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Research review paper

Endophytes as *in vitro* production platforms of high value plant secondary metabolites

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ABSTRACT

Many reports have been published on bioprospecting of endophytic fungi capable of producing high value bioactive molecules like, paclitaxel, vincristine, vinblastine, camptothecin and podophyllotoxin. However, commercial exploitation of endophytes for high value-low volume plant secondary metabolites remains elusive due to widely reported genomic instability of endophytes in the axenic culture. While most of the endophyte research focuses on screening endophytes for novel or existing high value biomolecules, very few reports seek to explore the possible mechanisms of production of host–plant associated or novel secondary metabolites in these organisms. With an overview of host–endophyte relationship and its possible impact on the secondary metabolite production potential of endophytes, the review highlights the evidence reported for and against the presence of host-independent biosynthetic machinery in endophytes. The review aims to address the question, why should and how can endophytes be exploited for large scale *in vitro* production of high value phytochemicals? In this regard, various bioprocess optimization strategies that have been applied to sustain and enhance the product yield from the endophytes have also been described in detail. Further, techniques like mixed fermentation/co-cultivation and use of epigenetic modifiers have also been discussed as potential strategies to activate cryptic gene clusters in endophytes, thereby aiding in novel metabolite discovery and overcoming the limitations associated with axenic culture of endophytes.

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1. Introduction

Fungi have been known to be a rich repository of medicinally important compounds since the discovery of penicillin. Today, the range of drugs derived from fungi stretch from antibiotics to immune-suppressants to anti-cholesterol drugs (statins). While plants still remain the major source of drugs or their lead molecules, with every

new bioactive molecule reported from a plant source, there follows reports of endangered status or even extinction of a medicinally important plant due to over-harvesting. Hence, the focus turned toward fungi namely the “endophytes”, which reside within these medicinally important plants and thus may have acquired their medicinal abilities. The landmark in this area of endophyte bioprospecting was undoubtedly the discovery of *Taxomyces andreanae* (Stierle et al., 1993), the first

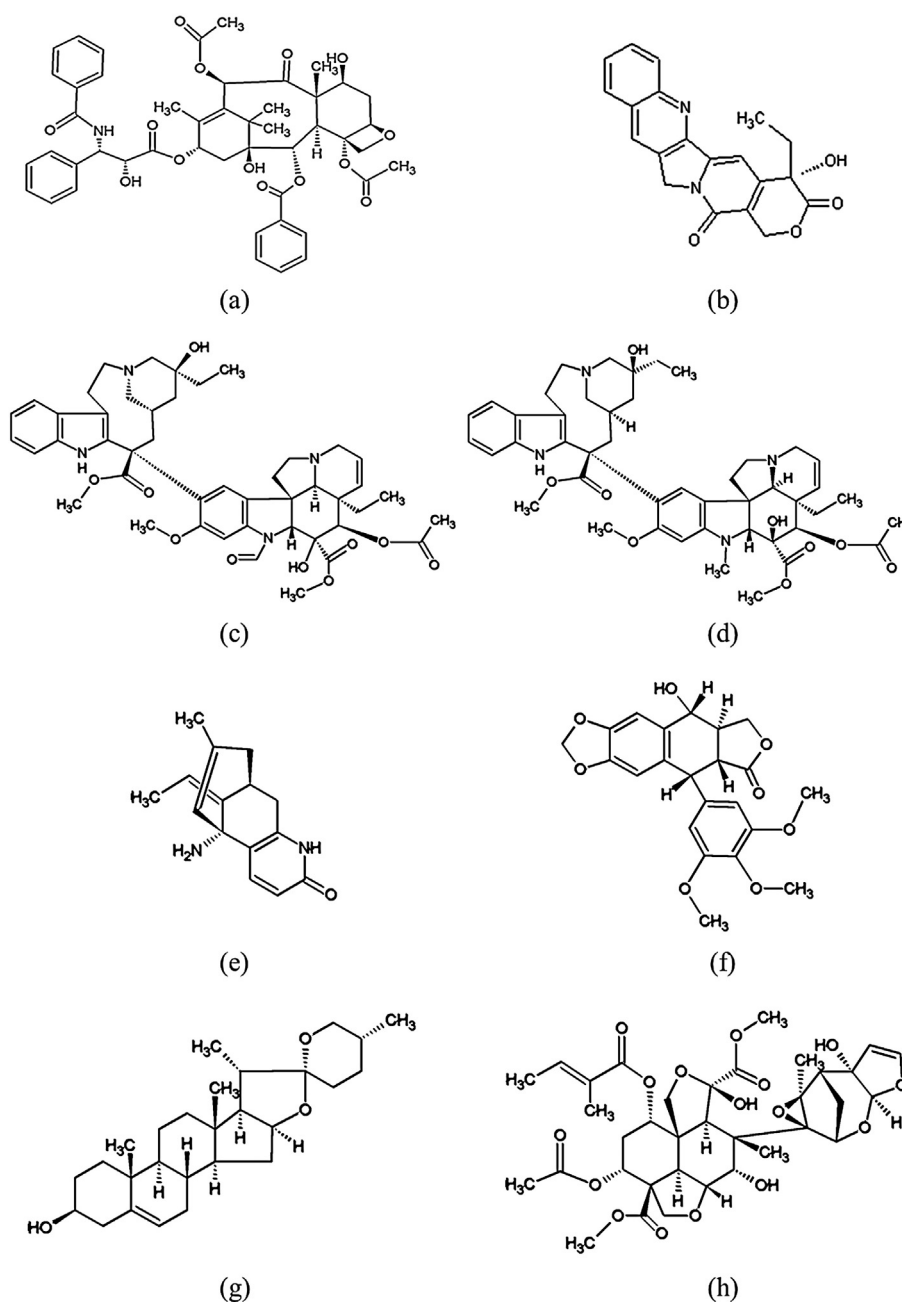


Fig. 1. Structures of various bioactive molecules produced by endophytes. (a) Taxol, (b) camptothecin (c), vincristine (d), vinblastine (e), huperzine (f), podophyllotoxin (g), diosgenin and (h) azadirachtin.

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