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Md. Merajul Haque Nomani
Department of Botany and Environment & Water Management, Millat College, Darbhanga, Bihar, India

Shikha Shirsh
Department of Zoology, DS College, Katihar, Bihar, India

Corresponding Author:
Md. Merajul Haque Nomani
Department of Botany and Environment & Water Management, Millat College, Darbhanga, Bihar, India

Endophytes: An asset for their hosts

Md. Merajul Haque Nomani and Shikha Shirsh

Abstract
Endophytes are beneficial for the plants in various ways as they fix nitrogen and solubilise phosphate. Moreover, they also produce different compounds like antimicrobial compounds, secondary metabolites, terpenoids, phytohormones and defense enzymes, phenols, antibiotics and plant growth regulators which further help the plants to survive better in their environment. This attribute of endophytes needs to be further investigated so that endophytes can be used as a source to extract these bioactives efficiently.

Keywords: Endophytes, antimicrobila compounds, secondary metabolites, enzymes

1. Introduction
Endophytes are a great asset for the plants. So far there has been not a single plant found which does not dwell endophytes. Gradually, the interaction of microorganisms with plant became a subject of immense interest for the scientists. Consequently, plants constitute niches for endophytic organisms. Endophytic bacteria usually occupy internal tissues of plants without causing damage to them. An understanding of the mechanisms which enables these microorganisms to interact with plants will help to achieve the biotechnological potential of plant–bacterial interactions. Moreover, first we need to assess the ways in which the endophytes are beneficial to the plants. Hence, here is the review of the benefits which the endophytic bacteria confer to their hosts.

2. History and definition of endophytes
Endophyte term comes from Greek word endon which means within and phyton means plant and it was first named by de Bary (de Bary, 1866) [9]. If microorganism like Bacteria or fungi spends its whole life or some parts of its life inside the healthy tissues of plant either intra- or inter cellular and mostly does not show any symptom of disease is recognize as endophyte (Wilson, 1995) [64]. In 1898 Vogl detected endophytes in the grass seed *Lolium temulentum*. In Germany in 1904, Freeman identified an endophytic fungus in Persian darnel (annual grass). Bacterial endophytes have been known for more than 100 years. In 1926, Perotti was the first who depicted non-pathogenic flora in the tissue of roots and after 14 years, Henning (1940) also accounted the harboring of bacteria in leaves and stems of the plants appear well. And endophyte could also be isolated from even surface sterilized plant organs. Since 1940, there have been a lot of reports from different parts of the country as well as the world on endophytic bacteria in various plant tissues (Hallmann *et al.*, 1997) [17]. Moreover, the term 'endophyte' basically refers to interior colonization of plants by bacterial or fungal microorganisms. Furthermore, endophytes have been defined in several different ways and the definitions have been modified with the advancement of the research in this field. Among the definitions given to endophytic bacteria the following by Hallmann *et al.*, (1997) [17] seems to be the most accurate. Hallmann *et al.* (1997) [17] defined endophytic bacteria as all bacteria that can be recognized or extracted from surface sterilized plant tissues showing no any visibly harmful effect on the host plants. According to endophytic life strategies, bacterial endophytes can be broadly classified as 'obligate' or 'facultative'. Obligate endophytes are those endophytes which strictly depend on the host plant for their growth, development and survival and transmission of such endophytes occurs vertically or via vectors to other plants. On the other hand, facultative endophytes have a stage in their life where they lead free life in the soil outside host plants along with internal colonization. Facultative endophytes have a free life in the soil and colonize the plant internally during some stage of their life cycle.

3. Biodiversity of endophytes
Endophytic bacteria in a single plant host are not restricted to a single species but comprise several genera and species (Ryan *et al.*, 2008) [46].

Mundt and Hinkle (1976) [41] reported as many as 46 different bacterial species from 27 plant species. In planta and ex-planta populations of *Pseudomonas* species could be differentiated by biochemical characteristics (van Peer *et al.*, 1991) [59]. Mavingui *et al.* (1992) [39] found that there are different populations of *Bacillus polymyxa* in soil, rhizosphere, and rhizoplane and that wheat roots select specific populations as endophytes. Sturz *et al.* (1997) [52] characterized 15 bacterial species from red clover nodules and estimated endophyte population densities to be in the range of 104 viable bacteria per gram of fresh nodule. Germida *et al.* (1998) [13] found that the endophytic population was less diverse than the root-surface population and the endophytes appeared to originate from the latter. Zinniel *et al.* (2002) [66] isolated 853 endophytic strains from aerial tissues of four agronomic crop species and 27 prairie plant species. As a whole, fewer isolates were recovered from perennial plants than from the agronomic crops. Surette *et al.* (2003) [53] have reported the isolation of up to 360 endophytic microorganism strains from *Daucus carota*, which were classified into 28 genera, with *Pseudomonas*, *Staphylococcus* and *Agrobacterium* being predominant.

4. Beneficial effects of endophytes

The intimate association of bacterial endophytes with plants offers a unique opportunity for their potential application in plant protection and biological control. However, several studies have also suggested that many endophytic associations are not neutral at all but are beneficial to plants (Barka *et al.*, 2002; Bailey *et al.*, 2006) [3, 2]. The growth stimulation by the microorganisms can be a consequence of nitrogen fixation (Hurek *et al.*, 2002; Iniguez *et al.*, 2004) [21, 22] or the production of phytohormones, biocontrol of phytopathogens in the root zone (through production of antifungal or antibacterial agents, siderophore production, nutrient competition and induction of systematic acquired host resistance, or immunity) or by enhancing availability of minerals (Sessitsch *et al.*, 2002; Sturz *et al.*, 2000) [49, 51].

4.1. Nitrogen fixation by endophytes

In 1986, Brazilian scientists (Cavalcante and Dobereiner, 1988) [5] discovered in the sugarcane stem N_2-fixing endophytic bacteria called *Gluconacetobacter diazotrophicus*. Their pioneering work was confirmed by other scientists in USA, UK, and Germany and led to the identification of two other N_2-fixing endophytes, *Herbaspirillum seropedica*e and *H. rubrisubalbicans* (Boddey *et al.*, 1995) [4]. Endophytic diazotrophs seem to constitute only a small proportion of total endophytic bacteria (Ladha *et al*,. 1997; Martínez *et al.*, 2003) [32, 38]. Such microbes include *Azospirillum lipoferum, Klebsiella pnemoniae* and *Azorhizobium caulinadans* (Schloter *et al.*, 1994) [48].

Endophytic bacteria are found in legume nodules as well. In red clover nodules, some species of *rhizobi*a were found, including *Rhizobium (Agrobacterium) rhizogenes*, in addition to *R. leguminosarum bv. trifolii*, which is the normal clover symbiont (Sturz *et al.*, 1997) [52]. Inside wheat, *Klebsiella sp*. strain Kp342 fixes N_2 (Iniguez *et al.*, 2004) [22] and it has been reported that it increases maize yield in the field (Riggs *et al.*, 2001) [45].

During a survey in Tamil Nadu with sugarcane varieties, four isolates belonging to the genus *Burkholderia* were studied. *Burkholderia vietnamiensis* was found more active in reducing acetylene than the others (Govindarajan *et al.*, 2006) [15]. Jha and Kumar (2007) [26] isolated and characterized endophytic diazotrophic bacteria from a semi-aquatic grass (*Typha australis*) which grows luxuriantly with no addition of any nitrogen source. Amplification of nifH by polymerase chain reaction (PCR) and detection of dinitrogenase reductase by western blot confirmed the diazotrophic nature of an isolate,GR3.

4.2. Phosphate solubilisation by endophytes

Seventy-seven endophytic bacterial isolates were isolated from roots, stems and leaves of black nightshade plants *(S. nigrum*) grown in two different native habitats in Jena, Germany by Long *et al.* (2003) [36] and six isolates were able to solubilize inorganic phosphate. Vendan *et al.* (2010) [60] reported that 9 out of 18 endophytic isolates from gingseng plants had phosphate solubilizing ability by detecting extracellular solubilization of precipitated tricalcium phosphate with glucose as sole source of carbon. Out of 18 endophytic isolates obtained from tomato by Patel *et al.* (2012) [42], 8 showed phosphate solubilisation activity.

4.3. Bioactive compounds synthesized by endophytic bacteria

Bacterial endophytes have found potential applications in pharmaceutical and drug discovery (Guo *et al.* 2008) [16]. Amines and amides are the common metabolites from endophytes that are toxic to insects but not mammals. Endophytes also produce extracellular hydrolyases such as cellulases, proteinase, lipases and esterases to establish resistance against plant invasions (Tan and Zou 2001) [56].

4.3.1. Secondary metabolites synthesis

Secondary metabolites play an adaptive role in functioning as the defense compound or the signaling molecule during ecological interactions and environmental stresses. Endophytic microorganisms produce low-molecular weight secondary metabolites that include antimicrobial compounds, phytohormones or their precursors, vitamins like B12 (Ivanova *et al.* 2006) [23] and B1 (Mercado and Bakker 2007) [40], bioprotectants (Trotsenko and Khmelenina 2002) [58]. Several secondary metabolites are alkaloids, steroids, terpenoids, peptides, polyketones, flavonoids, quinols and phenols. These compounds also have important role in therapeutic applications such as anti-cancer, antioxidant, antimicrobial, anti-inflammatory and immunosuppressive agents (Korkina 2007) [29]. Endophytes synthesize secondary metabolites via a variety of pathways e.g., polyketide, isoprenoid or amino acid derivation (Jalgaonwala 2013) [24].

4.3.2. Terpenoids

Terpenes are derived biosynthetically from isoprene units. Approximately, 50,000 terpenoid metabolites including monoterpenes, sesquiterpenes, and diterpenes representing nearly 400 distinct structural families have been isolated from plants, fungi and bacteria. The sesquiterpenoid antibiotic, pentalenolactone is the common metabolite isolated from more than 30 species of *Streptomyces* (Takahashi *et al.* 1983) [55]. *Streptomyces exfoliatus* UC5319 produced pentalenene synthase (ADO85594); the first characterized, cloned, and sequenced terpene synthase from *Streptomyces* (Lesburg *et al.* 1997) [34].

4.3.3. Alkaloids

Alkaloids, the low-molecular-weight, nitrogen-containing compounds, are important in pharmaceutical industries because of their high biological activities. Endophytes produce alkaloids as the secondary metabolites that have diverse biological potential as anti-fungal, anti-cancer, and anti-viral agents (Silva *et al.* 2007) [50]. Endophytic *Bacillus cereus*, *Aranicola proteolyticus*, *Serratia liquefaciens*, *Bacillus thuringiensis* and *Bacillus licheniformis* isolated from *Pinellia ternata* have the ability to produce alkaloids (guanosine and inosine) in fermentation broth similar to their host plant (Liu *et al.* 2015) [35].

4.3.4. Phenols

Among the different dietary bioactive compounds, polyphenols constitute an interesting group as some possess important biological activities including antioxidant, anti-carcinogenic or antimicrobial activities. They have been reported to lower the risks of many chronic diseases including cancer, cardiovascular diseases, chronic inflammation and many degenerative diseases.

Endophytic bacterial isolates *P. fluorescens* Endo2 and Endo35 on inoculation induced systemic resistance against dry root rot of black gram (*Vigna mungo* L.) caused by *Macrophomina phaseolina* under glasshouse conditions. The black gram plants inoculated with dry root rot pathogen showed increased activities of peroxidase (PO), polyphenol oxidase (PPO), phenylalanine ammonia lyase (PAL) in addition to accumulation of phenolics and lignin (Karthikeyan *et al.* 2005) [28]

4.3.5. Phytohormones and defense enzymes

Phytohormones are signal molecules that coordinate cellular activities and control plant growth and development. They play crucial roles in regulating plant responses to various stresses at extremely low concentrations. Bacterial endophytes and plants interactions result in the production and modulation of plant hormones (Lopez *et al.* 2008; Glick 2012) [14]. IAA is the most common naturally occurring plant hormone of the auxins class. The endophytic *B. cereus* (ECL1), *B. thuringiensis* (ECL2), *Bacillus sp.* (ECL3), *Bacillus pumilis* (ECL4), *Pseudomonas putida* (ECL5) and *Clavibacter michiganensis* (ECL6) isolated from *C. longa* L. produced IAA (Javid *et al.* 2011; Kumar *et al.* 2016) [25, 29]. *Pseudomonas*, *Agrobacterium* and *Bacillus* isolated from the root of *Cassia tora* produced phytohormones and solubilized tricalcium phosphate (Kumar *et al.* 2015) [28]. Endophytic *Artherobacter* EZB-4 and *Bacillus* EZB-8 isolated from the pepper plant (*Capsicum annum* L.) produced IAA and increased the plant biomass.

4.3.6. Antimicrobial compounds

Antimicrobial metabolites produced from the endophytes are the bioactive natural compounds (Guo *et al.* 2008) [16]. Endophytes have developed a resistance mechanism to control pathogenic intrusion by producing secondary metabolites (Tan and Zou 2001) [56]. A large number of endophytic actinomycetes were isolated from 26 medicinal plants from Panxi plateau with the huge spectrum of antimicrobial activity being the valuable reservoirs of novel bioactive compounds (Zhao *et al.* 2011) [65]. Endophytic *Streptomyces sp*. TQR12-4 isolated from Elite *Citrus nobilis* fruit showed antimicrobial activity and inhibited test pathogens *Colletotrichum truncatum, Geotrichum candidum, F. oxysporum* and *F. udum* (Hong-Thao *et al.* 2016) [20].

4.3.7. Anti-cancerous compounds

Several bioactive compounds produced by endophytes have been identified as anti-cancer agents (Firakova *et al.* 2007). Endophytic bacterial strain, EML-CAP3 isolated from *C. annuum* L. (red pepper) leaf showed potent anti-angiogenic activity. This endophytic bacterial strain produced lipophilic peptides which inhibited the proliferation of human umbilical vein endothelial cells and also exhibited anti-angiogenic potential in tumor progression (Jung *et al.* 2015) [27]. Ginseng (*Panax ginseng*) is known for its ginsenosides that have anti-cancerous property. The transformed *Paenibacillus polymyxa*, an endophytic bacterium of Ginseng leaf, showed high ginsenoside concentration. This endophytic bacterial strain on inoculation to Ginseng plants through foliar applications combined with irrigation enhanced plant growth and the concentration of ginsenosides (Gao *et al.* 2015) [12]. *Bacillus* serves as a source of first discovered anti-tumoral EPS, a natural product of high therapeutic value for cancer treatment as a new anti-cancer agent (Chen *et al.* 2013).

4.3.8. Antibiotics

Antibiotics are natural compounds produced by microorganisms as secondary metabolites to kill or inhibit other microorganisms. *Streptomyces sp.* are such organisms which produce about 80% of the total antibiotics (Sathiyaseelan and Stella 2011; Thenmozhi and Krishnan 2011) [47, 57]. Endophytic *Streptomyces* sp. LJK109 isolated from *Alpinia galangal* root produces 3-methylcarbazoles which is major anti-inflammatory component and also suppresses macrophage production of the inflammatory mediators NO, PGE2, TNF-α, IL- 1β, IL-6 and IL-10 in a dose-dependent manner (Taechowisan *et al.* 2012) [54] The majority of endophytic bacteria like other bacteria produce different kinds of antibiotics.

Ecomycin, pseudomycins and kakadumycins are some of the novel antibiotics produced by endophytic bacteria (Christina *et al.* 2013) [7]. *Pseudomonas viridiflava*, an epiphyte or endophyte of the leaves of many grasses produced ecomycin, an antibiotic which is used for the treatment of skin, eye, gut, respiratory and urinary tract infections. Endophytic *Streptomyces sp*. isolated from *Aucuba japonica* and *Cryptomeria japonica* produced two new novobiocin analogs and cedarmycins respectively. A new naphthoquinone antibiotic, alnumycin was also isolated from the endophytic *Streptomyces sp*. from *Alnus glutinosa.*

4.4 Production of plant growth-regulators by endophytes

The plant growth-promoting capabilities of various endophytic bacteria have been researched. By improving nitrogen, phosphate and other nutrients and minerals cycle endophytic bacteria increase plant growth and regulation. Plant growth mechanisms include phosphate solubilisation activity (Verma *et al.*, 2001; Wakelin *et al.*, 2004) [61, 63], indole acetic acid production (Lee *et al.*, 2004) [33] and the production of a siderophore (Costa and Loper, 1994) [8]. Adhikari *et al.* (2001) [1] reported the ability of strains of endophytic bacteria to control seedling disease of rice and promote plant growth. In plants, the fulfillment of essential vitamins can also be done by endophytic organisms (Pirttila *et al.*, 2004). On applying endophytic bacterial strain in the banana plant under greenhouse and field conditions Harish (2005) [18] observed and reported a considerable increase in growth and some physiological parameters of plants, such as height and girth of the stem, leaf count, the resistance of stomata, transpiration and chlorophyll stability index. In 2007 finding of IAA in the culture filtrate of endophytes from *Typha australis* were reported by Jha and Kumar (2007) [26], and they also reported that out of ten seven endophytic isolates were positive for IAA production. Twelve endophytic isolates from gingseng plants produced significant amounts of IAA in nutrient broth supplemented with tryptophan as precursor (Vendan *et al.*, 2010) [60].

5. Conclusion

Endophytes are a boon for the plants. They help the plants in numerous ways to grow and survive by releasing various novel compounds and also by making the nutrients readily available. Endophytes are a promising source of many bioactives and drugs but till date the potential of endophytes has not been analysed fully. More sincere work need to be done in this field to completely assess the ability of endophytes to produce different compounds. Also, there is a need to find out the ways in which these compounds can be extracted efficiently from the plants. This will not only pave the path of using these endophytes as inexhaustible source of some crucial compounds but also ensure better productivity of crop plants.

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