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Review Article

Role of Endophytic Fungi in Preservation of Plant Biodiversity

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ABSTRACT

Biodiversity, the diversity of all life forms on earth, is the variety and variability between genes, species and ecosystem. India is blessed with rich and diverse heritage of plants along with their use in a very broad area. The origins of most drugs are directly from plants and are constantly exploiting in pharmaceutical industry. Apart from pharmaceutical industries plants are also used in paper industries, timber industries and textile industries and also in bio-fuel production. This further leads to a great loss in the plant biodiversity. For the sake of our valuable plants, an effort was made to use endophytic fungi in a new approach to exploit them in pharmaceutical industry which will conserve plant biodiversity. These are the excellent source of bioactive compounds with tremendous medicinal value, as they do mimicry of plants and produce compounds similar to that of host plant, which would be beneficial for human race. So without going beyond our nature or by exploiting least, if a microbial source is available then we must have to use these microbes.

KEYWORDS: Plant biodiversity, Endophytic fungi, Bio-active compounds, Antimicrobial compounds, Bio-fuel.

INTRODUCTION

The planet earth comprise of about 3,00,000 plant species among which 87% flowering plants, 0.32% non-flowering plants, 4.4% ferns, 5% mosses, 3.3% of red and green algae[1]. The variety of the World's plant organisms, including their genetic diversity and the assemblage is known as plant biodiversity[2]. It is not distributed in a regular manner across the earth but diversity is rich in tropics comparison to polar region[3]. As per World Health Organization a large part of world population trust on traditional form of medicine and are mostly dependent on plants for their primary health care needs[4]. Growing pharmaceutical industrialization causes increase in human interference which results in the habitat loss of medicinal plants, so that endemic species having medicinal value become threatened in its own land. This suggest the over utilization and over exploitation of the valuable plant resources[5]. So there must be a need of an alternate to protect our slow growing valuable plants from habitat loss. Plant as source of drugs leads to somewhat exploitation of natural biodiversity so without going beyond our nature or by exploiting least some alternate as microbial source must be needed. Choosing endophytic fungi as source of drugs may ameliorate the conservation of plant biodiversity.

DIVERSITY OF PLANTS USED IN MEDICINES

The natural product made from plants with therapeutic potential is very ancient as human civilization and exploited as far as possible for medicines[6]. Therapeutic potential of plants are used in several ways as herbal tea and homemade medicines. Supplemented fractions of plant compounds are used as tincture, pills, capsules, powder *etc*. these are considered as phyto-pharmaceutical preparations of plants. The product prepared by following legal and technical procedures which is used for diagnosis, prevention and treatment of disease and characterized scientifically in terms of effectiveness, safety and quality is medicine. The compound which is component of medicine and is of natural, biotechnological or synthetic origin along with pharmacological activity is known as drug[4]. A total of 25% of drugs used all over world are from plants among which 252 drugs are considered as most important by WHO, 11% are obtained directly from plants and remaining are synthetic and obtained indirectly from natural precursors. In a broad way the 50% of antitumor and anti-infectious drugs which are present in market and in clinical trial are from plants[7]. Most of plant based drugs can be synthesized in the laboratory but it is sometime more beneficial to extract them directly from nature. Examples are d-tubocurarine, atropine, quassin and psoralen. d-tubocurarine is very important medically as it is used for relaxation of skeletal muscles during abdominal surgery and also to control tetanus convulsions[8]. In order to promote natural products in Latin America and Africa, Universities, industries and government adopted a multidisciplinary and sustainable program 'International Program of Co-operation for Biodiversity' (IPCB) in 1993[9]. In this regard, for the development of phytomedicinal products Eastern countries, such as China and India, established herbal medicinal industries and Latin America have been in research for the standardization and regulation of these plant products, behind this European countries, such as France and Germany are also added in this race[10]. 95% of all steroidal drugs on the market are derived from Diosgenin (obtained from plant *Dioscorea* sp.). It is used in oral contraceptives, sex hormones, as well as a variety of steroids such as cortisone and hydrocortisone, also used for treating rheumatoid arthritis, rheumatic fever, several allergies, and skin diseases such as contact dermatitis[11]. In a research by Prakasha *et al.* it was estimated that in India about 3000 plant species were known to have medicinal origin[12]. There are large numbers of pharmaceutical companies as Merck, CIBA, Glaxo, Boehringer and Syntex now have research and development departments devoted to study the new drugs from plants having medicinal value[13]. A large number of plants with their compound, action, nature and family were well tabulated below (Table 1)[14-18].

DESTRUCTION OF PLANTS IN DRUG DEVELOPMENT

The drug development from a plant resource depends on aim, whether drug obtained in which form and which part of plant is used. In an industry, initially plant is subjected to continuous extraction and purification to obtain the compounds which is active and used as drug. Some examples of drugs which are as the direct plant compound are quinine, digoxin, and ergotamine while some are synthesized from these compounds for example diosgenin[19]. From the knowledge point of view for making a plant into medicine basic sciences such as Botany, Chemistry and Pharmacology, including Toxicology are involved along with this other fields knowledge are also taken into account as Anthropology, Agronomy, Biotechnology, Pharmaceutical technology all these joint action makes a drug of plant origin[20,21].

The average yield of bioactive compounds from a starting crude raw material to its development, launch and supply requires a vast amount of starting compound, as presented by Mc Chesney, that in the production of 500mg of pure compound a total of 50kg of raw material is required which is used for bioassays, toxicology and *in vivo* evaluation, full pre-clinical and clinical trial requires about two kg of pure compound on exploiting 200 tons of raw material[22]. For the development of a drug a total investment of around US$ 100–360 million and a minimum of 10 year are required. In field of clinical trials, on producing compound one in 10,000 is being selected as promising and only one in four get approval as a new drug. For the testing of activity against HIV and Tumor, NCI, USA has tested 50,000 and 33,000 plant samples respectively and among this only three plant extract were chosen as promising against both HIV and Tumor[23]. This suggests the exploitation and destruction of Earth's biodiversity in huge manner. In this series, it was also mentioned that Taxol is the most important natural product with anti-tumor activity, isolated from plant *Taxus brevifolia* and *Taxus baccata*, however obtaining its compound from plant is the biggest hindrance because tons of plant raw material is exploited to obtain very minute amount of taxol. As 27,000 tons of bark of *T. brevifolia* is required to obtain two and half kg of taxol, about 12,000 trees must be cut down. This suggests that if we continue with process, then soon we must have to face the extinction of this plant, if no alternative is discovered[24,25].

The present state of exploiting the world's biodiversity including India for products such as drugs, papers, fuels, timber *etc.* leads to endanger the world's vegetation and species. This results in the loss of natural compounds as phytochemical drugs and also the loss of gene pool which may be used in development or biosynthesis of new compound[19]. Hence, in the way of protection of valuable plant biodiversity a new source of these drugs must be discovered, therefore the present review is based on alternative for obtaining drugs, fuels, enzymes *etc*. from microbial source such as 'Endophytic Fungi'.

Hence, it is directed to bring to the fore, the consequences of this vandalism. It's the time for us to stop ailing and perishing the biodiversity. Let us return the Mother Nature, its lost glory back. Making drugs by endophytic fungi will be a very important step in this direction.

Endophytes are microorganisms mostly bacteria and fungi that inhabit plant host for all or part of their life cycle. Endophytes are the chemical synthesizers inside plants which are symbionts living within the above ground tissue of their angiosperm hosts and are not affected by surface sterilization techniques[26]. Endophytism is thus a unique cost benefit plant microbe association defined by location that is transiently symptomless, unobstructive and established entirely inside the living host plant tissue[27]. Here we focused towards endophytic fungi (the fungi which reside inside plants body) whose few taxa have been tested for biological application and has ability like drug production and bio-control management[28].

ENDOPHYTIC FUNGI

They establish a very significant and quantifiable part of biodiversity of fungi which are known to affect the plant diversity and organization[29]. The term 'endophyte' was first of all introduced by De Bary for the organisms that occurring within plant tissues or 'All organisms inhabiting plant organs that at some time in their life, can colonize internal plant tissues without causing apparent harm to the host'[30].

Host Plant–Endophytic Fungi Relationship:

Any plant and endophyte interaction is a physical encounter between plant tissue and fungal mycelia followed by several physical and chemical barriers, which must be overcome to establish an association. The relationship that exist between plant and endophytic fungi range from mutualistic or symbiotic (beneficial to both host and fungi) to antagonistic (aggressive to both host and fungi) or slightly pathogenic (harmful to host)[31,32]. The mutualistic relationship ranges from commensalism to parasitism where in commensalism fungi derive benefit from plant without reciprocating, and in parasitism host injures from fungi. While showing mutualistic relationship fungi benefit the provision supply of energy, nutrients, shelter and protection from unfavorable environmental conditions. In contrast to this on producing secondary metabolites and enzymes host benefitted indirectly from fungi such as plant growth, adaptation to abiotic stresses like light, drought *etc*. and biotic stresses like herbivory, insect and other pathogenic attack[33]. There is a balanced mutualistic interaction between host and endophyte under environmental, physiological and genetical aspects, which is beneficial to both host and endophyte. In case of unbalanced symbiosis; parasitic interaction, the host along with environment controls the genes of both endophyte and plant itself[34].

Properties of Endophytic Fungi:

1. Taxonomically endophytic fungi mostly belong to class Ascomycetes, Deuteromycetes and Basidiomycetes[35,36].
2. Host specificity studies suggest that endophytic fungi are non-host specific[37], but depend on ecological and geographical condition; a same class of fungi can be isolated from different plants[35].
3. According to Petrini genetic variability of endophytic fungi explains specificity at family level but it was also explained by Carroll and petrini; that strains of same fungus isolated from different parts of same plant differ in their ability[38,39].
4. Endophytic fungi reproduce by two ways; *via* vegetative growth and *via* spores.
5. These fungi have wide host range, *i.e.* one endophytic fungus can infect more than one host[40]. *Epichloe typhina* infects up to 26 different grasses[41].
6. Physiologically endophytic fungi protects host from pathogen, insects and herbivore on taking nutrition, protection *etc.* from host[42].
7. They produce bioactive compound having diverse chemical structures and are evolved to possess biological activities, these have varied roles as defensive compounds against competitors/parasites/predators, growth and reproduction facilitators, or as cell signaling compounds[44].

ENDOPHYTIC FUNGI AS PRODUCER OF BIOACTIVE COMPOUND

On showing mutualism with plant, endophytic fungi gains property of producing bioactive compounds, these compounds are active as anti-microbial (anti-bacterial, anti-fungal, anti-viral, anti-protozoal), anti-cancerous, anti-oxidant, immunomodulatory agents *etc.* which are beneficial to the human race[43]. The production of bioactive compounds by endophytes especially those exclusive to their host plants is not only important from an ecological point of view but also from a biochemical and molecular perception. Use of endophytic fungi for production of secondary metabolites and its optimization led to discovery of novel compound. Recently much effort have been done in potential endophytic fungal strains regarding the production of bioactive metabolites like taxol, pestaloside, torreyanic acid and enzymes, *i.e.* Xylanase**,** Isoflavonoids**,** Asparaginase[44]. Endophytic fungi *Pestalotiopsis fici* is an important source of bioactive natural products, including chloropupukeananin isolated from tea plant. The genome sequence of this fungus was reported, this encodes the secondary metabolite synthesizing genes, *viz.* 27 polyketide synthases (PKSs), 12 nonribosomal peptide synthases (NRPSs), five dimethylallyl tryptophan synthases, four putative PKS like enzymes, 15 putative NRPS like enzymes, 15 terpenoid synthases, seven terpenoid cyclases, seven fatty acid synthases and five hybrids of PKS NRPS. This shows the potential of secondary metabolites of the endophyte *Pestalotiopsis fici.*[45] Hence use of endophytic fungi would be interesting and beneficial to research and commercial approach.

Endophytic Fungi as Anti-microbial Agent:
It was observed that bioactive compounds from endophytic fungi have ability to resist the growth of many pathogenic microbes like bacteria, fungi, viruses and protozoans[46]. The screening of anti-microbial compounds is an approach to combat the drug resistance in microbes and for this bioactive compound from endophytic fungi is one of the most convenient ways[43,47], instead of using plants and their parts. These anti-microbial compound also take part in our nutrition along with drugs they are used as food preservatives in order to regulate bacterial growth in our food and control food spoilage and food-borne diseases[48]. In a research by Sandhu *et al*., endophytic fungi from different parts of the plant *Calotropis procera* (Linn.) R.Br. were isolated and identified on the basis of morphology and characteristics of fungal spores[49]. The highest colonization frequency of isolated fungi was observed as *Aspergillus niger*, 33.33 %, *Altenaria alternate*, 33.33% and *Curvularia lunata*, 33.33% in leaf, stem and root respectively, along with this the endophytic fungi that displayed broad spectrum antibacterial activity include: *Fusarium solani*, *Cladosporium herbarum*, *Curvularia pallescens*, *Alternaria alternata* and *Drechslera nodulosa*. A medicinal plant, *Tripterigeum wilfordii* which is native to Eurasia results an endophytic fungus *Cryptosporiopsis quercina*, this fungus shows an excellent anti-fungal activity against some important human pathogens *viz.* *Candida albicans* and *Trichophyton* sp. Cryptocandin an anti-mycotic peptide was isolated and characterized from *Cryptosporiopsis quercina*[46]. The secondary metabolite of endophytic fungus *Penicillium sclerotiorum* was extracted and a compound sclerotiorin was isolated (Figure 1). Sclerotiorin was evaluated for its action to inhibit the effect of enzyme HIV-1 (Human Immunodeficiency Virus) integrase and protease, this shows that sclerotiorin have anti-HIV-1 integrase and protease activity with 45.88 and 198.41 µM IC_{50} values respectively. The sclerotiorin also showed weak anti-fungal activity against *Candidia albicans* and *Cryptococcus neoformans* with MIC (Maximum Inhibitory Concentration) values of 202.53 µM and 101.26µM respectively[50].

The bioactive compounds from endophytic fungi isolated from different regions of Jabalpur district show tremendous antibacterial activity against five pathogenic bacteria *viz. Escherichia coli, Bacillus subtilis, Salmonella typhimurium, Streptococcus pyogenes, Klebsiella pneumoniae.* This may lead to novel natural product for use in pharmaceutical industries[51].

Endophytic Fungi as Anti-Cancerous Agent:
The unregulated proliferation of cells which leads to spread an uncontrolled growth of tissues or abnormal cells is known as 'Cancer' and the compounds used in chemotherapy either inhibit or destroy the cancerous cells[4]. The way for investigation of anti-cancerous activity of secondary metabolites of endophytic fungi was unlocked from the discovery of taxol–producing endophytes. With this work the first major class of anti-cancer agent produced from endophytic fungi includes the Paclitaxel and some of its derivatives. The existence of this highly functionalized diterpenoid paclitaxel is generally found in each of the World's Yew (*Taxus*) species. In a cancerous cell, paclitaxel prevent the tubulin molecules from depolymerizing during the process of cell division results in no abnormal cell growth[46]. The enzyme catalyzing the first committed step for taxol biosynthesis was encoded by the gene *Taxadiene Synthase (TS)*; in recent times this gene was identified in the endophytic fungi *Stemphylium sedicola* SBU 16 isolated from the inner bark of tree *Taxus baccata*[52]. Meanwhile a number of anti-cancer agents were discovered, some important anti-cancer alkaloids are Camptothecin (Figure 1) and their derivatives, used as anti-neoplastic agents for treatment of integumentary related infection in China[53].

The two important clinically useful anti-cancer drugs, topotecan and irinotecan are synthesized from camptothecin and its derivative 10-hydroxycamptothecin; these two compounds are used as precursors for the synthesis of topotecan and irinotecan[54]. In this series Deshmukh *et al.* explains a dimeric xanthene Ergoflavin (Figure 1) which belongs to the class ergochromes. This ergoflavin was isolated from the endophytic fungi growing in the leaves of medicinal plant *Mimusops elengi* and was reported as a novel anti-cancer agent[55].

Endophytic Fungi as Anti-Oxidant Agent:

Anti-oxidant agents are the agents which readily reacts, neutralize or scavenge with Reactive Oxygen Species (ROS) such as superoxide anion, hydroxyl radicals and hydrogen peroxide. ROS are the chemically reactive molecules derived from oxygen and are generated as by-products of the metabolic pathways of the living organisms[56]. A large number of diseases like Alzheimer, Parkinson's, Rheumatoid arthritis, cardiovascular diseases, *etc.* from ROS are well documented. Plethora of anti-oxidants are present in our natural diet, some enzymatic anti-oxidants are synthesized in our biological systems. Presently, researches have been going on the endophytic fungi as a promising source of anti-oxidant agent[56]. Shukla *et al.* were isolated endophytic fungi from *Ocimum sanctum* showing anti-oxidant activity[57]. A strong anti-oxidant activity was found in the endophytic fungus *Phyllosticta* sp. isolated from plant *Guazumato mentos*[58]. Endophytic fungi and their associated higher plants are shown to be a good source of novel anti-oxidants. The most potent anti-oxidant agent Pestacin and Isopestacin (Figure 1) were extracted from the culture of endophytic fungus *Pestalotiopsis microspora* isolated from host plant *Terminalia morobensis*. These two compound Pestacin and Isopestacin show anti-mycotic and anti-fungal activities respectively, along with anti-oxidant activity. The anti-oxidant activity of isopestacin was credited due to the structural similarity with flavonoids; in the solution it is able to scavenge superoxide and hydroxyl free radicals. The anti-oxidant activity of Pestacin was found to be 11 times greater than a vitamin E derivative Trolox. Pestacin activity arises principally through cleavage of an extraordinarily reactive C-H bond and to somewhat *via* OH abstraction[59,33].

Endophytic Fungi as Insecticidal Agent:

Insecticidal activity of the metabolite is the lethal action of the fungal metabolite over pathogenic or harmful insects. Several endophytes are known to have insecticidal activity. Recently, a number of alkaloids having dynamic insecticidal activity have been discovered from the endophytic fungi[60]. In this series Bills *et al.* extracted a pantropical insecticide from the fungus *Hypoxylon pulicicidum*[61].

A total of 86 endophytic fungi were isolated by Han *et al.* from the plant *Tripeterygium wilfordii*. The bioactive compounds of fungi were extracted in ethyl acetate and their ability to kill mosquito larvae were tested; only 16 strains (18.6%) out of 86 were found to have larvicidal activity, further only nine strains out of 16 showed larvicidal activity when its fermentation broth of ethyl acetate extract was tested. The genera of the active strains were *Aspergillus*, *Penicillium*, *Phoma* and *Pesalotiopsis.* The active component of one strain is Wilforgine. Endophytic fungi from this plant was isolated in order to protect the plant from destruction as the active phytochemical compound content of this plant is very low and its wild variety is very rare. In artificial cultivation *Tripeterygium wilfordii* grows slowly and need long harvesting period, resulting its production is unable to meet commercial demand. Thus the insecticidal compound of endophytic fungi from the plant *Tripeterygium wilfordii* will so far combat the market demand[62].

Endophytic Fungi as Precursors for Bio-Fuel Production:

With globalization and climate change, the fuel reserve decreases continuously, this lead to generate biologically derived fuel such as bio-fuel from various biological matters. Bio-fuel like Bio-diesel is defined as the fatty acid methyl esters obtained from various biologically renewable lipid resources like rapeseed oil, soybean oil, palm oil, *etc*[63]. Recently production of bio-diesel from plants and their parts made a conflict between fuel and food security[64]. Hence, a proposed alternative to this is endophytic fungi, this on interaction with host plant become the good source of lipid resources[63]. Endophytic fungi have the ability to degrade cellulose and produce a diversity of astonish metabolites. With this concept the filamentous endophytic fungus *Ascocoryne sarcoides* when grown in cellulose based medium, has ability to produce potential bio-fuel metabolites[64]. The genome of the *Ascocoryne sarcoides* was characterized and by using transcriptomic and metabolomic data, genes for cellulose degradation and bio-fuel production pathway was hypothesized. A total of 80 biosynthetic clusters were identified, some of them were previously found in plants also[65]. Thus a support to endophytic fungi as a precursor for bio-fuel may combat the fuel problem. A list of bioactive compounds from Endophytic fungi with their activity and host plant is tabulated in Table 2[66-81].

Taxol an anti-cancerous compound is accepted as a drug against breast and ovarian cancer by Food and Drug Administration (FDA), USA[82].

CONCLUSION

India is blessed with remarkable heritage of plant biodiversity. This biodiversity is often exploited for manufacturing various useful products; like furniture, medicines, food items, textiles, bio-fuel *etc.*, by which we have made unprecedented progress throughout our life. One of the most useful products from plants is drugs and medicines. Ayurveda and ethno medicinal plants have its own importance in the development of the modern medicines. India export and imports significant quantity of plant raw material to pharmaceutical industries for drug manufacturing. Commercialization of herbal drugs and medicines are exploring day by day. Because of drug manufacturing process and its recurrent use habitat and future of medicinal plants are being threatened. This leads to increase in ecological imbalance, global warming, pollution and many more problems. On understanding the seriousness of this loss, we must have to select the better alternative.

One of the suitable alternate to protect plant biodiversity from exploitation is endophytic fungi from medicinal plants.

Table 1

Drugs derived from plants with their ethno-medical correlations and sources.

S. No.	Drug	Nature	Clinical use	Plant Name	Family
1	Acetyldigoxin	Glycoside	Cardiotonic	*Digitalis lanata* Ehrh.	Plantaginaceae
2	Agrimophol	Alkaloid	Anthelmintic	*Agrimonia eupatoria* L.	Rosaceae
3	Aescin	Saponins	Anti-inflammatory	*Aesculus hippocastanum* L.	Sapindaceae
4	Aesculetin	Phenolic compound	Antidysentery	*Fraxinus rhynchophylla* Hance.	Oleaceae
5	Adoniside	Cardenolides	Cardiotonic	*Adonis vernalis* L.	Ranunculaceae
6	Ajmalicine	Alkaloid	Circulatory disorders	*Rauvolfia serpentina* (L.) Benth ex. Kurz	Apocyanaceae
7	Allylisothio-cyanate	Organosulfur compound	Rubefacient	*Brassica nigra* (L.) Koch.	Brassicaceae
8	Andrographol-ide	Diterpene lactone compound	Bacillary dysentery	*Andrographis paniculata* Nees.	Acanthaceae
9	Anisodamine	Alkaloid	Anticholinergic	*Anisodus tanguticus* (Maxim.) Pascher	Solanaceae
10	Anisodine	Alkaloid	Anticholinergic	*Anisodus tanguticus* (Maxim.) Pascher	Solanaceae
11	Atropine	Alkaloid	Anticholinergic	*Atropa belladonna* L.	Solanaceae
12	Asiaticoside	Glycoside	Vulnerary	*Centella asiatica* (L.) Urban	Apiaceae
13	Arecoline	Alkaloid	Anthelmintic	*Areca catechu* L.	Piperaceae
14	Bergenin	Tannin	Antitussive	*Ardisia japonica* Bl.	Myrsinaceae
15	Berberine	Alkaloid	Bacillary dysentery	*Berberis vulgaris* L.	Berberidaceae
16	Bromelain	-	Anti-inflammatory; proteolytic agent	*Ananas comosus* (L.) Merrill	Bromiliaceae
17	Caffeine	Xanthine alkaloid	CNS stimulant	*Camellia sinensis* (L.) Kuntze	Theaceae
18	(+)-Catechin	Phenolic compound	Haemostatic	*Potentilla fragaroides* L.	
19	Chymopapain		Proteolytic; mucolytic	*Carica papaya* L.	Caricaceae
20	Codeine	Alkaloid	Analgesic: Antitussive	*Papaver somniferum* L.	Papaveraceae
21	Cocaine	Alkaloid	Local anaesthetic	*Erythroxylum coca* Lamk.	Erythroxylaceae
22	Colchicine	Alkaloid	Antitumor agent; antigout; anti-inflammatory	*Colchicum autumnale* L.	Liliaceae
23	Convallotoxin	Glycoside	Cardiotonic	*Convallaria majalis* L.	Liliaceae
24	Curcumin	Phenolic compound	Choleretic	*Curcuma longa* L.	Zingiberaceae
25	Cynarin	Phenolic acid	Choleretic	*Cynara scolymus* L.	Asteraceae
26	Danthron	Quinone	Laxative	*Cassia* sp.	Fabaceae
27	Deserpidine	-	Antihypertensive; tranquilizer	*Rauvolfia canescens* L.	Apocyanaceae
28	Deslanoside	Glycoside	Cardiotonic	*Digitalis lanata* Ehrh.	Plantaginaceae
29	Digitoxin	Glycoside	Cardiotonic	*Digitalis purpurea* L.	Plantaginaceae
30	Digitalin	Glycoside	Cardiotonic	*Digitalis purpurea* L.	Plantaginaceae

31	Digoxin	Glycoside	Cardiotonic	*Digitalis lanata* Ehrh.	Plantaginaceae
32	Emetine	Alkaloid	Amoebicide; emetic	*Cephaelis ipecacuanha* (Brotero) A. Richard	Rubiaceae
33	Ephedrine	Alkaloid	Sympathomimetic	*Ephedra sinica* Stapf.	Ephedraceae
34	Etoposide	Glycoside	Antitumour agent	*Podophyllum peltatum* L.	Berberidaceae
35	Gitalin	Glycoside	Cardiotonic	*Digitalis purpurea* L.	Plantaginaceae
36	Glaucaroubin	Terpenes	Amoebicide	*Simarouba glauca* DC.	Simaroubaceae
37	Glycyrrhizin	Terpenes	Sweetener	*Glycyrrhiza glabra* L.	Fabaceae
38	Gossypol	Terpenes	Male contraceptive	*Gossypium* sp.	Malvaceae
39	Hemsleyadin	-	Bacillary dysentery	*Helmsleya amabilis* Diels	Cucurbitaceae
40	Hydrastine	-	Hemostatic; astringent	*Hydrastis Canadensis* L.	Ranunculaceae
41	Hyoscamine	Atropine	Anticholinergic	*Hyoscamus niger* L.	Solanaceae
42	Kainic acid	Pyrrolidine	Atropine	*Digenea simplex* (Wulf.) Agardh	Rhodomelaceae
43	Kawain	Pyran	Tranquilizer	*Piper methysicum* Forst. f.	Piperaceae
44	Khellin	Coumarin	Bronchodilator	*Ammi visnaga* (L.) Lamk.	Apiaceae
45	Lanatosides – A, B, C	Glycoside	Cardiotonic	*Digitalis lanata* Ehrh.	Plantaginaceae
46	Lobeline	Alkaloid	Smoking deterrent; respiratory stimulant	*Lobelia inflate* L.	Campanulaceae
47	Monocrota-line	Alkaloid	Antitumor agent	*Crotolaria sessili* flora L.	Fabaceae
48	Morphine	Alkaloid	Analgesic	*Papaver somniferum* L.	Papaveraceae
49	Neoandro-Grapholide	Diterpene glucosides	Bacillary dysentery	*Andrographis paniculata* Nees	Acanthaceae
50	Noscapine	Alkaloid	Antitussive	*Papaver somniferum* L.	Papaveraceae
51	Ouabain	Glycoside	Cardiotonic	*Strophanthus gratus* Baill.	Apocyanaceae
52	Papain	Protein	Proteolytic; mucolytic	*Carica papaya* L.	Caricaceae
53	Papaverine	Alkaloid	Sympatholytic musculotropic	*Papaver somniferum* L.	Papaveraceae
54	Phyllodulcin	Coumarin	Sweetener	*Hydrangea macrophylla (*Thunb.) DC	Hydrangeaceae
55	Physostig-mine	Indole alkaloid	Cholinesterase inhibitor	*Physostigma venenosum* Balf.	Fabaceae
56	Picrotoxin	Cycloparaffin	Analeptic	*Anamirta cocculus* (L.) W. & A.	Menispermaceae
57	Pilocarpine	-	Parasympathomimetic	*Pilocarpus jaborandi* Holmes	Rutaceae
58	Podophyllotoxin	Lignans	Condylomata	*Podophyllum peltatum* L.	Berberidaceae
59	Protoveratrines A &B	Alkaloid	Antihypertensive	*Veratrum album* L.	Liliaceae
60	Pseudoephedrine	Phenethyl-amine	Sympathomimetic	*Ephedra sinica* Stapf.	Ephedraceae
61	Quisqualic acid	Azoles	Anthelmintic	*Quisqualis indica* L.	Combretaceae
62	Quinine	Alkaloid	Antimalaric	*Cinchona ledgeriana* Moens ex. Trimen	Rubiaceae
63	Rescinnamine	Alkaloid	Antihypertensive; tranquilizer	*Rauvolfia serpentine* (L.) Benth ex. Kurz	Plantaginaceae

Table 2
List of bioactive compounds from Endophytic fungi.

Host Plant	Endophytic Fungi	Compound	Activity	References
Taxus brevifolia	*Taxomyces andreanae*	Taxol	Anti-cancerous	[66]
Torreya taxifolia	*Pestalotiopsis microsporum*	Pestaloside	Anti-microbial	[67]
Torreya taxifolia	*Pestalotiopsis microsporum*	Torreyanic acid	Anti-microbial	[67]
Tripterigeum wilfordii	*Cryptosporiopsis cf. quercina*	Cryptocandin	Anti-microbial	[68]
Tripterigeum wilfordii	*Cryptosporiopsis cf. quercina*	Cryptocin	Anti-fungal	[69]
Salix gracilostyla var. melanostachys	*Phomopsis* sp.	Phomopsichalasin	Anti-bacterial	[70]
Bontia daphnoides	*Nodulissporium* sp.	Nodulisporic acid	Insecticidal	[71]
Paullina paullinoides	*Muscodor vitigenus*	Naphthalene	Insecticidal	[72]
Terminalia morobensis	*Pestalotiopsis microsporum*	Pestacin and isopestacin	Anti-oxidant	[73]
Cassia spectabilis	*Phomopsis cassia*	Phomosilactilis	Anti-fungal	[74]
Taxus cuspidate.	*Periconia* sp.	Periconicins A and B	Anti-bacterial	[75]
Nothapodytes foetida	*Enthrophospora infrequens*	Camptothecin	Anti-neoplastic	[76]
Sinopodophyllum hexandrum	*Alternaria neesex*	Podophyllotoxin	Anticancer, antimicrobial	[77]
Cardiospermum helicacabum	*Pestalotiopsis pauciseta*	Paclitaxel	Anticancer	[78]
Huperzia serrata	*Acremonium* sp.	Huperzine A	Insecticidal	[79]
Paris polyphylla var. yunnanensis	*Cephalosporium* sp.	Diosgenin	Anticancer, antiviral	[80]
Hypericum perforatum	*Chaetomium globosum*	Hypericin,	Antiviral	[81]
Hypericum perforatum	*Chaetomium globosum*	Emodin	Antiallergic, Antitumour.	[81]

The biologically active compounds from these could be produce commercially on large scale as these fungi are easily cultured in laboratory and fermented. These aureate resources could be manipulated further for higher production by applying new and improved biotechnological approaches like recombinant DNA technology, metabolic and fermentation technology.

On the other hand in bio-fuel production, many plants like euphorbia, jatropha, castor *etc.* are exploited commercially. With the expansion in commercialization and transport system, scarcity of fossil fuels is also observed. This again destroys biodiversity and ecosystem to some extent. If we continue of exploiting biodiversity in this way then disasters like volcano eruption, earthquakes, tsunami and storms becomes very common to all of us, resulting a dismal failure of ecosystem. So, there is a need to develop some renewable source as an alternate to fossil fuel. Choosing endophytic fungi as efficient enzymes producer to convert biomass into fermentable substrate in order to produce bio-fuel is a tremendous work in the field of endophytes.

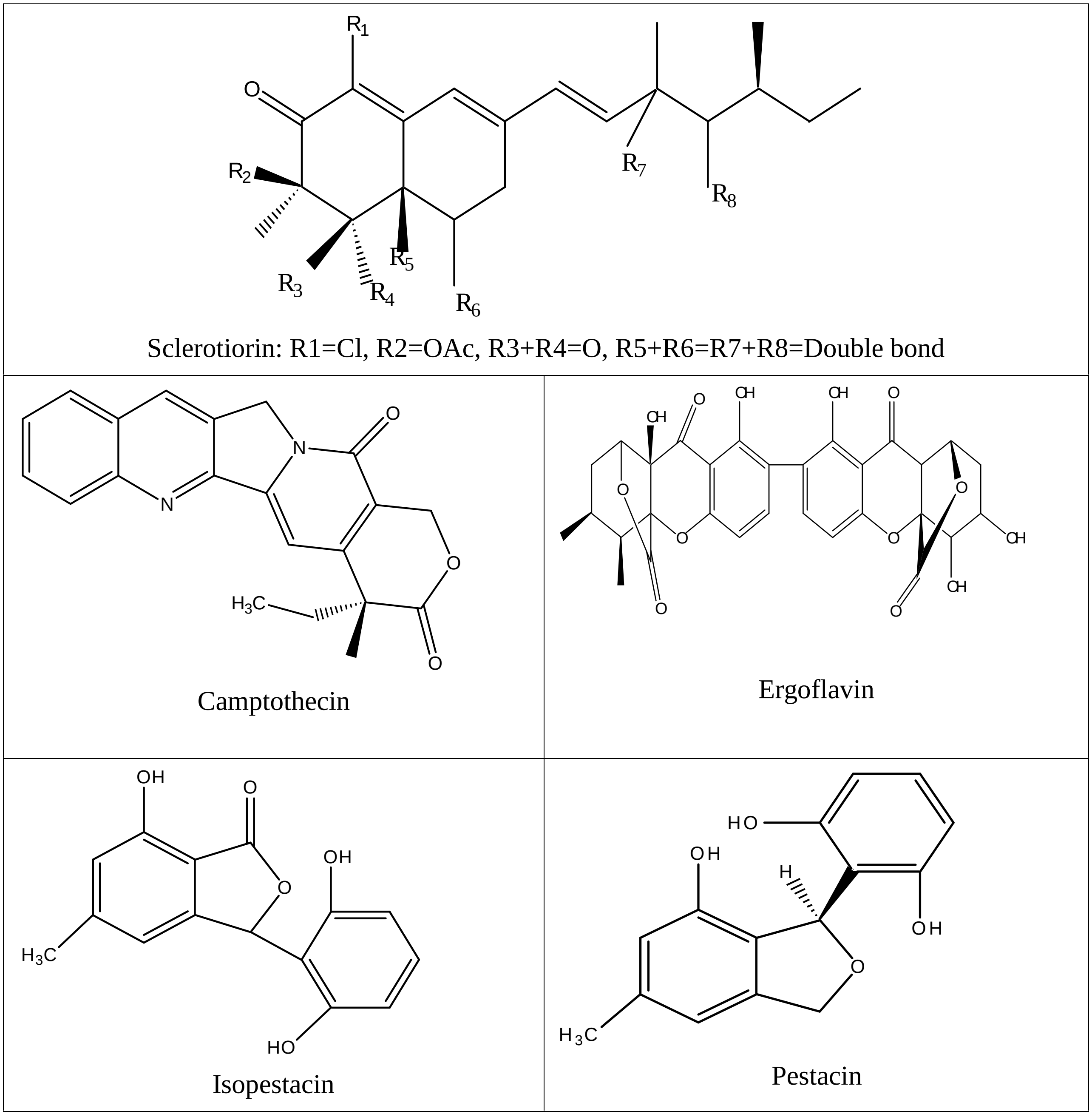

Figure 1
Chemical structure of some Bio-active compounds from Endophytic fungi

In 20th century, fungal bioprospecting had its focus on the search for traditional secondary metabolites having drugs and enzymes value with good applications in plant improvement, disease control and in developing eco-friendly environment. This offers a great opportunity in field of agriculture, industries and medicines.

Finally, endophytic fungi are novel and important source of bioactive compounds having potential activities (anti-microbial, anti-oxidant, anti-cancerous, immunomodulatory *etc.*). These are the good source of enzymes too for production of bio-fuel. Exploiting endophytic fungi across the world could conserve plant biodiversity and establish an eco-friendly ecosystem to large extent.

CONFLICT OF INTEREST

There is no potential conflict of interests between the authors regarding the publication of this article.

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