i>	USA	US Patent No. 6,113,949	Grain (2006)
9	Samoa	<i>Homalanthus nutans</i>	USA	US Patent No. 5,599,839	
10.	Thailand	<i>Croton sublyratus</i>	Japan	N/A	Sahai et al. (2007)
11.	Andean countries	<i>Chenopodium quinoa</i>	USA	US patent no. 5,304,718	Adhikari (2005)
12.	Amazon	<i>Banisteriopsis caapi</i>	USA	US patent PP 05751	
13.	South Africa	<i>Hoodia spp.</i>	UK	WO 9846243	
14.	Mexica	<i>Phaseolus vulgaris</i>	USA	US patent no. 5,894,079	Ratray (2002)
15.	Asia-Pacific	<i>Piper mythesiticum</i>	USA	US Patents Nos. 6405948, 6277396, 6080410, 6025363, etc.	Afreen and Abraham (2008)

Thus, bioprospecting can improve the ideal distribution of valuable plant chemical compounds throughout world, but the biopiracy weakens global justice (George, 2011).

## 1.5 BIOPROSPECTING MEDICINAL PLANTS FOR DRUG DISCOVERY AND THEIR CHALLENGES

Current world generation is more inclined and showing interest toward the alternative treatment especially, therapy based on plant-derived compounds (Simoes et al., 1999). The reason lies into important points such as side effect and inaccessibility of currently used therapeutics to poor people. Natural products from plant sources have long been recognized as a huge source of novel components. Many medicinal plants used are not associated with disease cure only, but several of them have religious values too. However, the industrial revolution has aggravated the formation of synthetic products for disease treatment purpose. Globally, approximately 25% of the drugs recommended for disease therapy are plant-originated, and currently, 121 bioactive molecules are under extensive application (Rates, 2001). World Health Organization has recognized 252 drugs as primary and necessary for human health management among which 11% are entirely plant derived. Some important plant produced bioactive molecules associated with human health are quinine and quinidine from *Cinchona* spp, atropine from *Atropa belladonna*, digoxin from *Digitalis* spp, vincristine and vinblastine from *Catharanthus roseus*, morphine, taxol from *Taxus baccata*, curcumin from *Curcuma longa*, azadirachtin from *Azadirachta indica*, reserpine from *Rauwolfia serpentina* and codeine from *Papaver somniferum*. According to an estimate (Yue-Zhong Shu, 1998), more than sixty percent of drugs commercially available in market or under clinical investigations, applied for treatment of tumor and infectious diseases are originated from natural sources indicating the significance of biomolecules synthesized by plants. So far, many of these drugs could have not been synthesized for commercial application and are still acquired from either cultivated or wildly growing plants, necessitating the conservation of medicinal plants diversity. Natural compounds from a large pool of plant's diversity can give the opportunity for designing as well as the synthesis of novel active principles with characteristics not yet demonstrated by many present-day used drugs (Hamburger and Hostettmann, 1991).

In spite of many evidences of drug discovery from medicinal plants, searching new drugs for diseases treatment is not so easy task. The process

needs the interdisciplinary efforts of expertise from medicinal chemistry, modern medical sciences, biotechnology, and molecular biology to improve the compounds at qualitative as well as quantitative level and also for maintaining harmony with other efforts being performed for drug discovery (Butler, 2004). According to an estimate, continuous effort for drug discovery may involve more than 10 years (Reichert, 2003) and cost greater than 800 million dollars (Dickson and Gagnon, 2004). Often, many of these rigorous, expensive experimental efforts result in no fruitful outcome. Surprisingly, only one out of 5000 lead phytochemicals has been estimated to be successful under clinical trials and approved for therapeutic purposes (Balunas and Kinghorn, 2005). The process of drug discovery is exhaustive and involves the key steps including lead identification, lead optimization, and lead development. Since the new drug development from medicinal plants is time-consuming, appropriate methods for plant collection, techniques of compound extraction as well as purification and equipments for the screening of active phytochemicals should be developed further for better results (Koehn and Carter, 2005). Advanced instrumentation techniques for compound identification such as NMR and MS should be applied for drug discovery purposes. One of the major hindrances in drug discovery is very low availability of bioactive principles that may not be sufficient for important steps of drug discovery. The problem can only be resolved by synthesizing these compounds under laboratory conditions which are again a hurdle for chemists as already has happened with many phytochemicals. Another solution to the problem may involve the synthesis of a compound with similar therapeutic properties.

## **1.6 FUTURE PROSPECTS**

Bioprospection of medicinal plants offers several advantages to human society especially the drug development. Analytical techniques have revealed the enormous diversity of components from medicinal plants. Many of the components have been found suitable for disease prevention in humans, and still, many more are under investigation for commercial application. Development in analytical instrumentation techniques like HPLC, NMR, XRD, FT-IR, and GC-MS will speed up the process of drug designing and synthesis. Essential oil components give the idea for the synthesis of lead molecules used in disease therapy. In view of widespread interest and importance of medicinal plants, research and development in the area should be promoted to get the maximum benefit.