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A.N.M. Alamgir

Therapeutic Use of Medicinal Plants and Their Extracts: Volume 1

Pharmacognosy

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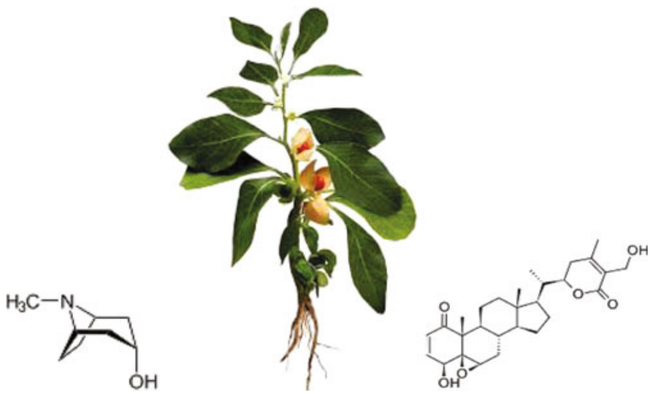
Therapeutic Use of Medicinal Plants and Their Extracts: Volume 1

Pharmacognosy

(Botany, pharmacology, therapy, culture and commerce of medicinal herbs)

For B. Sc. and M. Sc. Students



Tropane alkaloid - Tropine, *Withania somnifera*, Steroidal lactone - Withaferin A

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Dedicated to the memory of my beloved parents

Contents

Abbreviations

2,4,5-T	2,4,5-trichlorophenoxyacetic acid
2,4-D	Dichlorophenoxy acetic acid
4 CPA	4-chlorophenoxyacetic acid
5-MeO-DMT	5-methoxy-N,N-dimethyltryptamine, buffotoxin
AAS	Atomic absorption spectrophotometer
ABA	Abscisic acid
AC	Activated charcoal
AD	Anno domini
ADA	Adenosine deaminase
ADP	Adenosine diphosphate
AHAs	Alpha hydroxy acids
AHP	American herbal pharmacopoeia
AIDS	Acquired immunodeficiency syndrome
ALA	Alpha-lipoic acid
AMP	Adenosine monophosphate
ANF	American National Formulary
ANS	Autonomic nervous system
AP	African pharmacopoeia
API/APP	Active pharmaceutical ingredient/product
ATC	Anatomical therapeutic chemical
ATP	Adenosine triphosphate
BA	6-benzyladenine
BAP	6-benzylaminopurine
BC	Before Christ
BCG	Bacillus calmette-guerin
BDNF	Bangladesh national formulary
BHC	Benzene hexachloride
BNF	British National Formulary
BOL	Barcode of Life
BoNT	Botulinum neurotoxins

BP	British pharmacopoeia
BPC	British pharmaceutical codex
BSS	Balanced salt solutions
BTC	Behind-the-counter
C3/C4 pathway	Calvin-Basham (3 carbon acid) pathway / HatchSlack (4 carbon acid) pathway of CO2 assimilation
CA	Conservation agriculture
CAD	Charged aerosol detector
CAMs	Complementary and alternative medicines
CBD	Convention on biological diversity
CBOL	Consortium for the barcode of life
CCD	Charge-coupled device
CCEE	Countries of Central and Eastern Europe
CCK	Cholecystokinin
CE	Capillary electrophoresis
CE-DAD	Capillary electrophoresis with diode array detector
CF	Cystic fibrosis
CHD	Coronary heart disease
CIPIH	Commission on intellectual property rights, innovation and public health
CLA	Conjugated linoleic acid
CML	Cordyceps militaris lectin
CNS	Central nervous system
COMT	Catechol-o-methyltransferase
COMTRADE	Common format for transient data exchange
COX-1/2	Cyclooxygenase-1/2
CSIR	Council of scientific and industrial research
CTD	Common Technical Document
CTM	Chinese traditional medicine
CUOXAM	Ammoniacal solution of copper oxide
CZE	Capillary zone electrophoresis
DAD	Diode array detector
DDT	Dichlorodiphenyltrichloroethane
delta-9-THC	delta-9-tetrahydrocannabinol
DIM	Diindolylmethane
DMEM	Dulbecco's Modified Eagle's Medium
DMSO	Dimethyl sulfoxide
DMT	Dimethyltryptamine
DNA	Deoxy ribonucleic acid
DO	Doctor of osteopathy
DSHEA	Dietary Supplement Health and Education Act
ECM	Extra cellular matrix
ED	Erectile dysfunction
EDQM	European Directorate for the Quality of Medicines
EDTA	Ethylenediaminetetraacetic acid

EGCG	Epigallocatechin-3-gallate agency
ELISA	Enzyme-linked immunosorbent assay
ELSD	Electric light scattering detector
EMA	European medicines agency
EMEA	European medicines evaluation agency
EMEM	Eagle's Minimum Essential Medium
ENT	Ear, nose, and throat
ER	Endoplasmic reticulum
ESCOP	European Scientific Cooperative on Phytotherapy
EU	European union
FAO	Food and agriculture organization
FDA	Federal food and drug administration
FDCA	Federal food, drug, and cosmetics act
FID	Flame ionization detector
FOSHU	Foods for specified health uses
FYM	Farmyard manure
GA3	Gibberellic acid
GABBA	Gamma-aminobutyric acid A
GACP	Good agricultural and collection practice
GACPs	Good agricultural and collection practices
GC	Gas chromatography
GC-MS	Gas chromatography mass mapectrophotometry
GI	Gastrointestinal
GI	Geographical indications
GLC	Gas–liquid chromatography
GLP	Good laboratory practice
GMP	Good manufacturing practice
GnRH	Gonadotrophin-releasing hormone
GP	General practitioner
GPAIP	Good Plant Authentication and Identification Practice
GRs	Genetic resources
HA	Hyaluronic acid
hCG	Human chronic gonadotropin
HCH	Hexachlorocyclohexane
HEPA	High efficiency particle air filter
hGH	Human growth hormone
HILIC	Hydrophilic interaction chromatography
HIV	Human immunodeficiency virus
HMPC	Committee on herbal medicinal products
HMPC	Herbal medicinal products
HPLC	High-performance liquid chromatography
HPLC-DAD	HPLC coupled to diode-array detection
HPLC-ELSD	HPLC-evaporative light scattering detector
HPTLC	High-performance TLC
HR-MS	High-resolution mass spectrometry

HRs	Hairy roots
HSCCC	High-speed counter-current chromatography
HTS	High-throughput screening
HYV	High yielding variety
I3C	Indole-3-carbinol
IAA	Indole-3 acetic acid
IBA	Indole butyric acid
ICDRA	International conference of drug regulatory authorities
ICN	International code of nomenclature
ICP	Inductively coupled plasma
ICP-OES	Inductively coupled plasma-optical emission spectrometry
IDO	Indoleamine 2,3-dioxygenase
IGC	Intergovernmental Committee
IgE	Immunoglobulin E
IP	Indian pharmacopoeia
IP	Intellectual property
IPR	Intellectual property right
IR	Infrared
IRS	Infrared spectroscopy
IUCN	International union for conservation of nature
ITS	International transcribed spacer
JKMA	Japan Kampo Medicines Manufacturer Association
kD	Kilo dalton
KTTKS	Collagen pentapeptide: Lys-Thr-Thr-Lys-Ser
LC	Liquid chromatography
LC-MS	Liquid chromatography coupled to mass spectrometry
L-DOPA	Levodopa or L-3,4-dihydroxyphenylalanine
LHRH	Luteinizing hormone-releasing hormone
LOD	Loss on drying
LS	Longitudinal section
LSD	Lysergic acid diethylamide
MAO	Monoamine oxidase
MAOIs	Monoamine oxidase inhibitors
matK	Maturase K, a plant plastidial gene
MC	Moisture content
MCf	Maximum final moisture content
MD	Medical doctor
MEM	Minimum essential medium
MECC	Micellar electronic capillary chromatography
MEKC	Micellar electrokinetic chromatography
MEP pathway	Methyl D-erythritol 4-phosphate pathway/non-mevalonate pathway
MHRA	Medicines and healthcare products regulatory agency
MIR	Mid-infrared

MJ	Methyl jasmonate
MPAs	medicinal and aromatic plants
MPs	Medicinal plants
MPS I	Mucopolysaccharidosis type I
MS	Mass spectrometry
MS medium	Murashige and Skoog medium
Mw	Mass of water
NA	Numerical aperture
NAA	Neutron activation analysis
NAA	Naphthaleneacetic acid
NAPRALERT	Natural Medicines Comprehensive Database
NBSB	National Biological Standards Board
NCCAM	National Center for Complementary and Alternative Medicines
NE	Norepinephrine
NF	National formulary
NGA	N-acetyl-glucosamine
NHPD	Natural health products directorate
NIRS	Nearinfrared spectroscopy
NIS	Newly independent states
NMR	Nuclear magnetic resonance
NPK fertilizers	Nitrogen, phosphorus, and potassium fertilizers
NPs	Natural products
NSAIDs	Non-steroidal anti-inflammatory drugs
NTA	Notice to Applicants
omega-3 PUFAs	Omega-3 polyunsaturated fatty acids
MEG-3 brand omega-3 EPA/DHA	Eicosapentaenoic acid/docosahexaenoic acid
OPLC	Over-pressured layer chromatography
OTC	Over-the-counter
PAF	Platelet activity factor
PBS	Phosphate-buffered saline
PCPA	p-chlorophenoxyacetic acid
PEITC	Phenethyl isothiocyanate
PEP	Phosphoenolpyruvate
Ph. Int.	International pharmacopoeia
PIPs	Plant-incorporated protectants
POM	Prescription only medicines
POPs	Persistent organic pollutants
PP2A	Protein phosphatase-2A
PVP	Polyvenyl pyrrolodin
QDG	Quality Drafting Group
QP	Qualified Person
QTLC	Quantitative TLC
R&D	Research and development

Rad-br	Radium bromatum
RBC	Red blood corpuscles
rcbL	Ribulose bisphosphate carboxylase large chain
RECOMBIVAX HB	Recombinant hepatitis B vaccine
Rf	Retention factors or relative to front, determined as distance moved by the compound/distance moved by the solvent
RH	Relative humidity
RIA	Radioimmunoassay
RNA	Ribonucleic acid
RP	Reversed phase
RP-IPC-HPLC	Reversed-phase ion pair chromatography-HPLC
RPMI	Roswell park memorial institute
SA	Salicylic acid
SAX-HPLC	Strong anion exchange-HPLC
SCID	Severe combined immunodeficiency
SEC	Size exclusion chromatography
SH medium	Schenk and Hildebrand medium
SI	Stomatal index
SOD	Superoxide dismutase
SSM	Siddha system of medicine
STN	Scientific and technical network
TBGRI	Tropical Botanic Garden and Research Institute
TCA cycle	Tricarboxylic acid cycle
TCAM	Traditional/complementary and alternative medicine
TCM	Traditional Chinese Medicine
TEM	Transmission electron microscope
T DNA	Transfer DNA
TeNT	Tetanus neurotoxin
THM	Traditional herbal medicine
TK	Traditional knowledge
TKDL	Traditional knowledge digital library
TKRC	Traditional knowledge resource classification
TLC	Thin-layer chromatography
TL DNA	Left T DNA
TMK	Traditional medical knowledge
tPA	Tissue plasminogen activator
TR DNA	Right T DNA
TS	Transverse section
UNCTAD	United Nations Conference on Trade and Development
UNESCO	United Nations Educational, Scientific, and Cultural Organization
US	Ultrasound
USP	United States Pharmacopeia
USPTO	United States Patent and Trademark Office

UV	Ultraviolet
VIDS	Venation Image Database System
wb	Wet basis
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WWF	World Wide Fund for Nature
XRFS	X-ray fluorescence spectroscopy

Chapter 1
Introduction

Abstract Pharmacognosy is the scientific study of crude drug principles of natural origin including their history, collection, preparation, standardization, use, cultivation, and commerce. Herbal preparations from plant, animal, and mineral are medicinal and promote health beyond basic nutrition. Pharmacognosy is a multidisciplinary subject and requires knowledge of botany, ethnobotany, phytochemistry, microbiology, pharmacology, pharmaceutics, etc. Botany and ethnobotany are important for identification, genetics, cultivation, etc. of drug plants; chemical characterization includes isolation, identification, and quantification of drug plant constituents; and pharmacology informs about the biological effects of the crude drugs on cell cultures, animals and humans. The majority of the drugs available in the market today are obtained mostly from natural sources, and about 80% of the world's rural people rely on herbal medicine for primary health care. The renaissance of herbal medicine in the recent years has created an urge for intensive studies in the field of pharmacognosy to ascertain the quality, efficacy, and safety of the herbal products. Medicinal plants are widely used across the world in different traditional systems of medicine including Ayurveda, Unani, Homeopathy, Chinese, as well as in the medicinal systems of aborigines. Medicinal plants are the sources of drug components, lead compounds, excipient, etc. of modern medicine. The secondary metabolites (e.g., alkaloids, phenolics, terpenoids, etc.) of drug plants provide the therapeutically active principles of herbal medicine, and more than 180 therapeutic principles of natural origin are used in modern medicine (e.g., ajmalicine, allicin, aspirin, artemisinin). In addition to wild sources, medicinal herbs are now cultivated by agronomic and biotechnological methods to meet the requirement of their smoothness and quality to consumers and trade market. The international market is expanding, about 2500 species of medicinal plants having about 400000 tons, and US$ 1.2 billion were traded during the 1990s and the value is likely to touch US$ 5 trillion by 2050.

Keywords Pharmacognosy · Crude drugs · Secondary metabolites · Herbal trade

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Pharmacognosy is involved in the studies of plants, animals, and other natural sources that yield crude drugs and drug substances including their taxonomic identity; chemical, physical, and biological properties of crude drugs; and methods of cultivation, harvesting, processing, storing, and marketing as well as extraction, preparation, and therapeutic use of crude drugs.

1.1 Therapeutic Use of Medicinal Plants and Their Extracts: A Historical Perspective

The medicinal use of plants and their extracts in health care is as old as the history of human society. Since ancient times, the natural products (e.g., products from plants, animals, minerals) have been the basis of treatment of human diseases in many cultures across the world. The beginning of the medicinal use of plants or their extracts was instinctive, people tried to use plants of their living environment for curing illness or discomfort, and they acquired knowledge about the therapeutic use of plants through tireless indiscriminate random efforts years after years but the exact time is yet to be explored. The archeological evidence related to the medicinal use of plants dates back to the Paleolithic period (at least 60,000 years ago), while the written evidence dates back to the Sumerians (over 5000 years ago). Papyrus, baked clay tablets, parchments, manuscript herbals, etc. are some examples of ancient recorded documents on the medicinal use of plants.

Different ancient cultures developed their own herbal system independently, almost in isolation but also some systems were developed elaborately in a more organized way (e.g., Chinese herbal medicine, Ayurveda, Unani) in the past. It is only at the beginning of the nineteenth century the term 'pharmacognosy' was coined for the first time by J.A. Schmid (1759–1809) in his handwritten manuscript 'Lehrbuch der Materia Medica', published in 1811 after his death, and later C.A. Seydler in 1815 use the term in his book 'Analectica Pharmacognostica' to mean the scientific study of medicinal herbs. Modern medicine recognizes herbalism as a form of alternative medicine. Phytotherapists use extracts from plants or parts of plants (e.g., whole herbs, roots or leaves seeds) but do not isolate particular phytochemicals. However, they now try to explain herb's actions in terms of their chemical constituents (Vickers and Zollman 1999; Langmead and Rampton 2001).

Medicinal plants are capable of synthesizing thousands of diverse bioactive constituents including alkaloids, terpenoids, phenolics, which are more efficient compared to a modern biosynthetic laboratory. The search for isolation of the active drug principles from plant extract began in the early part of the nineteenth century, and the first purely synthetic drugs based on natural products were formulated in the middle of the nineteenth century (Schulz et al. 2001). A large number of plant-derived active compounds is now used in modern medicine, and these compounds show a positive correlation between their modern therapeutic use and traditional use of the source plants (Fabricant and Farnsworth 2001; Pan et al. 2013).

Chemical compounds of herbal origin and that of the conventional drugs mediate their effects on the human body through similar processes, i.e., herbal medicines do not differ greatly from conventional drugs in terms of their mechanism of action and this enables herbal medicines to be as effective as conventional medicines (Lai and Roy 2004; Tapsell et al. 2006). Phytochemicals of medicinal plants and their extracts may function as analgesics, antitussives, antihypertensives, cardiotonics, antineoplastics, antimalarials, antioxidant, antiseptic, diuretic, nervous system stimulant, sedative, expectorant, digestive agent, etc. and play important role in the development of many clinically useful agents. Medicinal plant constituents like aspirin, atropine, opium, digitalis, dioxin, codeine, morphine, quinine, etc. have a long history of use in traditional as well as modern medicine. Drug principles like inulin, digoxin, morphine and codeine, quinine are derived from dahlias, foxglove, poppy, cinchona respectively (Meskin et al. 2002). Seven drug principles are now in use clinically for various types of cancers, e.g., taxol, vinblastine and vincristine, topotecan and irinotecan, and etoposide and teniposide derived from *Taxus* sp., *Catharanthus roseus*, *Camptotheca accuminata*, and *Podophyllum peltatum*, respectively (Patwardhan et al. 2003).

A large section of the population in developing countries, up to the present time, rely on traditional herbal medicine for their primary care need because it is affordable and easily accessible source of treatment (WHO 2001a, b, 2002a, b, c, 2005), although the development and mass production of chemically synthesized drugs over the past 100 years have revolutionized health care in most parts of the world. In Africa about 90% and in India 70% of the population depend on traditional medicine. In China, traditional medicine accounts for around 40% of all health care delivered, and more than 90% of general hospitals have units for traditional medicine (WHO 2005). Traditional medicine in the name of CAM is becoming more and more popular in the developed countries like Germany, Australia, Canada, USA, Belgium, France, etc. (Marstedt and Mochus 2002; WHO 2002a). Traditional systems' medicines have been serving the rural communities from antiquity; however, they were officially recognized in 1978 by the Alma-Ata Declaration on primary health care (PHC) as important resources in achieving health for all (WHO 1978). Safety, efficacy, and quality control of herbal medicines are still crucial and problematic because of many factors (e.g., lack of uniform standards and methods, inadequate research). Double-blind clinical trials may be helpful to ensure safety, efficacy, and quality of the herbal products (Vickers 2007).

Pharmacognosy has a long history of development, started with the desperate search for medicinal plants to alleviate illness in antiquity through guess work, trial and error, quackery, etc. and culminated into its development as a multidisciplinary science of crude drugs. It is now a branch of modern medicine that studies medicines from plant, animal, mineral, and other natural sources. Pharmacognosy includes phytochemistry as an important branch, concerned with the determination of the bioactive ingredients of medicinal plants, their origin, classification, quality and quantity assessment, methodology as well as analysis of their beneficial and harmful effects on human health. Phytochemistry also studies metabolomics in relation to functional genomics and systems biology.

1.2 Pharmacognosy: A Multidisciplinary Science of Crude Drugs

Pharmacognosy is the scientific study of crude drugs (fresh or dried and unprocessed material) from natural sources like plants, animals, and minerals. Pharmacognosy gives a sound knowledge of the vegetable drugs under botany and animal drugs under zoology. Plant, the oldest source of drugs, provides a large stock of rich, complex, and highly diversified structures of phytochemicals which are unlikely to be synthesized even in a biosynthetic laboratory. Almost all parts of the plants are used or drug source. For example, leaves of *Digitalis purpurea*, *Eucalyptus globulus*, *Nicotiana tabacum*, *Atropa belladonna*; flowers of *Syzygium aromaticum*, *Crocus sativus*, *Papaver somniferum*, *Catharanthus roseus*, *Rosa damascena*; fruits of *Coriandrum sativum*, *Citrullus colocynthis*, *Foeniculum vulgare*, *Senna* spp., *Physostigma venenosum*; seeds of *Nux vomica*, *Ricinus communis*, *Physostigma venenosum*, *Strophanthus* spp.; stem of *Chondrodendron tomentosum*, bark of *Cinchona* spp., *Holarrhena antidysenterica*, *Cinnamomum zeylanicum*, *Atropa belladonna*, *Hyoscyamus niger*; wood of *Quassia amara*, *Santalum album*; roots of *Carapichea ipecacuanha*, *Rauvolfia serpentine*; rhizome of *Curcuma longa*, *Zingiber officinale*, *Valeriana officinalis*, *Podophyllum peltatum*, etc. are some of the common crude drugs of plant origin. Similarly, animal source includes pancreas for insulin, urine of pregnant women for human chorionic gonadotropin (hCG), sheep thyroid for thyroxin, cod liver for vitamins A and D, anterior pituitary for pituitary gonadotropins, blood of animals for vaccines, stomach tissue for pepsin and trypsin, etc.; and minerals such as iron, mercurial salts, zinc as zinc supplement, gold salts, iodine, and iodine supplements are used for anemia, syphilis, wounds and in eczema, rheumatoid arthritis, antiseptic, and iodine supplements, respectively. Some of these, however, are now replaced by better drugs. Other animal sources include honey from bees, beeswax from bees, bufalin from toad, musk oil from musk, spermaceti wax from sperm whale, wool fat (lanolin) from sheep, carminic acid from cochineal, venom from snake, etc. Botanical source of crude drugs dominates over animal and mineral sources (Rates 2001). The term herb includes whole plant (e.g., *Eclipta alba, Euphorbia hirta, Centella asiatica*, etc.) and also different plant parts. Plant preparations, animal, and mineral products are said to be herbal or medicinal when they are used to promote health beyond basic nutrition.

The pharmacognostical study of crude drugs from plant and animal sources includes botany, zoology, chemistry, and pharmacology as basic subjects. Pharmacognosy embraces a broad spectrum of biological and socio-scientific subjects. Ethnobotany, marine biology, microbiology, biotechnology, phytochemistry, zoopharmacognosy, marine pharmacognosy, analytical pharmacognosy, herbal formulations, nutraceuticals, cosmeceuticals, etc. are also included as subject matter of pharmacognosy.

Botany and zoology include the identification (taxonomy), genetics, breeding, pathology, etc. Taxonomic identity is fundamental for pharmacopoeial and quality control purposes, and by applying broader biological knowledge, one can improve the cultivation and culture methods for both plants and animals of therapeutic importance. Chemical characterization includes isolation, identification, and quantification of constituents in plant and other animated materials. Pharmacology studies the biological effects that the chemicals in medicinal plants and other natural sources have on cell cultures, animals, and humans (including pharmaceutics, clinical pharmacy). However, in the nineteenth century and even at the beginning of the twentieth century, pharmacognosy was a branch of medical science involving crude drug practices and the main focus was on the botanical aspects of the crude drugs such as description and identification of drugs in their whole state and in powder form for pharmacopoeial identification and quality control purposes.

Ethnobotany plays important role in drug discovery and many important modern drugs like digitoxin, reserpine, tubocurarine, ephedrine, ergometrine, atropine, vinblastine, and aspirin have been discovered by following leads from the folk uses (Anyinam 1995). Chemistry, pharmacology, microbiology, and biochemistry play vital role in pharmacognostical studies involved in isolation, identification, characterization, biotransformation, and discovery of lead compounds and new drugs from natural sources. Molecular biology, genomic science, biotechnology, and bioinformatic tools have a deep impact on drug discovery and development. Marine-derived bioactive pharmaceuticals and nutraceuticals provide a plethora of health benefits including antioxidant, anticancer, antiviral, anticoagulant, antidiabetic, antiallergy, anti-inflammatory, antihypertensive, antibacterial, and radioprotective activities (Barrow and Shahidi 2008; Venugopal 2008; Wijesekara et al. 2011). Zoopharmacognosy is a branch of pharmacognosy that deals with the self-medication behavior of non-human animals, and such behavioral study of animals may definitely enhance the discovery and development of new drugs. Analytical pharmacognosy, by applying different analytical methods, determines different physical and chemical constants such as ash values, extractive values, moisture content and loss on drying (LOD), volatile oil content, bitterness value, microbial load, pesticides, heavy metals and radioactive contaminants, foreign matters in various herbal drugs. Determination of R*f* value following chromatography and chemical tests is important for quality control of herbal drugs. Adulteration of crude drugs is detected by microscopic, physical, organoleptic, chemical, biological, and other methods of evaluation. Herbal formulation indicates composition product (single or multiple herbs), dosage form (quantity), and provides other information regarding use (therapeutic, nutritional, cosmetic), benefits, and contradictions. Assessment of quality, stability, safety, and efficacy are essential for standard herbal formulation.

With the renaissance of pharmacognosy in the twenty-first century, the conventional botanical approach of pharmacognosy has been extended up to molecular and metabolomic levels (Huang et al. 2009; Dhami 2013). Pharmacognosy has been advanced and extended up to a significant extent to cover a wide spectrum of the natural medicine. Under the circumstances of prevalent adulteration, inappropriate formulation, intoxication, plant and drug interactions, etc. leading to life risk adverse or lethal reactions (Elvin-Lewis 2001; Talalay 2001), proper double blind clinical trials are needed for the improvement of quality (identity, purity, consistency, etc.), efficacy (therapeutic indications, clinical studies, pharmacological investigations), safety (adverse reactions, drug interactions, contraindications, precautions) of the herbal products before recommendation for therapeutic use (Ernst 2007; Vickers 2007; Shinde et al. 2008; Blondeau et al. 2010).

1.3 Importance of Pharmacognosical Study and Development CAMs Concept

Pharmacognosical studies put due emphasis on origin and use of natural products as drugs, sweeteners, flavorings, colorings, cosmeceuticals, nutriceuticals, etc. Drugs of natural origin are intended for use in the diagnosis, cure, prevention, etc. of diseases, and they are staging a comeback all over the world. Many modern drugs available in the market for use today are obtained either directly from natural sources like plants, microbes, animals, and minerals or indirectly from synthetic and semisynthetic mechanism using the lead compounds of natural origin as a template (Fabricant and Farnsworth 2001). The extracts of folk medicine, natural products, or related substances account for 30% of the top 35 natural product-based drugs sold worldwide in recent years (Butler 2004). Natural products and their derivatives represent more than 50% of all the drugs in modern therapeutics (Pan et al. 2013). Over three-quarters of the world population and about 80% of the worlds' rural people rely on herbal medicine for primary health care (Sarkar 1996; WHO 2002c; Sakarkar and Deshmukh 2011). In developed country like USA, plant drugs constitute as much as 25% of the total drugs, while in developing countries like China and India, the contribution is as much as 80% (Joy et al. 1998). Herbal medicines have all-natural ingredients, readily available, much cheaper compared to high-value Western medicine; they provide an excellent source of alternative medicinal therapy, very effective with chronic conditions (arthritis), do not result in long-term effects on the body, have multipurpose benefits (ginger, peppermint), good in boosting the immune system, best for people who are allergic to various types of drugs, and can be used to cure people of all ages. It is also believed that herbal drugs are safer and more effective with fewer side effects than modern pharmaceutical drugs. High value of the modern Western drugs discourses many people living in the developing countries as they need to spend about 40–50% of their total wealth for health care purposes Thus, the use and popularity of medicinal plants from which the herbal drugs are produced is much more in the developing countries than the developed world. However, herbal medicines have some negative aspects, e.g., non-availability of prescription or dosage for herbal medicines, they are slow in action, not good for serious trauma (broken bones) or heart attack, can react with the pharmaceutical drugs, unregulated, some are not safe to use, some are toxic and need professional supervision (calamus, comfrey, chaparral, etc.).

Table 1.1 Usage of TCAM in developing and developed countries in % of the population

Developing Country	Usage of CAM in %	Developed Country	Usage of CAM in %
Uganda	60	Belgium	31
Tanzania	60	USA	42
Rwanda	70	Australia	48
India	70	France	49
Benin	80	Canada	70
Ethiopia	90	–	–

Source WHO (2002a). Traditional Medicine Strategy 2002–2005, World Health Organization, Geneva

The herbal drugs, sweeteners, flavorings, colorings, cosmeceuticals, nutriceuticals, etc. today symbolize safety in contrast to the synthetics that are regarded as unsafe to human and environment. The dependence on synthetics of the modern age is over and people are returning to the naturals with hope of safety and security. The increase of population, inadequate supply, high price of allopathic drugs, high cost of treatment, side effects, and development of microbial resistance to antibiotic drugs have led to the increased dependence on the use of herbal medicines for a wide variety of diseases (Pathare and Wagh 2012). Plants have been used successfully as medicines in every continent throughout the history. The practice of herbal medicine is well established in Asia and Africa, and the use of herbal products as complementary and alternative medicines (CAMs) is becoming popular rapidly in Europe, North America, and Australia (Table 1.1). Now, the use of phytomedicines as well as phytonutrients (nutraceuticals) continues to expand rapidly across the world for the treatment of various diseases (WHO 2004).

1.4 Medicinal Plants and Their Metabolites of Pharmacognostical Importance

Out of the total 250,000–500,000 plant species on earth (Borris 1996), more than 80,000 are known as medicinal plants and about 35,000–70,000 species are used medicinally across the world. The number of medicinal plants used in different countries may exceed 1000 species (Sofowora 1993). A list of medicinal plants prepared by WHO from the late 1970s contained 21,000 species (Penso 1980), and now it is assumed that, out of the global total 422,000 flowering plant species, the number of plant species used for medicinal purposes across the world is more than 50,000 (Govaerts 2001; Bramwell 2002; Schippmann et al. 2002). However, only 1–10% of them have been studied chemically and pharmacologically for their potential medicinal value (Verpoorte 2000).

In China, 4941 species plants out of the total 26,092 are used (18.9%) as drugs in traditional medicine (Duke and Ayensu 1985). In India, more than 45000 different plant species grow, and out of them, about 15,000–20,000 plants (3.3–4.4%) have good medicinal value. However, only 7000–7500 species are used by traditional communities for medicinal purposes (Joy et al. 2001). In Bangladesh, more than 5000 higher plant species grow (Mia 1990) and about 1000 plant species (20%) are considered to have medicinal properties. About 455–747 plant species of Bangladesh have been described with their specific medicinal properties (Ghani 2003; Yusuf et al. 2009). Most of these medicinal plants are used in the preparation of Ayurvedic, Homeopathic, Unani, and other indigenous systems of medicine in Bangladesh. Among the indigenous systems of medicine, Ayurveda and Unani are most ancient (1500–800 BC), most developed, and widely practiced in the Indian subcontinent. Traditional medicines are also practiced in Tibet, Mongolia, and Thailand. China has demonstrated the best use of herbal medicine in providing primary health care, and its use dates back to 3000 BC, when the Chinese were already using over 350 herbal remedies.

The herbal drugs are derived from whole plant and different organs of plant (organized drugs), and also some drugs are prepared from excretory plant products (unorganized drugs). Green plants synthesize alkaloids, phenolics, terpenoids, and a variety of other secondary metabolites. The terms 'secondary metabolites' and 'natural products' are synonymous, exhibit very wide structural diversity (Kinghorn et al. 2009), and can be found as active ingredients in non-prescription and prescription drugs (pharmaceuticals) as well as in other herbal products (Gurib-Fakim 2006; Schmidt et al. 2007). Among the innumerable number of bioactive therapeutic principles of plant origin used in modern medicine, some of the examples are ajmalicine, allicin, aspirin, artemisinin, atropine, berberine, camptothecine, capscicine, catechin, cocaine, codeine, curcumin, digoxin, diospyrin, digitoxigenin, digoxigenin, elipticine, emetin, ephedrine, forskolin, glycyrrhizin, gossypol, homoharringtonine, indicine N-oxide, magnolol, morphine, nerrifolin, nimbidin, paclitaxel, pilocarpine, plumbagin, podophyllin, podophyllotoxin, pristimerin, quassinoids, quinine, rescinnamine, reserpine, ricin, scopolamine, sophoradin, taxol, thevenerin, topotecan, tubocurarine, vinblastine, and vincristine. These alkaloid, phenolic, and terpenoid compounds constitute the pharmacologically active drug principles, and these bioactive secondary metabolites are synthesized by two principal pathways: (i) shikimic acid pathway that produces a pool of aromatic amino acids leading to the synthesis of phenolics (lignins, tannins, quinines) and alkaloids and (ii) acetyl-CoA mevalonic acid pathway in which a vast array of terpenoids are formed (Eisenreich et al. 2004; Mustafa and Verpoorte 2007; Ramawat et al. 2009). They are the examples of single entity plant drugs, which mostly treat serious medical disorders and at present about 50% of the total plant-derived drug sales come from single entities, while the remaining 50% come from bulk herbal remedies. Where the active molecule cannot be synthesized economically, the product must be obtained from the cultivation of medicinal plant. Allicin, aspirin, artemisinin, atropine, camptothecin, capscicine, codeine, curcumin, digitoxigenin, digoxigenin, ephedrine, gitoxigenin, morphine, podophyllotoxin, taxol, and tubocurarine are among those major plant drugs for which no synthetic one is currently available. Some important chemical intermediates useful for manufacturing the modern drugs are also obtained from plants (e.g., diosgenin, solasodine, β-ionone). Modern medicine has adopted a number of plant-derived drugs, viz. (a) anticancer drugs (ajmalicine, vinblastine, vincristine from *Catharanthus roseus*), (b) hypotensive-tranquilizer drugs (rescinnamine, reserpine from *Rauvolfia serpentina*), (c) antimalarial drug (quinine from *Cinchona sp.*), and (d) antiglaucoma drugs (pilocarpine from *Pilocarpus jaborandi*). The estimated value of plant-based drugs is nearly US$ 45000 million a year.

1.5 Pharmacognosy and Trade of Medicinal Plants

Plant-derived drugs offer a stable market worldwide, and plants continue to be an important source for new drugs. The international trade in herbal products is a large and expanding trade. It is estimated that about 2500 species of medicinal plants are traded in the international market (Hersch-Martínez 1995). An average of 400,000 tons of medicinal plants, valued at US$ 1.2 billion, was estimated to be traded annually during the 1990s (Heywood 2000). The world market for plant-derived drugs and aromatics may account for >US$ 70 billion and is likely to touch US$ 5 trillion by 2050. The main markets include Europe, North America, and Asia. Europe, which accounts for about 50% of the world market, is the largest (Anonymous 2000). The three leading exporting countries are China, India, and Germany (Kate and Laird 1999). India, a close neighbor of Bangladesh, ranks second in the world after China in the export of medicinal plants. The global trade of medicinal plants stands at US$ 7592 million in 2011, and of these China and India's share were around US$ 1329 million and US$ 790 million, respectively. On the other hand, Bangladesh earns about US$ 20,000–25,000 annually by exporting roots of *Rauvolfia serpentina* and expends a huge amount of foreign exchange for importing many useful herbs. The scientific study of traditional medicines, derivation of drugs through bio-prospecting and systematic conservation of the concerned medicinal plants are thus of great importance.

Forests are veritable storehouses of biological diversity (at genes, species and ecosystems levels) and forest biodiversity is the basis for more than 5000 commercial products including herbal medicine, food and clothing (Anonymous 2011). Deforestation, forest degradation, depletion, indiscriminate extraction of forest resources etc. are major threats to biodiversity and generation of commercial products worldwide. With forest biotopes being an irreplaceable source of new drugs (e.g., taxol), deforestation can destroy genetic variations irretrievably. The major system of indigenous herbal medicine (e.g., Ayurveda, Unani) in Bangladesh, as elsewhere in the world, has reached a very critical phase due to scarcity of raw drugs because of deforestation, degradation, and others. Natural forests, the living treasure of plant and animal diversity, have already been destroyed, left about 8% only at present as against a mandatory 25% of the land area of Bangladesh. Many valuable medicinal plants are under the verge of extinction. The 'Red Data Book of Vascular Plants of Bangladesh' has 427 entries of endangered species, of which 28, 124, 81, 100, and 34 are considered extinct, endangered, vulnerable, rare, and insufficiently known species, respectively (Khan et al. 2001). Natural forest should be regenerated, and forest biodiversity should be conserved for the sake of the indigenous systems of herbal medicine and others because forest provides habitat for innumerable plants, animals and microorganisms; maintains delicate ecological balance, conserves soil and water, and controls floods, drought, and pollution.

1.6 Traditional and Modern Pharmacognosy

Herbal medicine as the oldest science has been in use to alleviate disease and suffering of human being ever since the onset of primitive civilization. The use of plant, animal, and mineral products in the treatment of disease as well as their trade between cultures have been known for thousands of years. About 200 years have been elapsed since the term 'pharmacognosy' was introduced by J.A. Schmidt (1759–1809) for the first time and C.A. Seydler used this term in his book in 1815. Traditional pharmacognosy at the beginning was concerned mainly with flowering plants and their products and later on other groups of organisms including animals, marine organisms, and microbes were considered as legitimate material for study by pharmacognosists. Pharmacognosy has evolved considerably during the past 200 years. At the beginning of the twentieth century, pharmacognosy was developed mainly on the botanical side and was concerned with the description and identification of the crude drugs as well as with their history, collection, preparation, storage, and trade. Before the advent of modern analytical chemistry, emphasis was on the traditional botanical techniques such as macroscopical and microscopical characterizations of plant material for identification of crude drugs, differentiation of crude drugs from related species, and detection of adulteration. Microscopy was the only method of much use when the drug was in powdered or finely broken form. Traditional pharmacognosy emphases identification, authentication, and quality control of crude drugs. Identification of crude drugs required the basic knowledge of the subject botany and which are evident from the earliest records of medical history depicted in many ancient stones, bones, papyri, and texts of herbal medicine. For centuries, botany was a part and parcel of medicine because plant identification was a prerequisite for all physicians in the development of drugs. In fact, there have been notable developments in different areas of traditional pharmacognosy including production, isolation, and characterization techniques of drug principles, conservation of source materials, and commerce of the crude drugs. Some plants when their local wild sources become exhausted due to over extraction (e.g., *Catharathus roseus*, *Coleus forskohlii*, *Arnica montena*, *Taxus brevifolia*, *Leucojum aestivum*) necessitate conservation, cultivation, and/or artificial production by cell or tissue culture in order to avert the supply crisis. In recent times, more significant is the acceptance and inclusion of crude drugs as potential plant products in different national and international pharmacopeia like the European pharmacopoeia, the British pharmacopoeia, Chinese pharmacopoeia, Japanese pharmacopoeia, Indian pharmacopoeia, etc. as well as in the pharmacopoeia compiled by the WHO in response to the continued public demand for herbal medicine. The guidelines outlined in such pharmacopoeia are mainly to ensure smooth supply and quality control of herbal products (WHO 1998, 2007). Traditional pharmacognosy is still of fundamental importance but developments in other scientific fields have enormously expanded and elevated the subject to the level of modern pharmacognosy.

In the recent years, pharmacognosy has made a revolutionary come back with a more significant role in primary health care of the rural people, and according to WHO, ~70% of the world population depend on herbal medicine for primary health care purposes and some 35,000–70,000 species of plants equivalent to 14–28% of the world 250,000 plants species have been used as medicaments (Farnsworth and Soejarto 1991; Akerele 1992; Padulosi et al. 2002). Medicinal plants are continuously contributing to the development of modern drugs, and >50 major drugs available in the global market are originated from tropical plants (De Padula et al. 1999) and 89 plant-derived drugs currently prescribed in the industrial world were discovered by studying traditional herbal use (Fransworth 1992; Balick and Cox 1997).

The nineteenth century was a significant period for pharmacognosy when several hundred texts on materia medica and medical botany were published describing thousands of medicines used then across the world and provided information regarding plant origin, harvest, chemistry, processing, and morphological characteristics. Pharmacognosy in the second half of the twentieth century has evolved considerably following advances in disciplines such as taxonomy, agronomy, enzymology, genetics, analytical chemistry, natural drug evaluation techniques, quality control, pharmacology. Modern pharmacognosy deals with phytochemical and pharmacological aspects of natural products along with their classical matters. Advances in chromatography, spectroscopy, thin-layer chromatography, etc. enabled the pharmacognosists for isolation and structural characterisation of phytochemicals. In recent years, pharmacognosy has regained importance due to the renewed interest in natural products as lead compounds for modern medicines and rise of popularity in use of natural products in the developed countries as complementary medicine. At present, pharmacognosy has expanded beyond traditional techniques and advances in molecular biology and high throughput screening (HTS) methods to identify chemical constituents in enormously large scale and therapeutic targets and bioassay-guided fractionation have transformed the field. Plants are the inexhaustible source of new drug compounds, and a large number of plant species are constantly being screened for their cytotoxic, antibiotic, antiamoebal, anti-inflamatory, anti-hypertensive, anti-hyperglycemic, anti-Parkinsonism, etc. activities. Currently, new methods of drug discovery utilizing computer simulation models have been developed to complement the traditional process of investigating potential new drugs based on ethnopharmacological observations. High throughput screening is a quick process of drug-discovery and is widely used in the pharmaceutical industry to quickly assay the biological or biochemical activity of a large number of drug-like compounds.

Modern pharmacognosy is a highly specialized science dealing with biological, biochemical, and medicinal properties of plants, natural raw material and its products. It is also a highly multidisciplinary collaborative science ensconced at the interface of so many subjects including biology, biochemistry, chemistry, sociology, computer science. The topics of study in pharmacognosy are medicinal plants, medicinal plant material, products of animal origin and minerals. Instead of the conventional Galancial preparation, the use of single pure compound, natural or synthetic, has become a general practice in herbal and homeopathic systems of treatment. Modern pharmacognosy as an interdisciplinary subject has entered a new era at molecular level, the molecular pharmacognosy, at the beginning of the twenty-first century.

1.7 New Trends in Pharmacognosy

Pharmacognosy was initiated as a descriptive botanical subject of crude drugs chiefly concerned with the description, identification, and authentication of crude medicinal materials of natural sources, their standards, relate their chemical build-up in relation to their geographical locations, their constituents and uses, etc. During the early nineteenth century, abotanico chemical approach was framed to Pharmacognosy. At the beginning of the twentieth century, pharmacognosy was still a descriptive botanical subject mainly concerned with the description and identification of the crude drugs as well as their history, collection, preparation, storage, and trade and continued up to the first half of the twentieth century, and before the advent of modern analytical chemistry pharmacognosy was taught and practiced as descriptive botanical subjects. In the second half of the twentieth century, pharmacognosy has evolved considerably following advances in disciplines such as taxonomy, agronomy, enzymology, genetics, phytochemistry, analytical chemistry, natural drug evaluation techniques, quality control, pharmacology. A new era of scientific development of pharmacognosy was initiated with the development and contribution of other branches of science. Different branches like clinical pharmacognosy, analytical pharmacognosy, industrial pharmacognosy, etc. have already been established, and these reflect the contemporary advancement and diversification of the subject (Dhami 2013).

With the advancement of other branches of science, e.g., biotechnology, molecular biology, phytopharmacology, etc., pharmacognosy as a subject has got newer directions and now has embraced many new areas of activities in the arena of natural medicine as indicated below:

(i) Pharmacognosy has evolved after the second half of the twentieth century from a descriptive botanical subject to a science embracing the chemistry and pharmacology of crude composites as well as pure active principles in the twenty-first century.

(ii) Development of phytochemistry and natural product chemistry led the discovery and development of valuable natural therapeutic agents including atropine, digitoxin, ephedrine, morphine, galanthamine, paclitaxel, artemisinin, etc. (Jones et al. 2006). Many other natural compounds such as curcumin, epigallocatechin-3-gallate (EGCG), resveratrol, and quercetin have attracted researchers' attention for treatment of cancer and cardiovascular diseases (Lin et al. 2012; Koeberle and Werz 2014; Zheng et al. 2014).

(iii) Using novel formulations, researchers have recently attempted to improve pharmacokinetics of the natural compounds, e.g., attachment of paclitaxel to gold nanoparticles via DNA linkers (Zheng et al. 2014), encapsulation of curcumin by beta-case in nanomicelle (Esmaili et al. 2011), etc. Various novel pharmaceutical systems such as nanoparticles, liposomes, micelles, and phospholipid complexes, drug-encapsulated polymer nanoparticles, nanogels, etc. have been used to improve bioavailability, stability, and efficacy of compounds such as curcumin, quersetin, sylimarin, and so on (Ajazuddin 2010; Coimbra et al. 2011).

(iv) Development of neuropharmacognosy as a discipline at the interface of both pharmacognosy and neurosciences and the complexity of neuropharmacognosy comes from the multidisciplinary characters of both pharmacognosy (includes pharmacology and phytochemistry) and neurosciences (covers neurobiology, neurophysiology and neuropharmacology). The existence of both pharmacological and toxicological aspects of neuropharmacognosy creates more challenges.

Plant neurobiology has emerged in recent years as a result of the incorporation of new research knowledge generated in the field of plant electrophysiology, cell biology, molecular biology, and ecology (Brenner et al. 2006). Plant neurobiology focuses on natural products whose biosynthesis is shared by animal and plant organisms, i.e., indoleamines (melatonin and serotonin) and catecholamines (dopamine, norepinephrine and epinephrine) (Iriti 2013).

(v) Advancements in isolation and purification techniques with the latest technology for bioassays and molecular techniques have encouraged the modern pharmaceutical science towards analytical aspects of Pharmacognosy. Pharmacognosy research started to emphasize on isolation and structure elucidation of biologically active principles from natural resources worldwide.

(vi) At present, cultivation, collection, authentication, identification, quality assessment, biochemical, biological, and molecular studies of natural drugs are being considered as the main aspects of Pharmacognosy. As a result, the modern curriculum of pharmaceutical sciences has undergone substantial changes, and pharmacognosy has become one of the core streams of pharmaceutical research and education.

(vii) Cell biotechnology is widely recommended now as a new possibility for the production of plant secondary metabolites of known pharmaceutical activities. Besides the enormous possibilities of biotechnological production of pharmaceuticals using microbial, plant, insect, or mammalian cells, biotechnology offers also genetic engineering as an important new technology for the production of high-tech herbal products. Clinical pharmacognosy, analytical pharmacognosy, and industrial pharmacognosy have been established that represent the contemporary advancements in the field of pharmacognosy. Furthermore, molecular pharmacognosy, genomic pharmacognosy, metabolomic pharmacognosy, etc. have been deemed as the promising approaches to pharmacognosy research.

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