

Antidiabetic and Antioxidant Bioactivity of Various Potential Endophytic Microorganisms in Indonesia: A Mini Review



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Abstract

Entophytes are reliable source of bioactive compounds and secondary metabolites to various natural drugs. This potential of entophytes is promising but not yet fully explored. This paper provides selected data for current research of entophytes with potency as antidiabetic and antioxidant in Indonesia.

Introduction

The term of entophytes or entophytic microorganisms/microbes includes an intriguing group of microorganism – 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 Haridoim 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, antidiabetic, 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, antiviral, and antifungal, or related potency such as anticancer bioactivity. Two others major findings of their bioactivities, namely antidiabetic 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 Indonesia 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 antidiabetic and antioxidant.

Anti Diabetic Activity

The prevalence of diabetes has increased rapidly for the last decade, and will continue to increase in numbers and significance for the next decades Mathers and Loncar [5]. Most people with diabetes live in low and middle income countries confirm the large burden of diabetes in developing countries Guariguata et al. [6]. Consequently, the screening of new and affordable sources including entophytes for antidiabetic effects is mandatory. *In vitro* test such as α -glucosidase inhibitor assay provides an ideal way for initial screening the potential endophytes with alleged antidiabetic bioactive and later can be tested *in vivo* to confirm their effects. Dompeipen et al. [7]. Reported some potential isolated endophytic fungi that produce antidiabetic compounds from *Andrographis paniculata*, *Orthosiphon spicatus*, and *Piper croctacum*. Interestingly, besides their entophytes, these Indonesian medicinal plants have potencies as antidiabetic compound sources as well.

However, understanding relationship between the host and their entophytes to show such similar antidiabetic bioactivity is remaining unclear. Purified coumarone compound 8-hydroxy-6,7-dimethoxy-3-methylisocoumarin of entophytic fungi *Xylariaceae* sp. that isolated from the stem of *Quercus gilva* shows strong inhibitory activity against α -glucosidase Indriyaningsih and Tachibana [8]. Along with the recognized finding of anticancer taxin in entophytic fungi from various *Taxus* species worldwide, study in entophytic

fungi *Colletotrichum sp.* from Indonesian grown *Taxus sumatrana* revealed that the α -glucosidase inhibitor compounds are the unsaturated fatty acids, namely oleic, linoleum, and linolenic acids Arrant et al. [9]. In the world of bacteria, screening of entophytic actinomycetes isolates from *Tinospora crisp* indicated a novel species that has 92% similarity with *Streptomyces 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]. Pham-Huy et al. [12]. Therefore, the search for effective and nontoxic natural source compounds with ant oxidative 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 harbours many entophytic fungi also possess anti oxidative activity Praptiwi et al. [15]. In Taxicab family, an isolated entophytic fungus associated with *Taxus 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 Elfita 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 Saraswati 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 entophytes. With approximately 11% of the globe's plant species, at least 33,000 entophytes can be found in Indonesia. Entophytes 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 entophytic fungi to the plants is potentially improve the drug quality and quantity Jia et al. [20].

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