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REVIEW ARTICLE

Natural Sources Play Vital Role in the Management of Health Care System

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Abstract

Natural sources of medicines are very crucial part of our society. These sources provide us always with promising therapeutic benefits to cure disorders of many kinds. They are easily available from our garden, wild forests, fields and cultivation methods. Natural medicines are needed to explore because lack of knowledge between societies and population decreases their application spectrum. We have mentioned the tremendous varieties and numbers of natural medicinal sources that can be used in the treatment of diseases from ancient times. Besides this disadvantages of these natural medicines are also clarify our vision when we need to use these natural remedies. Our review tried to covers as many as possible knowledge and outcomes of these natural remedies that have crucial role in traditional system of medicines. This also covers the need of conservation methods for sustainable harvesting to preserve potential of natural sources of drugs for upcoming future. This helps to prevent the extinction of threatened species worldwide. The study of these categories the various natural sources of medicines available in the kinds of sources and vary according to their varieties, chemical nature, taxonomical class, geographical distribution, analytical technique applied, methods of collection and processes to establish its pharmacological class.

Major Findings: We have determined that the natural sources are available in various forms and resources. They have shared the huge criterion of traditional, modern and advanced medical system. Besides this the contribution of plant based drugs are remarkable which facilitated the advancement, therapy generation and modifications in the health care systems.

Keywords: Conservation Methods, Economic Impacts, Folk Remedy, Global Importance, Natural Sources of Drugs

1. Introduction

High-throughput screening technologies are employed vigorously to develop new drugs from natural sources. As we know, natural products with diverse structural conformation constitute the wide range of therapeutic activities. Such type of novel moieties are always welcomed and searched for continuously developing new lead compounds and scaffolds. These new lead compounds are always responsible for their potentiating properties to treat human disorders, especially major ones. Multi-dimensional structural eligibilities of natural compounds showed promising results and the WHO reported that the majority of the population always look for medicine from nature. India and other countries of the world directly and indirectly depend upon codified medical systems (*Ayurveda*, *Unani*, Chinese, and *Siddha*), folk medicine, allied disciplines and modern system of natural medicines[1-3]. Higher plants nearly 80,000 species mentioned in the Figure 1 have medicinal value that is utilised by around 80% of the world's population. In India and China extensive use of traditional medicine increases its emergence to document accurately[4,10]. Ministry of AYUSH regulates the traditional system of medicine in India, which involved in the authentication of raw materials, hospitalization, education, research and development and industrialization in collaboration with many other countries[5].

The demand for medicines has always increased with time, which estimated that approximately 35% associated with natural origins. The global markets

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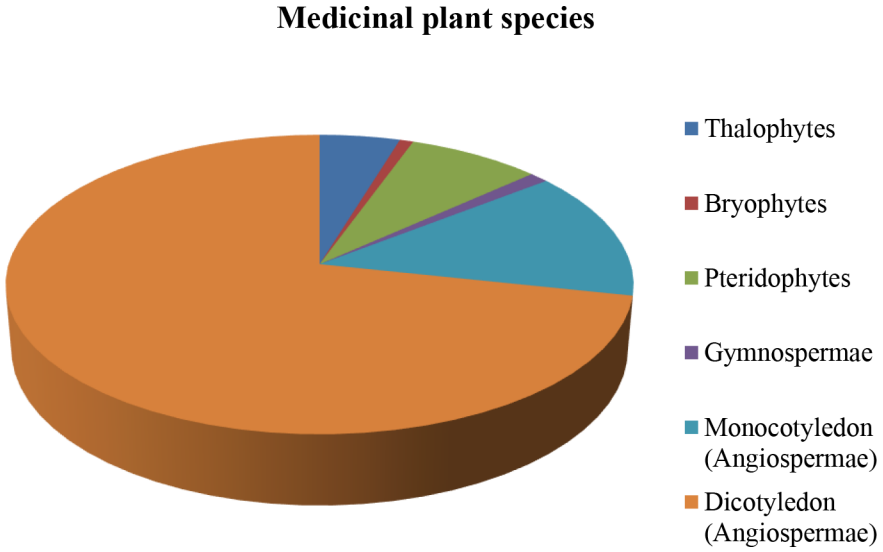


Figure 1. Medicinal plants are utilised worldwide.

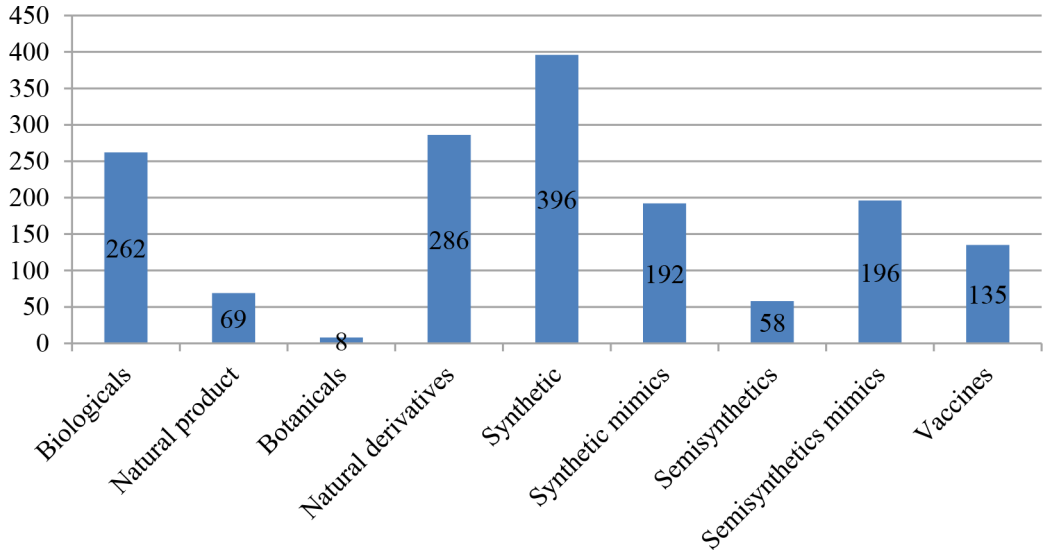


Figure 2. New chemical entity and biological activity approved for drug formulations reported till September 2019.

report more than 1 trillion US dollars in each year. The natural medicines have revolutionized healthcare through its ethnopharmacological importance, which presently overcomes the disease burden of societies worldwide. They facilitate us with medicinal plants, raw materials, prototypes for lead molecule designing and marker compounds for taxonomy[6]. Since 1981-2019 tremendous number of drugs approved that showed under Figure 2 are in the form of biologics, natural products, botanicals, semi-synthetic forms, synthetic forms motivated from existing natural sources, and vaccines. These utilised in the treatment of many diseases.

It has also been documented that a total of 1602 drugs have been approved since January 1981. Since January 1981 the total antibacterial drugs has been 176 from which 93 are purely from natural sources. The antiviral drugs approved from that year are 198 drugs and 6 are natural derivatives. The antifungal drugs approved from year 1981 are 34 and the anti-parasitic agents approved are 20 drugs. The anticancer drugs approved are 250 drug agents, among these 18 are natural products and 43 are natural derivatives. This also emphasizes that from the year 1946-1980 total of 74 drugs were approved and 39 chemical entities belong to natural products and their derivatives. The anti-diabetics approved drugs are

61 drugs and 9 directly obtained from natural products and its derivatives. Other included 13 approved drugs for multiple sclerosis and antibody drug conjugates under clinical trials of phase II and III are 17 drugs[7-9].

Medicinal mushrooms are also good sources of biologically active metabolites. The active chemical compounds obtained from mushrooms are lectin, glycoprotein, ergosterol, glutathione, flavonoids, alkaloids, tocopherol, carotenoids and terpenoids used to cure minor to major diseases. The medicinal mushrooms, namely *Trametes* sp., *Agaricus* sp., *Ganoderma* sp., *Hydnum* sp., *Coprinus* sp., *Morchella* sp., *Cantharellus* sp., *Amanita* sp., *Cortinarius* sp., *Tremella* sp., *Rigidoporus* sp., *Grifola* sp., *Lentinus* sp., *Pleurotus* sp., *Calocybe* sp., *Huitlacoche* sp. and *Cordyceps* sp[10].

2. Impact of Diseases on Society

The disaster of epidemic and pandemic diseases manifests the populations in many ways. The rapid spread of diseases in the population has always been a concern for scientists, health workers, policy makers, and economic aspects. The impacts of these healthcare issues are largely faced by the developing countries. In China, COVID-19 (Coronavirus disease) causes isolation of cities, transport, economic impact, closing of schools and other departments to prevent spread of the virus. COVID-19 pandemic also impart major stress and mental effects on society, which makes them vulnerable to metal diseases[11,12]. Obesity is the disease that related with economic misbalance like financial disturbance, immature mortality, productivity loses and wastage of time[13]. The allergic disease can produce many symptoms that may be fatal in few cases if untreated. These included asthma, allergic rhinitis, atopic dermatitis and food allergies. They are responsible for abnormal epithelial barrier functionality. These reactions can cause socioeconomic imbalance and other health care managing issues[14]. Zoonotic diseases can cause many illnesses to humans. Zoonoses effect the life style, financial lose, mortality and morbidity. They also isolate the affected individuals and causes mental issues. The economical impact is also very high because of decrease in productivity that are associated with prevention involving animal care, quarantine, diagnosis, transportation, treatment, vaccination and inspection of animal products. COVID-19 brings Severe Acute Respiratory Syndrome (SARS) that induce the health emergency, economical manipulations, deaths, mutations and global disturbance. Therefore, infectious diseases always produce the major impacts on our societies in many forms. These changes induced are problematic from past history and should be managed well in future. The demands of new policies, healthcare workers, transportation, migration, hospitalization and community understanding are much needed to finalize these disorders and prevent its economic consequences[15-18].

3. Natural Sources of Drugs

3.1 Medicinal Plant Sources of Drug

Medicinal plants have its own rich history to cure humankind with their therapeutic properties; traditional herbs are mainly used for the common cold, cough, diarrhea, skin conditions, and other ailments. Plant parts like leaves, stem, root and fruit are reported to be utilized extensively; however, plant secretions, flowers, and other aerial parts have many advantages. Many herbals are being studied in preclinical and clinical research and development. Some of the active principles like morphine, paclitaxel, vinblastine, and etoposide are reported for their biological responses by acting upon μ-opioid receptor, β-tubulin, α-tubulin and type II topoisomerase respectively[19,20]. Medicinal plant utilization has been increased moderately from past few years, this was because of wide spread of knowledge of the important herbs. The main concern about increased consumption of medicinal plants suggested that there is increased awareness in developed countries and easy availability for poor population in developing and developed countries. Therefore, the availability of variety and a structured framework motivated the increased demand of plant derived drugs[21-23]. Severe Acute Respiratory Syndrome-related Corona virus 2 (SARS-CoV-2) or novel Corona Virus (COVID-19) infection attracts the demand of medicinal herbs. This utilised the medicinal plant as a single herb, a mixture of herbs and isolated pure chemical constituents that are further represented in Figure 3, which suggests its appropriate methods of processing[24].

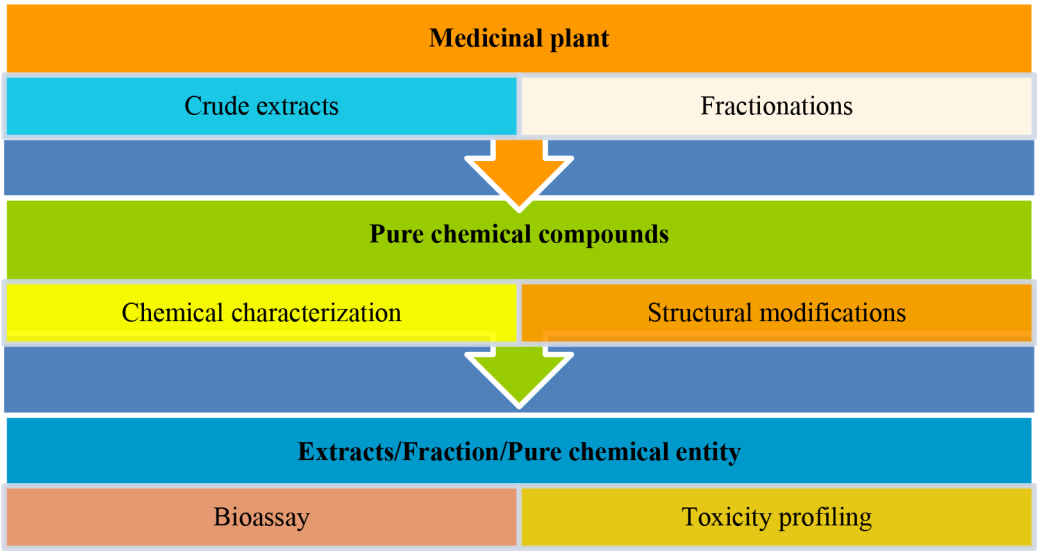


Figure 3. General criteria for verification of novel chemical entity[25].

3.1.1 Traditional Chinese Medicinal Plants

The Chinese system of alternative medicines included the followings *Pueraria lobata, Panax ginseng* (*P. japonicas*, *P. quinquefolium*, *P. vietnamensis, P. fuscidiscus*), *Polygonatum sibiricum*, *P. cyrtonema*, *P. officinale*, *P. odoratum*, *Cornus officinalis*, *Whitmania pigra*, *Coptis chinensis*, *Lycium barbarum*, *Poria cocos*, *Atractylodes lancea*, *A. chinensis*, *A. japonica*, *Anemarrhena asphodeloides*, *Ophiopogon japocicus*, *Ligustrum lucidum*, *Morus alba*, *M. insignis*, *Schisandra chinensis*, *S. sphenanthera*, *Gynostemma pentaphyllum*, *Salvia miltiorrhiza*, *Phragmites communis*, *Alisma orientale*, *Cuscuta chinensis*, *Epimedium sagittatum*, *Clematis chinensis*, *Dendrobium nobile*, *D. officinale*, *D. chrysanthum*, *D. loddigesii*, *Ephemerantha fimbriata*, *Ostrea gigas*, *O. talienwhanensis*, *O. rivularis*, *Lithospermum erythrorhizon*,*Acanthopanax senticosus*, *Paeonia veitchii*, *P. lactiflora*, *Arctium lappa*, *Xanthium sibiricum*, *Bombyx mori*, *Gekko gecko*, *Stephania tetradra*, *Sinomenium acutum*, *Polygonum cuspidatum* (*P. multiflorum*, *P. aviculare*, *P. orientale*), *Platycodon grandiflorum*, *Codonopsis pilosula*, *Scrophularia ningpoensis*, *Ligusticum chuanxiong*, *Angelica sinensis*, *Momordica charantia*, *Zea mays*, *Fagopyrum cymosum*, *Litchi chinensis*, *Punica granatum*, *Allium sativum*, *Allium cepa*, *Asparrausi officinalis*, *Cordyceps sinensis*, *Ganoderma lucidum*, *Tremella fusiformis*, *Gymnema sylvestre*, *Trigonella foenum-graecum*, *Prunella vulgaris*, *Ephedra sinica* (*E. distachya*, *E. intermedia*), *Agrimonia pilosa*, *Anisodus tanguticus*, *Catharanthus roseus*,*Stevia rebaudiana*, *Psidium guajava*, *Aralia elta*, *A.decaisneana*, *Caesalpinia sappan*, *Rhodiola sachalinensis*, *Eriobotrya japonica*, *Amorphophallus rivieri*, *A. konjack*, *A. sinensis*, *Oenothera erythrosepala*, *Tribuluks terrestris*, *Euonyrnus alatus*, *Nelumbo nucifera*, *Fritillaria cirrhosa*, *Rheum palmatum*, *Fallopia multiflora*, *Eucommia ulmoides*, *Ligusticum sinense*, *Houpoea officinalis*, *Rhodiola crenulata*, *Neopicrorhiza scrophulariiflora*, *Rhus chinensis*, *Aristolochia mollissima*, *Epimedium brevicornum*, *Campsis radicans*, *L. erythrorhizon*, *Lobelia chinensis*, *Lonicera japonica*, *Dianthus superbus*, *Tripterygium wilfordii*, *Terminalia chebula*, *Artemisia annua* (*A. argyi*, *A. capillaries*), *Aster tataricus*, *Carthamus tinctorius*, *Centipeda minima*, *Chrysanthemum indicum* (*C. morifolium*), *Cirsium setosum*, *Eclipta prostrate*, *Inula britannica*, *Taraxacum mongolicum*, *Xanthium sibiricum*, *Cuscuta chinensis*, *Cornus officinalis*, *Sedum sarmentosum*, *Isatis indigotica*, *Trichosanthes kirilowii*, *Imperata cylindrical* (*I. major*), *Juglans regia*, *Lycopus lucidus*, *Prunella vulgaris*, *Salvia miltiorrhiza*, *Scutellaria baicalensis* (*S. barbata*), *Cinnamomumcassia*, *Acaciacatechu*, *Astragaluscomplanatus* (*A.membranaceus*, *A.mongholicus*), *Caesalpiniasappan*, *Cassiatora*, *Glycyrrhizauralensis*, *Psoraleacorylifolia*, *Sophoraflavescens* (*S. japonica*, *S. tonkinensis*, *S. tonkinensis*), *Spatholobus suberectus*, *Smilax glabra*, *Viscum coloratum*, *Magnolia officinalis*, *Schisandra*

chinensis, *Forsythia suspense*, *Ligustrum lucidum*, *Matteuccia struthiopteris, Dendrobium nobile* (*D. lindl*), *Areca catechu*, *Plantago asiatica*, *Polygala tenuifolia*, *Fagopyrum cymosum*, *Rheum officinale*, *Drynaria fortune*, *Pyrrosia lingua*, *Portulaca oleracea*, *Pteris multifida*, *Cimicifuga dahurica*, *Paeonia lactiflora* (*P. suffruticosa*), *Pulsatilla chinensis*, *Crataegus pinnatifida*, *Rosachinensis*, *Rubus chingii*, *Sanguisorba officinalis, Gardenia jasminoides, Hedyotis diffusa, Rubia cordifolia*, *Uncaria macrophylla*, *Citrus aurantium, Phellodendron amurense*, *Zanthoxylum nitidum*, *Houttuynia cordata*, *Picrorhiza scrophulariiflora*, *Rehmannia glutinosa*, *Brucea javanica*, *Hyoscyamus niger*, *Solanum nigrum*, *Stemona sessilifolia*, *Camellia sinensis*, *Bupleurum scorzonerifolium*, *Foeniculum vulgare*, *Patrinia scabiosaefolia*, *Vitex trifolia* (*V. simplicifolia*), *Viola yedoensis*, *Curcuma longa* (*C.wenyujin, C. rhizome*), *Zingiber officinale*, *Alpinia officinarum*, *Aconitum brachypodum* (*A. carmichaelii*), *Akebia trifoliate*, *Amomum tsaoko, Anoectochilus roxburghii*, *Asarum* L., *Calanthe*, *Chuanmingshen violaceum*, *Cichorium intybus* (*C. glandulosum*), *Citri reticulatae*, *Citrus reticulate* (*C. chachiensis*), *Clerodendrum* L., *Codonopsis lanceolate, Codonopsis pilosula, Coix lacryma-jobi*, *Dioscorea opposite (D. rhizome), Dipsacus asper, Epimedium acuminatum, Eupolyphaga sinensis*, *Ferula syreitschikowii, Forsythia suspensa*, *Fritillaria* L., *Gardenia jasminoides*, *Gastrodia elata*, *Gentiana straminea*, *Geranium wilfordii*, *Goodyera* L., *Hedysari radix, Hirudo nipponica, Illicium difengpi, Istais indigotica*, *Leonurus artemisia*, *Marsdenia*, medicinal leech, *Microcos paniculata*, *Notopterygium incisum*, *Paeonia suffruticosa*, *Paris polyphylla* (*P. yunnanensis), Pesudostellaria heterophylla*, *Pholidota cantonensis*, *Pinellia ternate, Pleione bulbocodioides*, *Potentilla* L., *Psammosilene tunicoides*, *Rhodiola* L., *Rubus* L., *Sarcandra glabra*, *Siraitia grosvenorii*, *Sophora alopecuroides*, *Stemona tuberose*, *Stephania kwangsiensis*, *Tamarix chinensis*, *Taxus chinensis* (*T. mairei*), *Tetrastigma hemsleyanum*, and *Trichosanthis fructus*[25-28].

3.1.2 Traditional Medicinal Plants in India

The traditional Indian system of medicine mentioned these followings like *Asparagus racemosus*, *Commiphora mukul*, *Cyperus scariosus* (*C. rotundus*), *Garcinia cambogia*, *Glycyrrhiza glabra*, *Gymnema sylvestre*, *Melia azadirachta*, *Momordica charantia*, *Moringa pterygosperma*, *Mucuna pruriens*, *Nardostachys jatamansi*, *Piper longum* (*P. nigrum*), *Bergenia ligulata*, *Terminalia chebula*, *Tinospora cordifolia*, *Withania somnifera*, *Zingiber officinale, Phyllanthus emblica (P. amarus), Tephrosia purpurea*, *Plumbago zeylanica* (*P. ovate*), *Glycyrrhiza glabra*, *Solanum xanthocarpum*, *Adhatoda vasica*, *Curcuma zedoaria* (*C. longa*), *Ocimum sanctum*, *Terminalia chebula* (*T. bellerica, T. arjuna*), *Ricinus communis*, *Bauhinia variegate*, *Crataeva nurvala*, *Holarrhena antidysenterica*, *Cassia angustifolia*, *Azadirachta indica* (*A. arabia*), *Areca catechu*, *Achyranthes aspera*, *Ficus benghalensis* (*F. glomerata*, *F. religiosa*), *Quercus infectoria*, *Symplocos racemosa*, *Aegle marmelos*, *Syzygium cumini*, *Centella asiatica*, *Mentha piperita*, *Eclipta alba*, *Tribulus terrestris*, *Butea monosperma*, *Psoralea corylifolia*, *Sida cordifolia*, *Picrorhazia kurroa*, *Pterocarpus marsupium*, *Rauwolfia serpentine*, *Commiphora wightii*, *Mucuna pruriens* and *Curcuma longa*[29,30].

3.2 Medicinal Animal Sources of Drug

In India, Brazil, China, South Africa, Latin America and the rest of the countries have traditionally considered animal products for their medicinal values. They has been conserving their traditional knowledge through documents and practicing till date, which mainly categorised the health promotion activities through providing strength, wound healing, anti-asthmatic, GIT disorders, paralysis, malaria, aphrodisiac, immunity booster, anemia, respiratory diseases, menstrual problems, anthelmintic, blood related complications, rheumatism, sore throat and eye disorders. Mainly, they included the animals like *Lepus nigricollis*, *Rana tigrina*, *Calotis versicolor*, *Schizothorax richardsoni*, *Spirobolus* spp., *Palamnaeus* spp., *Hemidactylus* spp., *Cimex rotundatus*, *Vipera russelli*, *Ancistrodon Himalayans*, *Cervus duvauceli*, *Equus cabalus*, *Panthera pardus*, *Bubalus* spp., *Muntiacus muntjak*, *Sus scrofa cristatus*, *Rattus rattus*, *Macaca mulatta*, *Capra falconeri*, *Ptyas mucosus*, *Hemitragus jemlahicus*, *Paratalphusa* spp., *Catreus wallichii*, *Hystrix indica*, *Strix aluco nivicola*, *Bos indicus*, *Columba livia*, *Oryctolagus quiniculus*, *Canis aureus indicus*, *Bos grunniens*, *Equus* spp., *Felis domesticus*, *Moschus moschiferous*, *Martes flavigula*, *Cypselus affinis*, *Vanellus indicus* and *Selenarctos thibetanus*, *Caudisona durissa*, *Iguana iguana*, *Caiman*

latirostris, *Phrynops geoffroanus*, *Gallus domesticus*, *Cerdocyon thous*, *Apis mellifica*, *Physeter catodon*, *Sepia officinalis*, *Tubipora musicas*, *Bos Taurus*, *Capra hireus*, *Sus scrofa lybicus*, *Scorpiones* spp., *Hystrix indica*[31,32]. Medicinal compounds from animals like exenatide, lixisenatide, bivalirudin, desirudin, captopril, enalapril, tirofiban, eptifibatide, batroxobin and cobratide. These products have medicinally approved to treat human ailments. Batroxobin used in angina pectoris, topical medications and acute cerebral infarction; bivalirudin in anti-coagulant; captopril in heart diseases; cobratide used in chronic arthralgia; desirudin in venous thrombosis; enalapril in hypertension; eptifibatide in acute coronary syndrome; exenatide in Type 2 diabetes mellitus; lixisenatide in Type 2 diabetes mellitus and tirofiban in acute coronary syndrome[33-36].

3.3 Medicinal Marine Sources of Drug

Marine sources covered the wide range of medicinal products in the form of food and active compounds, which utilized for the treatment of minor to major diseases. Medicinally important marine species included are *Electrophorus electricus, Hippocampus reidi*, *Thunnus obesus*, *Gadus macrocephalus*, *Theragra chalcogramma*, *Rhinchodon typus*, *Thaleichthys pacificus*, *Echinast erbrasiliensis* (*E. echinophorus*), *Luidia senegalensis*, *Mellita quinquies perforata*, *Oreaster reticulates*, *Pteriomorphia* spp., *Haliotisasinine* and *Echinometra lucunter*, which have used for treatment of skin disorders, heart diseases, respiratory disorders and brain related ailments. Some of the seaweeds contain active constituents having therapeutic activities against cardiovascular diseases, viruses, inflammation and cancer, this included *Undaria pinnatifida* (Fucoxanthin), *Porphyra* spp. (Phycoerythrobilin), *Phaeophyceae* (Sulfated fucoidans), *Rhodophyceae* (Sulfated galactans), *Codium fragile* (Xyloarabino galactans), *Codium cylindricum* (Sulfated galactans), *Sargassum thunbergii* (Phlorotannins), *Saccharina japonica* (Fucoidans), *Eiseniabicyclis* (Phloroglucinol), *Taonamaria atomaria* (Stypoldion), *Laurencia microcladia* (Sesquiterpene elatol), *Schizymenia dubyi* (Sulfated glucuronogalactan), *Lobophora variegate* (Fucans), *Ecklonia cava* (Phlorotannin6,6- bieckol), *Poriphyria dentate* (Catechol, rutin and hesperidin). Coral reefs have showed promising activities against inflammation, cell lines toxicity and neuron-inflammation. Important coral reefs with active entities are *Sinularia flexibilis* (Flexibilin D, flexibiliquinone), *Sinularia gaweli* (5α, 8α-Etidioxysterol), *Sinularia granosa* (9,11-Secosterol), *Sinularia crassa* (Crassalone A), *Sinularia querciformis* (II-epi-Sinulariolide, sinularin, acetate), *Cladiella krempfi* (Kremptielins), *Capnella imbricate* (capnellenes), *Echinomuricea* spp. (*Echinoclrodane A.*), *Scleronephthya gracillimum* (Sclerosteroids), *Paraminabea acronocephala* (Paraminabic acid), *Lemnalia cervicomi tenuis* (Lemnalol), *Nephthea chabrolii* (Nebrosteroids Q, R and S). Marine organisms have significant role to combat cancer, malaria, inflammation and infections. We have mentioned some important marine organisms with active chemical compounds like *Bugula neritina* (bryostatin), *Ecteinascidia turbinate* (ecteinascidin), *Discodermia* (discodermolide), *Lissodendoryx* spp. (halichondrin B), sponge (cytarabine/ara-C), puffer fish (tetrodotoxin), *Pseudopterogorgia elisabethae* (pseudopterosins), cone snail (ziconotide), *tunicate* (piltidepsin), sponge (plakortin), *bryozoa* (pezizavesiculosa β-carboline), bacteria (pulicatin A), *alga* (floridosides), sponge (calyculin A), soft coral (capnellene), *tunicates* (didemnins, trabectedin), and *Dolabella auricularia* (dolastatins)[37-40].

3.4 Medicinal Micro-organisms Sources of Drug

Micro world has crucial role in the drug discovery and drug development process that are derived from definite mechanisms as showed in the Figure 4 related with time immemorial by providing platform for many medicines to the human kind. Some of these important microbes are *Streptomyces coelicolor*, *Escherichia coli, Saccharomyces cerevisiae*, *Saccharomonospora* spp., *S. coelicolor*, *S. cerevisiae*, *Streptomyces venezuelae*, *Streptomyces ambofaciens*, *Streptomyces viridochromogenes*, *Streptomyces albus*, *Staphylococcus aureus*, and *Lycium barbarum*[41]. The reported microbial natural products have antibacterial, antifungal, agriculture fungicides, antitumor, b-lactamase inhibitor, cholesterol biosynthesis inhibitor, immunosuppressant, lipase inhibition, insecticidal, anthelmintic and food additive applications. These included *Penicillium notatum* (Penicillin G), *Acremonium* spp. (Cephalosporin), *Streptomyces griseus* (Streptomycin), *Streptomyces fradiae* (Neomycin), *Micromonospora*

purpurea (Gentamicin), *Streptomyces kanamycetus* (Kanamycin), *Amycolatopsis orientalis* (Vancomycin), *Streptomyces roseosporus* (Daptomycin), *Streptomyces* spp. (Tetracycline), *Saccharopolyspora erythraea* (Erythromycin), *Lactococcus lactis* (Nisin), *Pleurotus mutilus* (Pleuromutilin), *Streptomyces venezuelae* (Chloramphenicol), *Streptomyces noursei* (Nystatin), *Streptomyces linconensis* (Lincomycin), *Fusidium coccineum* (Fusidic acid).

They also collected from *Amycolatopsis mediterranei* (Rifamycin), *Streptomyces clavuligerus* (Clavulanic acid), *Streptomyces nodosus* (Amphotericin), *Glarea lozoyensis* (Pneumocandin), *Strobilurus tenacellus* (Strobilurins), *Streptomyces verticillus* (Bleomycin), *Streptomyces peucetius* (Doxorubicin), *Micromonospora echinospora* (Calicheamycin), *Tolypocladium* spp. (Cyclosporine), *Streptomyces hygroscopicus* (Rapamycin) and *Claviceps* spp. (Ergotamine)[42,43].

3.5 Medicine Mineral Sources of Drug

Chinese traditional medicines have documented the applications of majority of the mineral origin substances in the kind of treatment. The naturally occurring stones, minerals or animal bones (Dragon's bone) as a medicine used in traditional Chinese medicines are pyrite (iron), cinnabar (mercury), mirabilite, calomel, white quartz, selenium, nickel, vanadium, cobalt, magnetite, beryllium, lithium, rubidium, zirconium, cesium, mica, galena (lead), sphalerite (zinc), copper (covellite, chalcocite and chalcopyrite), ophicalcitum, hydromuscovite, kaoline, green vitriol, halitum purpureum, azurite, stalactite, chloriteschist, pumice, stalactite, malachite, hanshuishi gypsum, halite (halitum), fluorite, hematite , magnet, amber, clay minerals, margarita, native gold, native silver, vermiculite, selenite, asbestos, stalactite, hematite, ophicalcitum, calcium carbonate and limonite. They help to treat borax for goitre and fluorosis, selenium for Kaschin-Beck disease; calcium, silicon, iron, magnesium, potassium, sodium, manganese, zinc, cobalt, iodine, chromium, copper, selenium and boron for cancer treatments; alum, borax, calomel, gypsum for infectious ailments, red halloysite (consists of hydrated aluminum silicate, ferric and manganese oxides), hydrous sodium sulphate, sulphur, fulonggan, hydrated copper sulphate, calcined alum for GIT disorders; hydrated calcium sulphates, powdered alum, Dragon's bones (consists of calcium carbonate and calcium phosphate) for treating nervous system disorders and mirabilite, talc (magnesium silicate) for treating urinary diseases[44-47].

3.6 Tissue Culture as Sources of Medicine

The collection and generation of secondary metabolites as medicines play important role in the pharmaceutical drug industry. The *in vitro* production of these medicinal compounds involves simple procedures and tremendous results. The production of bioactive moieties with *in vitro* plant tissue culture included like production of solasodine from *Solanum eleagnifolium*,

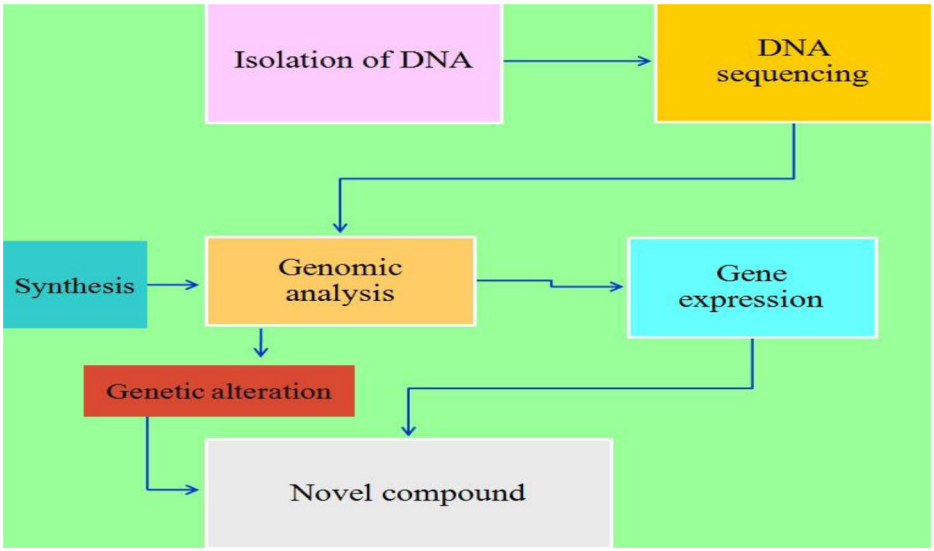


Figure 4. Isolation of novel compound(s) from medicinal micro-organisms.

Cephaelin and emetine from *Cephaelis ipecacuanha*, pyrrolizidine from *Senecio* spp., quinoline alkaloids from *Cinchona Ledgeriana*, diosgenin from *Dioscorea deltoidea*, cardenolides from *Digitalis lanata*, azadirachtin and nimbin from *A. indica* and lepidine from *Lepidium sativum*[48].

Similarly, production of secondary medicinal compounds like taxuyunnanine C and taxol (*T. chinensis*), saponins (*Panax quinquefolius*), glycyrrhizic acid (*Glycyrrhiza uralensis*), triterpenoid (*C. lanceolate*), valerenic acid (*Valeriana officinalis*), saikosaponin (*Bupleurum chinense*), triptolide (*Tripterygii wilfordii*), tanshinones (*Salvia miltiorrhiza*), artemisinin (*Artemisia annua*), flavonoids (*Ginkgo biloba* and *Saussurea involucrate*), licochalcone A (*Ginkgo uralensis*), catharanthine and vindoline (*C. roseus*), campothecin (*Campototheca acuminate*), atractylodin (*Atractylodes lancea*), ephedrine (*Ephedra sinica*), tropane alkaloids (*Anisodus acutangulus*), scopolamine and hyoscyamine (*Datura stramonium*), vincamine (*C. roseus*), coumarins (*Angelica archangelica*),rosmarinic acid (*S. miltiorrhiza*), antharaquinone (*Morinda officinalis*), aloe emodin (*Aloe vera* and *Aloe chinesis*), chrysophanol (*Aloe vera*), phytoecdysteroids (*Achyranthes bidentata*) and guggulosterone (*C. wightii*)[49]. The industrial production of medicinal compounds through in-vitro techniques has helps to biosynthesis berberine (*Coptis japonica, Thalictrum minus*), Echinacea polysaccharides (*Echinacea purpurea*), Geraniol (*Geraminea* spp.), Paclitaxel (*Taxus* spp., and *Podophyllum* spp.), Podophyllotoxin (*Podophyllum* spp., and *C. blumei*), Rosmarinic acid

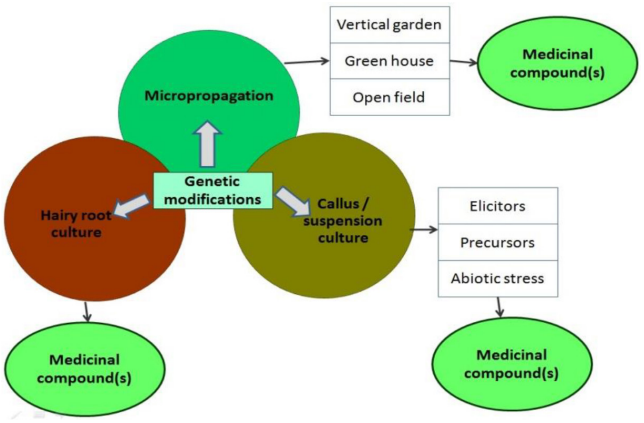


Figure 5. Harvesting of novel compound(s) from tissue culture technique[52].

(*Duboisia* spp.) and Scopolamine (*L. erythrorhizon*). The *in-vitro* techniques also gain importance in the biosynthesis of pharmaceuticals like taliglucerase-α (Carrot or tobacco), VEN150 (Rice seeds), Vaccine (NDV) from tobacco suspension cultures, Moss-GAA and Moss-GBA from Moss, Moss-AGAL (*Nicotiana benthamiana*), Vaccines (alfalfa), Antibody (Duckweed leafy biomass) and HIV, CaroRx, PBI-220 and DPP4-Fc from tobacco leaves for the treatment of various disorders. The methods adopted for the processing, isolation and purification have been discussed under Figure 5[50-52]. Many more secondary metabolites derived from plant tissue culture technique reported are quinolone alkaloids, furanocoumarins, acridone, flavonoids from *Ruta* spp.; Kaempferol, isorhamnetin, quercetin, bilobalide, ginkgolide A, B, C, ginsenoside from *G. biloba*; Phenolics, flavonoids, alkaloids, lignans, carboxylic acids, steroids, polysaccharides, quinochalcone C-glycosides, quinone-containing chalcones from *C. tinctorius*; Ephedrine alkaloids (1-ephedrine, d-pseudoephedrine, norephedrine, norpseudoephedrine, methylephedrine and methylpseudoephedrin), Flavonoids (eucodelphinidin, leucopelargonine, leucoanthocyanidin, lucenine, vicenin-1 and vicenin-2), proanthocyanidines from *Ephedra* spp.; Ajmaline, ajmalicine, solasodine, α-solanine, serpentine and reserpine, β-carboline, alstonine, rescinnamine, reserpiline from *Rauwolfia* spp.; Stilbene, procyanidins, resveratrol, anthocyanins, quercetin, myricetin, laricitrin, kaempferol, syringetin, isorhamnetin, epicatechin, flavonols, vineferin from *Vitis vinifera*; Paclitaxel, essential oils, flavonoids, taxol, baccatin III, lignans from *Taxus* spp.; Tropane alkaloids, phytosterols, saponins, tannins, phenolic compounds, antharaquinone glycosides, triterpenoids from *Rubia tinctorum*; Rosmarinic acid, β-sitosterol, forskolin, apigenin, chavicol, cavacrol, eugenol, quercetin from *Coleus blumei*; Sesquiterpenoids flavonoids, phytosterols, triterpenoids, lignans, phenolics, gallic acid, syringin, chlorogenic acid, ethyl gallat, rutin, isoquercitrin from *Saussurea medusa*; aspidin, deaspidin, filixic acid from *Dryopteris filixmas*; Borneol, α-terpineol, carvacrol, thymol, geraniol, carotenoids, rosmarinic acid from *Thymus* species; Pelletierine, ellagic acid, phenol, flavonoids from *Punica granatum*; Stevioside, steviol rebaudioside, essential oils from *Stevia rebaudiana*; Visnagin,

khellin, g-pyrones, scopoletin, dehydrogeijerin, furanochromones, pyrano-coumarins, apigenin, luteolin, chrysoeriol, essential oils from *Ammi visnaga*; Baccharine, clerodane, labdane diterpenoids, oleanane triterpenoids, cinnamic acid, coumarins, flavonoids from *Baccharis megapotamica*; Berberine, palmatine, epiberberine, coptisine, jatrorrhizine from *Coptis* species; Diosgenin, discoeine, cortisone, allantoin, phytic acid, coumaric acid, myricetin from *Dioscorea* species; Odoroside H, odorobioside G, verodoxin, glucodogifucoside, strospeside, digitoxin, digoxin, ouabain, oleandrin, proscillaridin from *D. lanata*; Betalains, apigenin flavonoids like vitexin, vitexin-2-O-rhamnoside, vitexin-2-O-xyloside from *Beta vulgaris*; Quinolozidine, alkaloids, nesodine, vertine, lyfoline, lythrine, demethylsubine I and II from *Heimia salicifolia*; Camptothecin, 10-hydroxycamptothecin, 10-methoxycamptothecin from *Camptotheca acuminate*; Hypericin, hyperforin from *Hypericum perforatum*; Scandenone, auriculasin, osajin and pomiferin from *Maclura pomifera*; monoterpenoids, sesquiterpenoids, diterpenoids, triterpenoids, steroids, flavonoids, guggulsterols, lignans from *C. wightii*; Puerarin, daidzin and daidzein from *P. lobata*; Phenols, saponins, flavonoids, alkaloids, tannins, steroids, triterpenoids, vitamins from *Chlorophytum borivilianum*; Bacosides from *Bacopa monnieri* and Saponins, steroids, alkaloids and flavonoids, curcubitacins from *Citrullus colocynthis*[53, 54].

4. Natural Sources for Advancement of Health Care System

Natural medicines has play very vital role in the treatment of diseases mentioned in the literatures and ancient sculptures. The folk medicines are utilized for disorders due to their cost effective treatment and easily availability. The importance of natural medicines are better understood through their extensive use in the treatment of malaria especially discovery of quinine and artemisinin. Natural medicines have potential cure for chronic diseases[55,56]. In India AYUSH and National Level Policy for betterment of health regulated the traditional practices for treatment and management of healthcare. There are number of plant metabolites employed to treat diseases which are obtained through extracts, isolation, purification, characterization and evaluation of biological activities of these novel moieties[57]. Ethnopharmacology and Ethnopharmacognosy has significant role in the management of health care system by providing natural medicines, pharmacological procedures, identification tools and phytochemical evaluations. The National Cancer Institute in the United States and the Central Drug Research Institute in India take initiative to randomly screen bioactive compounds through techniques like High throughput screening methods, genomics, and combinatorial chemistry[58].

5. Drawbacks with Natural Sources of Drug

The ethno-medicinal approaches from plants in the drug discovery suggested that not all the active principle from them is biologically safe, renewal of exhausted flora and fauna are difficult, patent protection of ethno-medicines are problematic, collection and evaluation is difficult, needs conservation of plant species and import or export of plants[59,60]. Moreover, the drug discovery from nature is still very lengthy, costly, difficult and with low success rates. There is also a risk of interaction between either herb-herb interactions, herb-drug interactions or herb-food interactions. Another disadvantage while dealing with natural substances is adulteration, shelf life, potency of collected natural material and pharmacokinetics and pharmacodynamic profile of formulations. Further, the pharmacokinetic and pharmacodynamic studies characterized by biological half -life, elimination rate studies and various types of interactions[61,62]. Sometimes, the over consumption of these natural herbs may cause side effects that are because of many factors including contaminations, quality, purity, age, sex, metabolic status, absorption disturbances, intake with other medications and presence of any other complications in the body. These can therefore results into major to minor side effects on our body. Medicinal plants that need care before administration or oral intake are like chamomile (vomiting, allergy, eczema and skin irritation), black peppers (excessive tears in the eyes, mouth burning sensation, stomach pain, diarrhea, vomiting, irritation of mucous membranes of nose or mouth, swollen lips, nasal congestion, hives, bloating, nausea, anaphylaxis), clove oil (seizures, liver damage,

fluid imbalances, and bleeding), cinnamon (liver injury, hypoglycemic attach), anise (hypoglycemia, hormonal disturbances), hibiscus (decrease in estrogen level and blood pressure), catnip (diarrhea, muscle pain, cramping, drowsiness, dizziness and low heart rate), dried lime (contact dermatitis, skin redness, severe itching, burning sensation, skin peeling and blisters) and cress seeds (hypothyroidism, GIT and urinary tract disorders). These effects are caused by the presence of definite type of chemical compounds in the plants[63-65].

6. Conservation of Natural Drug Sources

Conservation of natural sources of drugs especially medicinal plants needs attention and involvement of society and peoples. The strategies for conservation of medicinal plants has established through various meetings and involvement of governmental bodies from past time. The over-harvesting by peoples of developing countries leads to loss of land and biodiversity. So, sustainable use of these natural sources is much required[66]. Many animals used for medicinal purposes has threatened by loss of habitat and hunting like musk deer, rhinos, antelope and tigers. The extensive harvesting of medicinal animals has caused by personnel usage trends, growing market demands, increasing economical values and promise of awards to the hunters or harvesters. The targeted animal species for scientific research investigations that are misguided, misconduct or misdirected investigations directly manifest these wild species with results in no expressive discoveries[67].

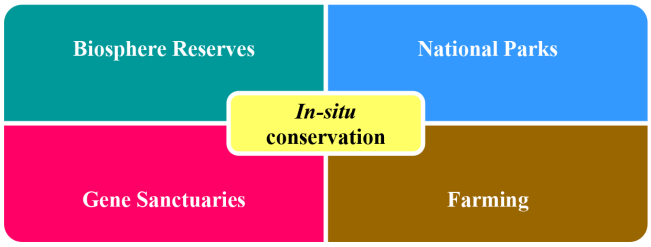


Figure 6. *In situ* conservation methods for sustainable usages[66,69].

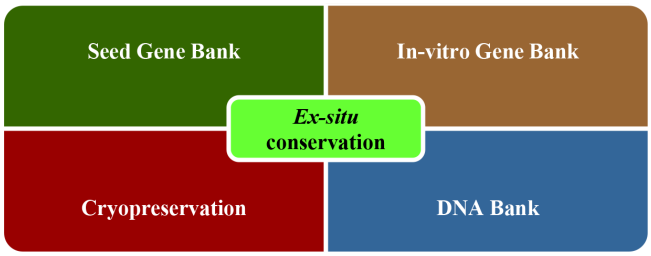


Figure 7. *Ex situ* conservation methods for sustainable usages[66,68,69].

The crucial steps of *in-situ* and *ex-situ* conservation techniques have been showed in Figure 6 and Figure 7. The medicinal plants conservation can be done through good agricultural practices, use of modern cultivation, collection and harvesting techniques, plant tissue culture, synthetic seeds, pollen storage and DNA storage methods[68-70].

7. Conclusion

Medicinal sources from nature have ancient history that dispensed in the form of crude extracts, tinctures and other formulations like *ayurvedic* formulations. These old applications of natural drugs increase its importance among developed and developing countries. These old documentations helped many researchers to explore the new formulations and treatment strategies with the applications of modern technologies. This has been proved that 75-80% population worldwide still using these traditional medicines and alternative medicines as well now a day. These are modified according to treatment strategies and suited dosage forms to treat ailments. There are mentioned numbers of natural sources of drugs in each alternative medicinal system. Our conclusion focuses on the knowledge of these drug sources and its therapeutic role in the cure of relative disorders. We also depicted the advantages of using natural sources of drugs as well as disadvantages of these natural treatment regimens. These findings associated with drawbacks of natural medicines helps to reduce the harmful effects and provide better treatment options that should be adopted. Although, the extensive harvesting of natural sources of drugs always a problem that may leads us to the vicinity of lack of these beautiful natural medicines, danger to biodiversity and bioprospecting. Therefore, this have been very crucial to categories these points for sustainable harvesting and preserving natural potential for future applications.

8. Authors Contribution

Shiv Kumar: Conceptualization, data collection, writing original draft, supervision, editing and proofreading.

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