Introduction

The term of entophytes or entophytic microorganisms/microbes includes an intriguing group of microorganisms – mostly fungi and bacteria - that colonize living and internal tissue of plants and exhibit complex interactions with their host, which involves mutualism, antagonism, but rarely parasitism (Strobel and Daisy [1]). Nair and Padmavathy [2]. In the sense of mutual interaction, many reports show that entophytic microbes can interfere the host in various way such as stimulating plant growth, production of antibiotics and other secondary metabolites, protection against biotic and a biotic stresses, promoting nitrogen fixation, and heavy metal homeostasis (Hardoim et al. [3]). Thus, the entophytic microbes are beneficial for many fields including agricultural fields as well as pharmaceuticals, mainly through the production of their natural products.

Entophytic microbes produce bioactive secondary metabolites that can serve as excellent source for various pharmaceutical agents, inasmuch as antimicrobial, anticancer, ant diabetic, antioxidant, immunosuppressant’s, and an arthritic Gouda et al. [4]. For this medicinal purpose, many studies are more focused on searching for antimicrobial potency such as antibiotic, ant viral, and antifungal, or related potency such as anticancer bioactivity. Two others major findings of their bioactivities, namely ant diabetic and antioxidant are also a promising prospect for further research in entophytes. Several laboratories in Indonesia have been searching for entophytes of these roles, including Lembaga Ilmu Pengetahuan Indonesia (LIPI) or Indonesian Institute of Sciences, a major research institution in Indonesia. This paper provides selected data obtained in Indonesia mainly for current research of entophytes and their secondary metabolites with potency as ant diabetic and antioxidant.
fungi *Colletotrichum sp.* from Indonesian grown *Taxes sumatrana* revealed that the α-glycosidase inhibitor compounds are the unsaturated fatty acids, namely oleic, linoleum, and linolenic acids Arrant et al. [9]. In the world of bacteria, screening of entrophic actinomycetes isolates from *Tinospora crisp* indicated a novel species that has 92% similarity with *Streptomycyes olivochromogenes* but shows potential anti diabetic bioactivity Pujiyanto et al. [10].

**Antioxidant Activity**

Antioxidants are substances that prevent free radical induced tissue damage by preventing the formation of the free radicals, scavenging them, or by promoting their decomposition, while excess free radical production originating from endogenous or exogenous sources might play a role in many diseases such as cancer, autoimmune disorders, and cardiovascular and neurodegenerative diseases Young and Woodside [11]. Therefore, the search for effective and nontoxic natural source compounds with antioxidant activity has been intensified in recent years. There are various *in vitro* and *in vivo* methods that are being used for the evaluation of antioxidant activity of the sample interest, in which DPPH method was found to be used mostly for the *in vitro* test Alam et al. [13]. After screening isolated entophytic fungi from *Curcuma longa*, Bustanussalam et al. [14]. Reported some isolates that have potential antioxidant activity.

Additionally, a more recent study indicated that rhizome of other various Zingiberaceae family plants that harbors many entophytic fungi also possess anti oxidative activity Praptiwi et al. [15]. In Taxicab family, an isolated entophytic fungus associated with *Taxes sumatrana* also exhibits anti oxidative activity Artanti et al. [16]. A sesquiterpene compound isolated from *Acremonium sp.* the entophytic fungi from the twigs of *Garcinia griffithii*, had been elucidated and reported to have antioxidant activity Elita et al. [17]. A significant amount of total phenolic content in ethyl acetate extract of endophytic fungus *Fennellia nivea* associated with *Typhonium divaricatum* confirms it’s high anti oxidative activity Saraswaty et al. [18].

**Future Research and Prospect**

In addition to find the novel species, exploration of entophytes opens the way to find many potential bioactive for medicinal purpose and to cope more understanding the complex mechanism of interaction between plants and microorganism. According to Strobel and Daisy [1], Earth is the home of nearly 300,000 species of plants, where each individual plant is host to one or more endophytes. With approximately 11% of the globe’s plant species, at least 33,000 endophytes can be found in Indonesia. Endophytes inhabiting these hosts are poorly studied, which leaves a promising but also challenging research for the future. In this case, Indonesian Culture Collection or Inca (http://inacc.biologi.lipi.go.id/), a part of LIPI, has significantly contributed to microbiological research in Indonesia by searching number of new species and exploring their bioactivities.

Collaborating with international networks, its collections have been used for generating natural product libraries to accelerate the high-throughput discovery of therapeutic leads and/or new molecular structures Johnson et al. [19] Furthermore, understanding the knowledge of relationship between the entophytes and their host will facilitate the ideal production of better drugs. Traditional way to produce natural product based drugs is extraction directly from the medicinal plants, which sometimes quantitatively gives small yields. Manipulating the growth conditions of medicinal plants by adding a particular group of entopic fungi to the plants is potentially improve the drug quality and quantity Jia et al. [20].

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