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 are still a problem in Indonesia, both humans and animals. The problem of bacterial resistance to antibiotics has an impact on increasing morbidity, mortality, and health care. The problem of bacterial resistance to antibiotics has also been found in livestock, which can threaten human health. 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 some aspects in 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 and 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). The requirement for potential new compounds to solve problems in various areas, particularly within the health sector, is very important. 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 bioprospect 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 contained in plant tissue is getting 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 exhibiting a variety of biological activities against different diseases. This 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 and White, 2000; Strobel & Daisy, 2003; Kumar and 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. Of the nearly 300000 plant species on the earth, each plant is the host to one or more endophytes (Strobel & Daisy, 2003). In this view of the particular colonization in certain hosts, it is estimated that there may be as many as one million different endophyte species (Andrew and Hirano, 1991).

Endophytic bacteria are microbes that live in plant tissues at certain 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 with various plant are thought to be produced by endophytic bacteria in these plants (Strobel and Daisy 2003). The ability of endophytic bacteria to produce secondary metabolites under 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, both Gram-negative, Gram-positive bacteria, and Actinobacteria.

Generally, endophytic bacteria in plants 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 of the endophytes are the chemical synthesizers inside the plants (Owen and Hundley, 2004). Many of them are capable of synthesizing bioactive compounds that plants can use for defense against human pathogens and some of these compounds have been proven helpful for novel drug discovery. Currently, 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 important secondary metabolites, including antibiotics, antimicrobials, and enzymes (Qin et al., 2011). Actinobacteria play an important role in recycling wastes in
the environment and produce of natural products which exhibit biological activity. Actinobacteria have been exploited successfully for their biologically potential bioactive compounds (Mohanraj and 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 due to Actinobacteria being prolific producers of secondary metabolites or bioactive compounds with biological activities. Bull and Stach (2007) reported that marine Actinobacteria as new opportunity for natural product search and discovery to new drugs, especially antibiotics. Actinobacteria continue to be productive for natural products 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, Streptomyces, 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 can 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 is in inhibiting the growth of *Staphylococcus aureus* and *Escherichia coli* bacteria. *S. aureus* is a Gram-positive bacteria and *E. coli* is a Gram-negative bacteria (Setianah et al., 2021). Testing of these two bacteria found that endophytic bacteria can form an inhibition zone, based on the test results, showing endophytic bacteria have a broad spectum 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, endophytic bacteria isolated from green betel plants showed efficacy as antibiotics 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 to inhibit the pathogenic bacteria *S. aureus*, *Pseudomonas aeruginosa*, *Pasteurella multocida*, and *B. subtilis*. The endophytic bacteria kill pathogenic bacteria by disrupting bacterial metabolism then inhibiting bacterial cell walls and protein synthesis and damaging nucleic acid synthesis from these pathogenic bacteria (Sari et al., 2020). The activity of endophytic bacteria in inhibiting the growth of pathogenic bacteria is characterized by the formation of a clear zone around the endophytic bacterial colony. 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 typhimurium*. 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 fraidae* is known to produce the antibiotic tylosin (https://pubchem.ncbi.nlm.nih.gov/c-compound/Tylosin), it is primarily used in
veterinary medicine for dogs, cats, and small mammals to treat diarrhea and inflammation of the gastrointestinal tract (https://vcahospitals.com/know-your-pet/tylosin). A common antibiotic such as streptomycin also produced by Actinobacteria Streptomyces. A common antibiotic such as gentamicin is produced by fermentation of Micromonospora purpurea or Micromonospora echinospora (https://pubchem.ncbi.nlm.nih.gov/compound/Gentamicin). Gentamicin is an aminoglycoside antibiotic for the treatment of a variety of bacterial infections. In veterinary it is normally used as the sulphate salt mainly as a solution for injection for pigs, cattle and horses and as an oral solution for poultry (ema.europa.eu/ European medicines agency). Another common antibiotic such as lincomycin that is produced by bacteria Streptomyces lincolnensis (https://pubchem.ncbi.nlm.nih.gov/compound/Lincomycin ). In veterinary It is commonly used in dogs and cats to treat bacterial skin infections, dermatitis, pyoderma and soft tissue infections (wedgewoodpharmacy.com).

Rabusin et. al. (2016), was reported that the combination of antibiotic Penicillin and streptomycin (PS) and gentamicin, tiolys, 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. Based on previous studies, several research reported the endophytic bacteria isolated from several plants and they have potency in veterinary medicine, such as for antibiotics, antifungal, etc. (Table 1).

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

<table>
<thead>
<tr>
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<th>Endophytic bacteria</th>
<th>Potency in veterinary medicine</th>
<th>References</th>
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<td>Antibacteria</td>
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<td>Paenibacillus sp. endophytic bacterium isolated from the root of aloe chinensis</td>
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<td>7.</td>
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**Conclusion**

The conclusion of this review is that the endophytic bacteria have the same bioactive compunds activity as their host plants and could be employed to improve animal health. Benefits could also be realized when 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. To bring about this future, we must more explore the endophytic bacteria from several medicinal plants and learn how to
optimize endophytic bacteria function for application in animal health.

References


Marler, M.J., C.A. Zabinski, and R.M. Callaway. 1999. Mycorrhizae indirectly enhance competitive effects of an


