



A mini review: endophytic bacteria from plants and their potential to produce bioactive compounds for veterinary applications

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Abstract

Infectious diseases caused by microorganisms, both humans and animals, are still a problem in Indonesia. The problem of bacterial resistance to antibiotics has an impact on increasing morbidity, mortality, and health care. The problem of bacterial resistance to antibiotics, which can threaten human health, has also been found in livestock. This situation has led many researchers to search for new bioactive compounds as alternative antibiotic candidates to fight multidrug-resistant bacteria such as *Mycobacterium tuberculosis*, *Staphylococcus* spp., and *Streptococcus* spp. This study aimed to discuss and determine the development of endophytic bacteria isolated from several plants so we can know the role of endophytic bacteria in producing bioactive compounds, especially for application in veterinary medicine. Endophytic bacteria provide great potential to produce various new bioactive compounds obtained from secondary metabolite compounds from their host. Plants are one of the hosts for endophytic bacteria. Bioactive compounds from endophytic bacteria are widely used in health and veterinary applications as antibacterial, antiviral, anti-inflammatory, and antioxidant. This shows that endophytic bacteria can be a promising source of new antibiotics to overcome the problem of pathogenic bacterial resistance and disease in the world of animal health, which also threatens human health. This review discusses aspects of the phytochemistry of endophytic bacteria producing bioactive compounds and its application in veterinary medicine.

Keywords: Animal health, antibacterial, antibiotics resistance, endophytic bacteria, infectious diseases.

Background

Numerous alternative and complementary medicines have expanded in popularity in recent decades (Joseph & Priya, 2011). In addition, there has been an expanding interest in the examination of diverse novel natural bioactive compounds from plants (Joseph et al., 2010). Potential new compounds are required to solve problems in various areas, particularly within the health sector. Therefore, the search for compounds that have the potential to overcome infectious diseases in humans and animals is still underway. The

importance of looking for these compounds is additionally due to the development of resistance to infectious microorganisms (such as the *Staphylococcus*, *Mycobacterium*, and *Streptococcus* species) against bioactive compounds that already exist and because of naturally resistant microorganisms. Recent trends show that the discovery rate of active novel chemical entities is declining (Lam, 2007). The product of natural bioactive compounds can naturally be obtained from microorganisms, plants, and or animals. These natural compound products have been exploited for

human needs for thousands of years and have become a major source of compounds for medicinal raw materials. Therefore, there is a need to bioprospecting new sources and, if possible, from less explored regions and habitats to maximize the discovery of novel bioactive compounds. In recent years, this excavation of microbial resources in plant tissue has gotten much attention. Endophytic microbes are being studied for various purposes, including for veterinary applications.

Endophytic bacteria are bacteria that live symbiotically inside the plant tissue, and they have novel metabolites that exhibit a variety of biological activities against different diseases. These bacteria living within plant tissues without causing any immediate overt negative effects have been found in every plant's species examined to be recognized as the potential source of natural products for exploitation in medicine, agriculture, and industry with more bioactive compounds isolated from the microorganism (Bacon & White, 2000; Strobel & Daisy, 2003; Kumar & Sagar, 2007).

Endophytic Bacteria and Their Interactions with Host Plants

The term endophytic comes from the word 'endon', which means inside and 'python', which means plant. The use of this term has a broad and literal meaning that endophytes are inhabited by potential organisms such as bacteria (Kobayashi & Palumbo, 2000), fungi (Stone et al., 2000), plants (Marler et al., 1999), insects in plants (Feller, 1995), as well as for algae in algae (Peters, 1991). Endophytes are ubiquitous, with rich biodiversity found in every plant species examined to date. Each plant hosts one or more endophytes of the nearly 300,000 plant species on the earth (Strobel & Daisy, 2003). In this view of the particular colonization in specific hosts, it is estimated that there may be as many as one million different endophyte species (Andrew & Hirano, 1991).

Endophytic bacteria are microbes that live in plant tissues at specific periods without causing danger and can be isolated

from plant tissue that has been surface sterilized or extracted from inner plant tissue (Hallmann et al., 1997). This bacterium is a potential natural source that can be assessed for benefits in agriculture, medicine and industry. Various bioactive compounds in various plants are thought to be produced by endophytic bacteria in these plants (Strobel & Daisy, 2003). The ability of endophytic bacteria to produce secondary metabolites with their host plants is an opportunity that can be optimized to produce secondary metabolites efficiently and quickly. Endophytic bacteria have been successfully isolated from various types of tissue from various plants including Gram-negative, Gram-positive, and Actinobacteria.

Generally, plant endophytic bacteria can be localized at the entry point or spread to all parts of the plant. This bacterium can be in cells, intercellular space, or vascular system. Endophytic bacteria enter plant tissue through roots, stomata, flowers, stems, and cotyledons. Specifically, bacteria can penetrate roots through root radicle germination and secondary roots. Sharma et al. (2005) state that lateral roots are the most populated part of plants by endophytic bacteria. This is because endophytic bacteria enter the plant tissue through lateral roots and then spread into the intercellular space and the vessels of vessels. Zinniel et al. (2002) also reported that the population of endophytic bacteria was most commonly found in the root area and decreased in the stem and leaf area. In this review, we discuss the endophytic bacteria isolated from plant and their interaction with host plants, the bioactive compounds from endophytic bacteria, and the potency of endophytic bacteria in veterinary applications.

Endophytic Bacteria as Producers of Bioactive Compounds

Some endophytes are the chemical synthesizers inside the plants (Owen & Hundley, 2004). Many of them can synthesise bioactive compounds that plants can use to defend against human pathogens and some of these compounds have been proven helpful for novel drug discovery.

Most of the natural products from endophytic bacteria are antibiotics, anticancer agents, biological control agents, and other bioactive compounds by their different functional roles.

Several members of actinobacteria produce essential secondary metabolites, including antibiotics, antimicrobials, and enzymes (Qin et al., 2011). Actinobacteria play an important role in recycling waste in the environment and producing of natural products that exhibit biological activity. Actinobacteria have been exploited successfully for their biologically potential bioactive compounds (Mohanraj & Sekar, 2013). Microbial bioactive compounds have been in the frontier in the discovery of novel antimicrobial agents for the pharmaceutical industry and nowadays all evidence suggests that novel bioactive compounds with potential therapeutic applications are still waiting to be discovered from bioactive compounds especially those produced by Actinobacteria (Alharbi, 2016). This because Actinobacteria are prolific producers of secondary metabolites or bioactive compounds with biological activities. Bull & Stach (2007) reported that marine Actinobacteria are a new opportunity for natural product search and the discovery of new drugs, especially antibiotics. Actinobacteria continue to be productive for natural product research, with many novel bioactive compounds of eminent pharmacological value. In addition, Actinobacteria can synthesize many different biological actives such as antibiotics, pesticides, antiparasitic substances, and enzymes. Genus *Streptomyces*, *Micromonospora*, *Actinomadura*, *Amycolatopsis*, *Streptoverticillium*, *Actinoplanes*, *Nocardia*, *Saccharopolyspora*, *Streptosporangium*, *Streptoalloteichus*, *Dactylosporangium*, *Frankia*, and *Streptosporangium* spp. are playing a role in the production of a wide range of antimicrobial and antibiotics metabolites of important to the pharmaceutical industries (Manivasagan et al., 2014).

Potency of Endophytic Bacteria for Veterinary Medicine Application

Endophytic bacteria are known to be used as antibacterial, antifungal, antiviral, and anti-inflammatory. Endophytic bacteria can produce several antimicrobial products that act as antimalarial, antibacterial, and antimicrobial. Endophytic bacteria can produce secondary metabolites with antimicrobial activity inhibiting bacterial growth (Irdawati et al., 2017). One of the antibacterial activities tested inhibits the growth of *Staphylococcus aureus* and *Escherichia coli* bacteria. *S. aureus* is a Gram-positive bacterium, and *E. coli* is a Gram-negative bacterium (Setianah et al., 2021). Testing of these two bacteria found that endophytic bacteria can form an inhibition zone, based on the test results, endophytic bacteria have a broad spectrum because they can inhibit the growth of Gram-positive and Gram-negative bacteria. The endophytic bacterial isolates used come from young plants that are known to contain secondary metabolite compounds. Similarly, Safira et al. (2014) reported that endophytic bacteria isolated from green betel plants were effective against pathogenic bacteria *S. aureus* and *Bacillus subtilis*. *S. aureus* is known to be the dominant bacterium that causes mastitis in livestock (Purwantiningsih et al., 2014). Sari et al. (2020) and Sari et al. (2023) reported that endophytic bacteria are capable of inhibiting the pathogenic bacteria *S. aureus*, *Pseudomonas aeruginosa*, *Pasteurella multocida*, and *B. subtilis*. Endophytic bacteria kill pathogenic bacteria by disrupting bacterial metabolism, inhibiting bacterial cell walls and protein synthesis and damaging nucleic acid synthesis from these pathogenic bacteria (Sari et al., 2020). The formation of a clear zone around the endophytic bacterial colony characterizes endophytic bacteria's activity in inhibiting pathogenic bacteria's growth. According to Sadikin et al. (2021), the antibacterial activity of secondary metabolite compounds is produced by microbes in the stationary phase, which is when the depletion of nutrients needed by bacteria and the stability of bacterial cell death and division. Research

conducted by Iqlima et al. (2017) showed that endophytic bacteria also have antibacterial activity against *Salmonella thypimurium*. Based on many studies that have been done show endophytic bacteria have antibacterial activity against Gram positive bacteria and Gram-negative bacteria.

Actinobacteria such as *Streptomyces fradiae* are known to produce the antibiotic tylosin; it is primarily used in veterinary medicine for cats, dogs and small mammals to treat diarrhoea and inflammation of the gastrointestinal tract. A common antibiotic such as streptomycin also produced by Actinobacteria, genus *Streptomyces*. A common antibiotic such as gentamicin is produced by fermentation of *Micromonospora purpurea* or *M. echinospora*. Gentamicin is an aminoglycoside antibiotic for the treatment of a variety of bacterial infections. In veterinary medicine, it is usually used as the

sulphate salt, mainly as a solution for injection for pigs, cattle, and horses and as an oral solution for poultry. Another common antibiotic is lincomycin, which is produced by the bacteria *S. lincolnensis*. It is commonly used in dogs and cats to treat bacterial skin infections, dermatitis, pyoderma, and soft tissue infections.

Rabusin et al. (2016) reported that the combination of antibiotic Penicillin and streptomycin (PS) and gentamicin, tiolysin, lincomycin and spectinomycin (GTLS) were effective for controlling the growth of bacteria in frozen semen of Friesian Holstein bovine. It could be an alternative to control bacteria growth so that good quality and safe semen can be produced. Previous studies, several research reported that the endophytic bacteria are isolated from several plants and have potency in veterinary medicine, such as antibiotics, antifungals, etc. (Table 1).

Table 1. Endophytic bacteria isolated from several plants and their potency in veterinary medicine

No.	Endophytic bacteria	Potency in veterinary medicine	References
1.	Endophytic bacterial strains from green algae	Antibacteria	Li et al., (2012) Habbu et al., (2016)
2.	<i>Paenibacillus</i> sp. endophytic bacterium isolated from the root of aloe chinensis	Antibiotic	
3.	Endophytic bacterial diversity isolated from young radish	Biocontrol agents	Seo et al., (2010)
4.	Endophytic bacterial populations isolated from medical plants	Antibacteria	Beiranvand et al., (2017)
5.	Endophytic bacteria isolated from sugarcane plants	Antibacteria	Yulianti, (2012)
6.	Endophytic bacteria isolated from srikaya	Antibacteria	Zulkifli et al., (2018)
7.	Endophytic bacteria isolated from garlic	Antifungal	Ibrahim et al., (2020)
8.	Endophytic bacteria isolated from <i>Fagonia indica</i>	Antibiotics	Rahman et al., (2017)
9.	Endophytic bacteria <i>Enterobacter hormaechei</i> isolated from Malaysian plants	Antimicrobial	Loh et al., (2013); Monowar et al., (2021)
10.	Endophytic bacteria f4 isolated from papaya leaf (<i>Carica papaya</i> l)	Antibacteria	Sarjono et al., (2021)
11.	Endophytic bacteria isolated from soursop (<i>Annona muricata</i> L.)	Antimicrobial	Aisyah et al., (2023)

Conclusion

This review concludes that the endophytic bacteria have the same bioactive compound activity as their host plants and could be employed to improve animal health. Benefits could also be realized when endophytic bacteria are a promising source of new antibiotics to overcome the problem of pathogenic bacterial resistance and disease in the world of animal health, which also threatens human health. To bring about this future, we must explore the endophytic bacteria from several medicinal plants and learn how to optimize endophytic bacteria function for application in animal health.

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