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Need Exploration of Endophytic *Streptomyces* - Review

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Endophytic actinomycetes especially *Streptomyces* are the most wanted genera in Biopharamaceutical industries. Inside the plants they plays critical role which promotes growth. Endophytic biology would be the new microbial niche is needed to explore more especially for Streptomyces genera. Their genetic co-evaluation with plants can create novel chemistry and its ability of producing plant chemicals has raised its importance to combat against various drug resistance organisms and to reduce the over harvesting of the plants. The current review describes the need of endophytes isolation from antimalarial ethanobotanical valued plants and its important chemicals also concentrated. Majorly, this report discusses the rational approach on selecting medicinal plants for endophytic Streptomyces against the specific disease.

Key words: Endophytic *Streptomyces*, Antimalarials, Medicinal plants.

Need of antimalarial drugs

Infectious disease remains one of the biggest killers in developing countries (Stella Hurtley *et al.*, May 2010) which are emerged due to climate change, might be caused by deforestation process. Further, the resistance pattern of Plasmodium falciparum to recent drugs and often creates new drug need (Arjen M dondorp, 2009). So the world countries spending lot of millions to find broad spectrum compounds identification. However this drug finding journey touches atleast some 70 years now. There is widespread agreement that action is required to reverse or at least slow down this process. The more prudent use of the antibiotic also sometime leads to the antibiotic resistance. (Richard Wise, 2008). There is an urgent need to study the most commonly used drugs for their potency in reducing parasite growths and symptoms of the disease. If the objective is discovery of novel antimalarial drug candidates, the choice of study plants that might possess compounds with antiplasmodial activity is an important but difficult task (Geme Urge Dori, 2008).

Endophytic actinomycetes

Endophytes are the microorganisms that colonize inside the plant tissues below the epidermal cell layers, and the host plant tissues are transiently asymptomatic (G A Strobel 2003). Almost all vascular plants harbor several endophytic actinomycetes, which would helps to improve host plants growth promotional activity against disease symptoms caused by plant pathogens and/or various environmental stress factors (Sachiko Hasegawa *et al.*, 2006). It is

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noteworthy that, of the nearly 300,000 plant species that exist on the earth, each individual plant host to one or more endophytes. Only a few these plants have ever been completely studied relative to their endophytic biology. Accordingly, the opportunity to find new and beneficial endophytic microorganisms among the diversity of plants in different ecosystems is considerable (Robert P Ryan, 2008). Consequently, the opportunity to find novel endophytic microorganisms causing the variety of plants in various ecosystems is great.

Plants have myriads of chemical and anatomical defenses, whose intensity level depend on biotic and environmental influences (Mika T. Tarkka *et al.*, 2008). Precursors often stimulate production of secondary metabolites either by increasing the rate of a limiting precursors, and unusual structures and their formation is regulated by nutrients, growth rate, feedback control, enzyme inactivation, and enzyme induction (Arnold Demain, 1998). The energy lost by the plant in the production of endophyte biomass is in all likelihood adequately compensated for by the improvements in plant health derived from the presence of mutualistic microorganisms (Backman, P A, Sikora, RA 2008). Thus, it appears that these biotypical factors can be important in plant selection, since they may govern the novelty and biological activity of the products associated with endophytic microbes (Strobel *et al.*, 2003). Sometimes extremely unusual and valuable organic substances are produced by these endophytes that are sources

Table 1. Recently identified endophytic Streptomyces with with antimicrobial and antimalarial active compounds

Organism	Plant association	Active agent	Activity	Reference
Streptomyces sp. (strain HK10552)	*Aegiceras corniculatum*	Four new p-aminoacetophenonic acids (Polyene macrolide antibiotics)	Antifungal	Fangfang Wang *et al.,* 2010
Streptomyces albidoflavus	Mangrove plants.	Antimycin A18	Bioactivity	Lei-Lei Yan *et al.,* 2010
Streptomyces sp GS DV232	Traditional Chinese medicinal plants	4-methyl-2-quinazolinamine (1)	Antiproliferative bioactivity	Daniel Vollmar *et al.,* 2009
Streptomyces sp Tc052	*Alpinia galangal*	Kempferol, isoscutellarin, umbelliferone, cichoriin	Antibacterial	Taechowisan *et al.,* 2008
Streptomyces aureofaciens CMUAc130	*Zingiber officinale*	4-Arylcoumarins	Anti-tumor active	Taechowisan *et al.,* 2007
Streptomyces NRRL 3052	*Kennedia nigriscans*	Munumbicins E-4. E-5	Antimalarial activity and broad specturum	Castillo *et al.,* 2006
Streptomyces griseus	*Kandelia candel*	p-aminoacetophenonic acid	Antimicrobial	Guan2005
Streptomyces aureofaciens CMUAc 130	*Zingiber officinale* Rosc	5, 7-dimethoxy- 4-p-methoxyphenylcumarin and 5,7-dimethoxy-4-phenylcumarin	antifungal activity	Taechowisan *et al.,* 2005
Streptomyces sp TP-A0569	Spring onion	Fistupyrone	Antifungal	Aremu *et al.,* 2003
Streptomyces NRRL 30566	*Grevillea pteridifolia*	Kakadumycins	Antibiotic	Castillo2003
Streptomyces sp. MSU-2110	*Monstera* sp.	Coronamycins	Antimalarial, antifungal	Ezra2004
Streptomyces NRRL 30562	*Kennedia nigriscans*	Munumbicins A, B,C Munumbicin D	Antibiotic, Antimalarial	Castillo 2002

of novel chemistry (T R Prashith Kekuda *et al.*, 2010). Thus, study of endophytic microbial diversity is more crucial to figure out new and emerging disease ills and to advance biotechnology. Enphytic microbes seem to fit perfectly into this natural 'warehouse' only a small part of which we have been able to tap into so far. (Agata Staniek *et al.*, 2008).

Currently, endophytic actinomycetes are looked at as a prominent source of bioactive natural products because there so many of them invading literally millions of unique biological niches (higher plants) growing in so many unusual environments. A specific rationale for the collection of each plant for endophytic isolation and natural products discovery is used. The plant selection can be adopted by the geographical nature of the plants and ethanobotanical value of the plants.

Table 2. Previously reported antimalarial compounds from medicinal plants

Compound	Plant name
Quinolinecarbinolamine quinine- Quinolines	Cinchona sp (Rubiaceae) (Casteel, 1997)
Augustine , crinamine , lycorine - isoquinoline alkaloids	Crinum amabile (Maryllidaceae) (Likhitwitayawuid e t al., 1993b).
Hervelines - a type of pavine- benzylisoquinoline alkaloids	Hernandia Voyoronii (Hernandiaceae)(Rasoanaivo *et al.*, , 1998)
korupensamine A, korupensamine B, 5-O_- demethyldionchophylline - Naphtylisoquinoline alkaloids	Triphyophyllum peltatum (Ancistrocladaceae) (Bringmann *et al.*, 1998; Hallock *et al.*, 1994)
Lissoclinotoxins- sulfur-containing alkaloids	Lissoclinum perforatum(Litaudon *et al.*, 1994).
Sarachine (Pseudoalkaloids)	Saracha punctata (Solanaceae) (Moretti *et al.*, 1998)
Licochalcone A	G. glabra (European liquorice), G. uralensis, or G. inflate (Fabaceae) (Christensen *et al.*, 1994)
Diuvaretin and uvaretin - dihydrochalcones	Uvaria sp (Annonaceae)(Nkunya *et al.*, 1991).
Neolignan nyasole(Lignans)	Asparagus africanus (Asparagaceae) (Oketchrabah *et al.*, 1997)
Termilignan	Terminalia bellerica (Combretaceae) (Valsaraj *et al.*, 1997)
5,6,7-trimethoxycoumarin, isofraxidin - coumarins	Artemisia abrotanum (Asteraceae)(Cubukcu *et al.*, 1990; Khalid *et al.*, 1986)
Anthraquinone	Morinda lucida (Rubiaceae)(Makinde *et al.*, 1994; Wijnsma and Verpoorte, 1986)
Plumbagin - Naphtoquinones	Nepenthes thorelii (Nepenthaceae) (Likhitwitayawuid et al., 1998a)
Cowanol - Xanthones	Garcinia cowa (Clusiaceae) (Likhitwitayawuid *et al.*, 1998b).
endoperoxide yingzhaosu A - Peroxides(Sesquiterpenoids)	Artabotrys unicinatus (Annonaceae) (Desmet, 1997)
Artemisinin - natural peroxide Artemether, arteether, sodium artesunate	Artemisia annua (Asteraceae)(Casteel, 1997; Murray and Perkins, 1996)
Quinone methides	Salacia sp , Maytenus sp, (Elastraceae) (Desmet, 1997; Gessler *et al.*, 1994; Sullivan *et al.*, 1998)
Limonoids	Azadirachta indica (Meliaceae) (Desmet, 1997; Phillipson and Wright,1991)
Bruceantin - Quassinoids - (triterpenoids)	Brucea antidysenterica Mill. (Simaroubaceae) (Phillipson and Wright, 1991)
Tumacoside A, tumaquenone - steroidal saponins	Solanum nudum(Solanaceae) (Saez *et al.*, 1998)
Fagaramide - alkamides	Fagara rhetza (Rutaceae) (Shibuya *et al.*, 1992; Sittie et al., 1998; Weenen *et al.*, 1990)

Plant based chemical compounds from Endophytes

Endophytes are a rich source of natural products displaying a broad spectrum of biological activities and the phytochemistry of endophytic microbes continues to increase in significance. As a general rule, a single endophytic strain will produce multiple bioactives (Strobel, A Stierle *et al.*,1993). However, the distribution of actinomycetes in the plants is mostly unexplored and the presence of indigenous endophytic actinomycetes in the plants in its infancy. Another significant observation is that novel compounds with biological activities have been isolated from these endophytic actinomycetes indicating they are the potential source for the discovery of novel secondary metabolites. There is an enormous possible for the isolation of novel secondary metabolites from endophytic Strptomyceys species. In this respect, future success trusts on our ability to find novel endophytic actinomycetes from the plants. Many fungal organisms were already reported for the production of similar plant chemicals. Broad spectrum active Guanacastepene (Singh *et al.,* 2000), antiviral active Cytonic acid A and B (Guo *et al.,* 2000), Hinnuliquinone (Singh *et al.,* 2004), Isobenzofuranones, Pestacin and Isopestacin (Strobel *et al.,* 2002), Paclitaxel (Shrestha K *et al.,* 2001). These nature gifted potential bioactive endophytes will play the greatest role for bioprospecting and will conserve the medicinal plants (G A Strobel, 2005) which mostly needed for novel drug discovery (Bhutani and Gohil, 2010).

Recently endophytic *Streptomyces artemisiae* identified from antimalarial plant *Artemisia annua* L. (Guo-Zhen Zhao *et al.,* 2010) and others were listed in Table 1.

Ethano botanical valued plants and its chemistry

Plants based phenols and polyphenols, flavonoids, isoflavones, terpenes and glucosinolates are responsible for bitterness and appear to lower the risk of various communicable and non-communicable diseases. (A Drewnowski and C Gomez-Carneros, 2000). These chemicals activating "cryptic pathways" for secondary metabolite biosynthesis in Actinomycete genome which are abundant(S Rigali *et al.,* 2008). Thereby offering new prospects in the fight against emerging diseases. The chemical and biological diversity of nature is immeasurable and provides an extraordinary resource for the discovery of drugs (T. Luke Simmons, 2005). The World Health Organization estimates that over 65% of the world's population relies on traditional medicine for their primary health needs (Ming-Wei Wang, 2007, Daniel S. Fabricant, 2001). Listed are a few examples of plant-derived therapies currently in clinical use for treatment of various forms of malaria (table 2).

One significant problem associated with natural product drug research is nature only produces a relatively small amount of these phytochemicals. Sometime, these compounds are the same as those produced by the particular host plants, thus triggering the expectation that endophytes that can serve as an alternative source of potential plant secondary metabolites (V. Priti et al., 2009). So, Plants with these like ethanobotanical history, also likely candidate for study, since the medical uses to which the plant may have been selected relates more to its population of endophytes than to the plant biochemistry itself. The microorganisms living inside the plant tissue for long duration will make the co-evaluation. This is due to the adaptation condition made by the organisms due to the genetic variation with the host. This paves the best way to produce some Phytochemicals by the guest organisms (H W Zhang *et al.,* 2006). Endophytic organisms found in all the types of plant tissues such as stems, roots, leaves, fruits, ovules, seeds, tubers, rachis, bark. Probably hundreds of endophytic species from a single plant is also possible, and among them, at least one generally shows host specificity. (Tan *et al.,* 2001). Thus, if endophytes can produce the same rare bioactive compounds as their host plants, this would not only reduce the need to harvest slow growing and possibly rare plants but also preserve the world's ever-diminishing biodiversity. Furthermore, it is recognized that a microbial source of a valued product may be easier and more economical to produce, effectively reducing its market price.

CONCLUSION

Vector transmitting pathogens causes high level threat to humans and animal life. The climatically changes will tremendously influence life cycles of arthropod vectors for the maximum productivity which resulting in changes in both vector and pathogen distribution and changes in the ability of arthropods to transmit pathogens (W.J Tabachnick, 2010). Endophytic are a poorly investigated group of microbial floras that constitute an ample and reliable source of bioactive and novel chemical compounds with possible for developments in a various biomedical disciplines biotechnology industries. Thus, it is essential that new groups of actinomycete from unexplored or underexploited niches be pursued as source of novel bioactive secondary metabolites (Kin S Lam, 2006). Although figure out on the usage of this vast resource of poorly understood microorganisms has just begun, it has already become apparent that a tremendous possible for organism, product, and utilization discovery in this field holds stimulating hope. Insights from such research may provide alternative methods of natural product drug discovery which could be reliable, economical and environmentally safe. Antibiotic productivity has been known to be closely related to the cultural conditions that exist in a relevant environment (Takao Okazaki 2006). Research attempts to discover new bioactive compounds from prokaryotic organisms, and in particular, Actinomycetes, appear to have been declining over the recent years. Recently, various new genera of Actinomycetes were found, resulting the discovery of new bioactive substances.

This is one of the most attractive and significant research themes for plant-microbe interactions (Sachiko Hasegawa *et al.*, 2006). Finding of new variety of antibiotics is one of the greatest events in the history of medicine which has a profound effect on human life, thus in society as a whole (B K Bhattacharyya and S K Sen, 2006).

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