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REVIEW ARTICLE

Physiological and AI-based study of endophytes on medicinal plants: A mini review

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Abstract

Research on the natural resources found in medicinal plants and endophytes makes important contributions to a wide variety of fields, including drug development, agribusiness, biotechnology, and sustainable development. Endophytes are a group of microorganisms that can be discovered in the rhizosphere of plants being used in medical treatment. These microorganisms have the capability of producing a wide range of primary and secondary metabolites by utilizing a variety of distinct biosynthetic pathways. Several different technologies, such as genetic modification and artificial intelligence (AI), play a significant role in the acceleration of endophytic research. These methods aid in the discovery and synthesis of novel compounds with medicinal promise, the predictive analysis of bioactive compounds, the identification and classification of endophytes, and the optimization of potential bioactive compounds. In light of this, the current review focuses on providing a concise comprehension of the influence of bioactive compounds secreted by specific endophytes on medicinal plants through the application of significant technologies in the field of endophytic research.

Keywords

Artificial Intelligence; bacteria; bioactive compounds; Endophytes; fungus; medicinal plants

Introduction

Microbes residing in plant roots tend to be beneficial for plants, showing plant-microbe interaction. Microbes acquire good nutritional values from plants and serve to produce various bioactive compounds (1). In return, they provide essential nutrients to plants and help them survive in extreme climatic conditions, as well as perform a crucial role in a sustainable environment (2).

Bioactive compounds such as quinols, phenols, steroids, alkaloids, peptides, flavonoids, polyketones, and terpenoids (3) are produced by the endophytes, including bacteria, actinobacteria, and fungi, that reside in symbiotic association with plants and are in great demand (4, 5, 6). Additionally, endophytes, which are found in the roots of plants used for medicinal purposes, are a crucial source of nutrients for plant growth and development. According to reports, three main kinds of exchanges that are advantageous exist between endophytes and host plants: (i) enhancement of the growth of the medicinal plant, (ii) enhancement of the medicinal plant's resistance to stress, and (iii) high

-value secondary metabolites (2). There is various advanced development against pathogenic species inhibiting their growth and modulating the nutrient balance in pathogens and providing benefits to existing endophytes (7). Various species of medicinal plants and endophytes produce similar groups of bioactive compounds Table 1 such as alkaloids, terpenoids, flavonoids, steroids, phenolics, etc. example from *Catharanthus roseus*, *Alternaria* sp. was isolated and found to produce vinblastine (also called vinca alkaloid), It was discovered that *Fusarium oxysporum*, another endophytic fungus, produces vincristine (vinca alkaloids) when it is isolated from *Catharanthus roseus* (1) possessing numerous advantages (3) as shown in Fig. 1. These secondary metabolites possess beneficial, multifunctional activity which promotes human health and wellness, and also used for drug development (1, 3) shown in Fig. 2.

However, research showed that genome sequencing of numerous endophytes exhibits the absence of comprehensive biosynthetic pathways for the production of phytochemicals (4). In addition, plant secondary metabolites (PSMs) themselves perform several types of roles in plant development and growth, including defence response signalling (8), innate immunity (9), and response to environmental stress (10). They also provide resistance to certain pathogens and pesticides, have significance over plant-microbe relations, and transform the microbial communities with plants (11). Rhizobacteria has been reported to encourage plant development by improving root hair branching, promoting early nodulation, improving nodule function, increasing leaf surface area and biomass, and most importantly, increasing nutrient use efficiency (12), however, decreasing the application of chemical fertilizers and pesticides (13). Furthermore, the secondary metabolites from fungal and bacterial endophytes contribute to the enhancement of the growth of medicinal plants. Additionally, these endophytes have antibacterial, anticancer, antioxidant, and anti-inflammatory properties as well (14) (Fig. 2). Moreover, there are certain biotechnological techniques such as CRISPR-Cas9, TALEN, and ZFN for the genetic improvement in endophytes which helps to enhance the production of targeted bioactive compounds and also helps to enhance the immune memory in the medicinal plants (15, 16, 17). The genetically modified endophytes provide the capacity to survive adverse situations and tolerate drought, which enhances the durability, yield, fertility, and health of to host plant (8) Fig. 3 depicts all phases of endophytic research on medicinal plants, from the identification of potential endophytic species to the commercialization of endophytic-derived medications.

Table 1. Enodpytes produce various bioactive compounds by using medicinal host plants.

S.No.	Bioactive Compound	Endophyte	Plant Species	References
1	Galanthamine	*Paenibacillus lautus*	*Leucojum aestivum*	(18)
2	Vinblastine	*Curvularia verruculosa*	*Catharanthus roseus*	(19)
3	Taxol (paclitaxel)	*Annulohypoxylon* sp. MUS1	*Taxus wallichiana*	(20)
4	Saikosaponin	*Fusarium acuminatum* *Fusarium oxysporum*	*Bupleurum scorzonerifolium*	(21)
5	Resveratrol	*Aspergillus stellifer* AB4 *Quambalaria cyanescens*	*Vitis vinifera*	(22, 26)
6	Ginsenoside Rg3	*Chaetomium* sp.	*Panax ginseng*	(24)
7	Emodin	*Epicoccum nigrum*	*Hypericum perforatum*	(25)
8	Dendrobine	*Trichoderma Longibrachiatum* MD33	*Dendrobium nobile*	(26)
9	Colchicine	*Diaporthe perseae*	*Glorosa superb*	(27)
10	Asiaticoside	*Colletotrichum Gloeosporioides*	*Centella asiactica*	(28)

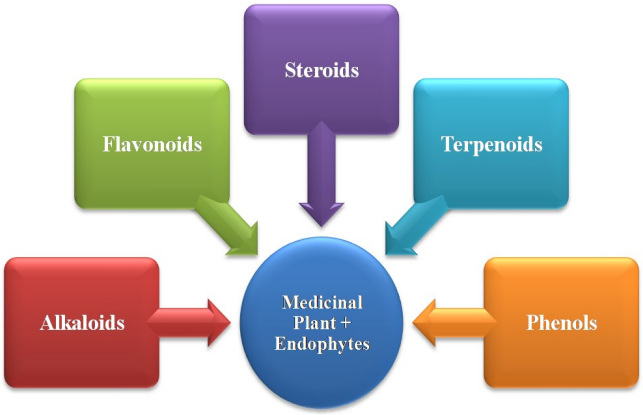

Fig. 1. Various secondary metabolites present in medicinal plants.

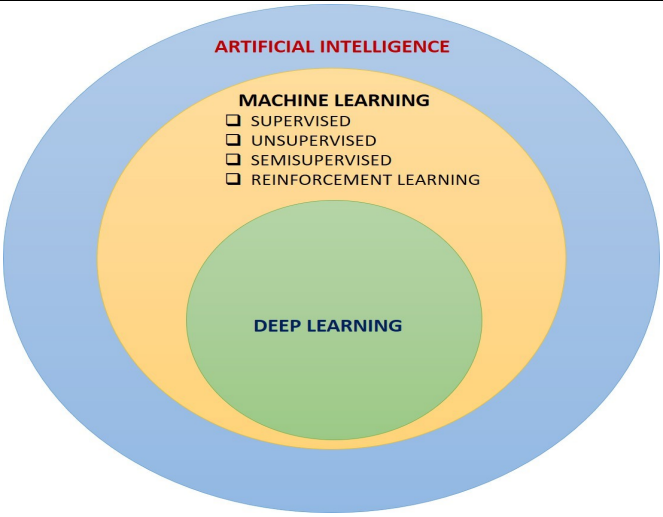

Fig. 2. The Schematic diagram of AI with its relation to ML and DL.

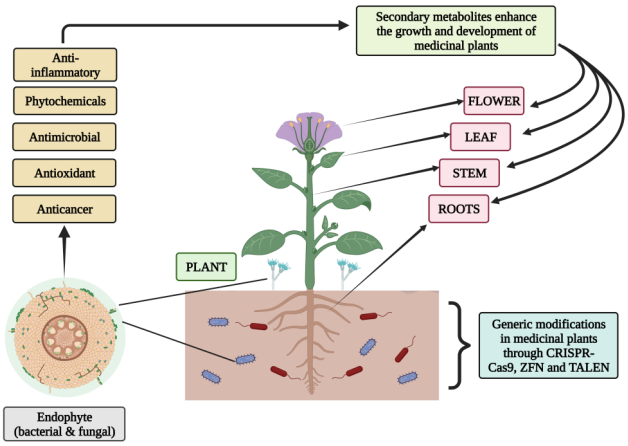

Fig. 3. Influence of bioactive compounds from entophytes in medicinal plants. (Bio Render software).

To analyze and interpret the vast amounts of data produced by such studies, artificial intelligence (AI) can be extremely important. Artificial intelligence could identify and classify endophytic microbes using their genetic and biochemical profiles (29). Machine learning algorithms can detect specific endophytes and their medicinal properties from large DNA and RNA sequence datasets (30). Artificial intelligence can help facilitate the discovery of promising medicinal substances (31). To predict the activity of newly identified endophytic bioactive compounds, machine learning algorithms can be trained on large databases of chemical compounds and their properties. This can aid in the discovery of novel agents and medications (32). Endophytic microorganism growth can also be optimized with AI. Machine learning algorithms can maximize endophytic growth by analyzing environmental factors like temperature, pH, and nutrient availability (33).

Role of endophytes on medicinal plants

Fungal endophytes

Endophytic fungi are responsible for the production of growth-promoting plant hormones (4), for example; *Azospirillum* spp. enhances the growth of *Triticum aestivum L.*, and they also produce bioactive compounds which increase the stress resistance in host plants (34, 35). By secreting indole acetic acid, *Mycena dendrobii* could encourage seed germination in addition to the growth of the host plant *Gastrodia elata* (36). Furthermore, it has been reported that by promoting the production of nitrate reductase and the starch-degrading enzymes, *Piriformospora indica* accelerated the growth in the roots of tobacco (37). The host plants of endophytic fungus belonging to the genus *Neotyphodium* may benefit from alkaloids produced by these organisms boosting their resistance to insect attacks (9). Table 2 shows the influence of fungal endophytes on various medicinal plants.

Bacterial endophytes

Bacterial endophytes are found in various plant components, including the seed, root, stem, leaves, and flowers (43-45). Endophytic bacteria enhance the biomass and seed germination in the host plants, they present at the different stages of plant development (46). Through a variety of methods, including the production of phytohormones, nitrogen fixation, and phosphorus solubilization, endophytes aid in the growth of plants (47, 48). Bacteria such as *Streptomyces*, *Bacillus*, *Paenibacillus,* and *Pseudomonas* (49-51) reported to promote the growth of plants, induce stress resistance, and enhance the metabolism of the medicinal plant (14). Actinomycetes support the ecology due to their environmentally favourable nature. They have been recognized to generate a range of antibiotics, biocontrol agents, and compounds that encourage plant growth (52-55). Actinomycetes enhance the soil fertility and production of the plant and also increase the nitrogen level (15). Table 3 shows the effect of bacterial endophytes on various medicinal plants.

Artificial intelligence and its subsets

Artificial intelligence (AI) refers to the mimicking of human intelligence processes by machines, particularly computer systems. It trains machines how to mimic human characteristics including learning, judging, and making decisions (61). Artificial intelligence (AI) seeks to replicate human intellectual activity by using knowledge as the object, obtaining knowledge, researching and analyzing the various ways in which knowledge is expressed, and then using these expressions (62).

Table 2. Effects of Fungal endophytes on medicinal plants.

S.No.	Medicinal Plant	Fungal Endophyte	Impact on Plants	References
1	*Cymbidium sinese*	*Mycena archdicola*	Increase hormones in the host plant.	(38)
2	*Dendrobium nobile, D. chrysanthum*	*Epulorhiza* sp., *Mycena* sp., *Tulasnellales, Sebacinales,Cantharellales*	Improve absorption of nutrients and promote seed germination in medicinal plants.	(39)
3	*Dendrobium candidum*	*Mycena dendrobii*	Increase hormones in the host plant.	(38)
4	*Sesbaniasesban*	*Funneliformis mosseae, Claroideoglomus etunicatum*	Secret the plant hormones	(40)
5	*Cucumis sativus*	*Phoma glomerata*, *Penicillium* sp.	Secret phytohormones	(41)

Table 3. Effects of bacterial endophytes on medicinal plants.

S.No.	Host Plant	Bacterial Endophytes	Impact on Host Plant	References
1	*Coriandrum Sativum*	*Bacillus siamensis*	Enhance the growth of stem and roots.	(56)
2	*Teucrium polium*	*Bacillus subtilis*	Improve the area, weight, and length of the root.	(57)
3	*Panax ginseng*	*Micrococcus luteus*	Enhanced biomass of seeds.	(58)
4	*Atractylodes Macrocephala*	*Pseudomonas fluorescens*	Increase yield of metabolites.	(59)
5	*Lonicera japonica*	*Paenibacillus*	Length of shoot, root, and fresh and dry weight increased.	(60)

The ability of a machine to learn by itself from data, improve its efficiency depending on prior experiences, and make predictions is known as machine learning, which is a subset of artificial intelligence (AI). The four basic categories of machine learning i.e., supervised, unsupervised, semi-supervised, and reinforcement learning are determined by the learning processes and methods (63). Deep learning (DL) is a member of a larger group of machine learning techniques built on artificial neural networks and representation learning (64). The Schematic diagram of AI and its relation to ML and DL is represented in Fig. 2.

AI and its functioning

The field of artificial intelligence is vast and includes numerous approaches and methodologies. Below is a general summary of how AI works and some of the important principles involved:

Data Collection: AI systems learn and make choices using massive volumes of data. The initial stage is to collect appropriate information from multiple data sources, such as images, text, audio, video, or numerical data (64).

Data Pre-processing: After gathering the data, it is frequently necessary to pre-process it, which involves cleaning, converting, and arranging it to make it appropriate for AI algorithms (64).

Machine learning: The procedure for ML modelling is to input data for training, use a machine learning algorithm for learning; and fine-tune the learning algorithm's parameters to improve accuracy. After the learning is completed, the model is now formed (63).

Neural networks: Modern AI and machine learning rely heavily on neural networks. They are inspired by the organization of the human brain and are made up of interconnected nodes or artificial neurons. Because neural networks can understand complex patterns and connections within data, they are highly effective for difficult jobs (65).

Deep learning: It emphasizes the application of multi-layered deep neural networks. These deep networks may automatically learn hierarchical data representations, allowing them to solve more complex problems (66).

Inference and decision-making: Following training, the AI model can make predictions or judgments on previously unknown data. This is referred to as inference. (67). For example, an AI system trained on diseased or healthy plants may be used to categorize newly acquired images as diseased or healthy.

Natural language processing: The field of artificial intelligence known as "natural language processing" (NLP) is concerned with designing algorithms to understand and interact with human language (68). Techniques such as language translation, digit recognition, handwriting recognition, and chatbots fall under this category.

Computer vision: Another important field of AI is computer vision, which enables intelligent machines to evaluate and comprehend visual data from images or videos (69). It is used in domains such as object detection, facial identification, autonomous vehicles, medicinal plant recognition, plant disease detection, and so on.

Role of AI in plant-based endophytic research

In endophytic research on medicinal plants, artificial intelligence (AI) has assumed an increasingly significant role. Here, are some examples of AI applications in this field shown in Fig. 4.

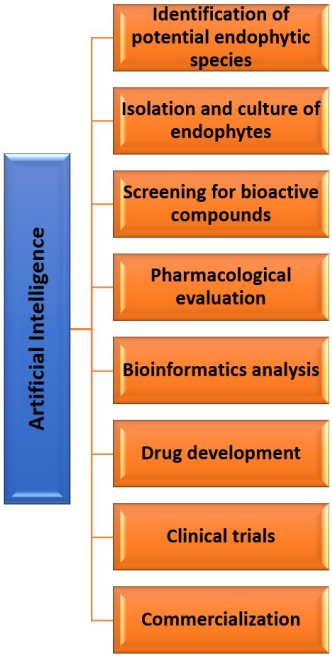

Fig. 4. AI assists in Endophytic research phases.

Prediction of bioactive compounds

Artificial intelligence can help to predict the bioactive compounds developed via endophytic microorganisms in medicinal plants. Predicting the production of bioactive metabolites by endophytic fungi in the medicinal plant *Panax ginseng* using machine learning algorithms is studied (70). Transcriptomics and artificial intelligence techniques for bioactive compound prediction and selection are also studied (71). On the extraction of bioactive chemicals from unripe *M. acuminata* peel using microwave-assisted extraction (MAE), the association between response surface methodology (RSM) and an artificial neural network prediction model was examined (72).

Discovery of new endophytes and natural products

Artificial Intelligence can aid in the discovery of novel endophytes and natural products with potential medical applications. AI is utilized to analyze the genome of the endophytic fungus *Aspergillus terreus* isolated from the medicinal plant *Huperzia serrata* to identify new natural products with anti-inflammatory and anti-tumor properties (73). In a review, emerging methods for discovering natural products from plant microbiomes were examined, with a focus on the potential of deep learning as a tool for bioprospecting, biochemical novelty prediction, and regulatory control of endophytes (74). For in-depth data analysis and forecasting in the search for anticancer leads, machine learning has provided potent

approaches to identify anticancer lead compounds with an emphasis on natural products from plants and their related microbes (75). Bioprospecting different species and running laboratory screening techniques are traditionally employed to identify natural compounds, producing complex data. This strategy, meanwhile, frequently confronts difficulties and high rates of loss. To solve these issues, machine learning (ML) and artificial intelligence (AI) are being used. The area of natural product-based drug discovery algorithms has undergone a revolution as a result of recent advances in AI, notably in ML. AI tools have shown success in classifying things, finding hidden patterns, and grouping compounds according to their properties (76, 77).

Optimization of endophyte-based production

Artificial Intelligence can improve medicinal plant endophytic microorganism bioactive compound production. Artificial Intelligence optimized bioactive compound synthesis by the endophytic fungus *Fusarium solani* isolated from the medicinal plant *Lithospermum erythrorhizon* (78). Response surface methodology (RSM) and an artificial neural network-genetic algorithm (ANN-GA) were investigated using a single-factor analysis of the efficacy of culture situations upon the quantity of cellulase produced by endophytic fungi of *T. cuspidata* to obtain factors for improving the enzyme activity process of production (79). For optimizing and predicting the 6-gingerol concentration in *Zingiber officinale* samples from 60 distinct locations around the state with varying agricultural and climatic circumstances, two deep learning algorithms of the Artificial Neural Network (ANN) model were used (80).

Identification of endophyte-host interactions

Artificial intelligence can be used to identify the associations between endophytic microorganisms and their host plants. It is used to examine the transcriptomes of the host plant *Camellia sinensis* and the endophytic fungus *Colletotrichum tofieldiae* and discover genes involved in their interaction (81).

Using genetic, morphological, and biochemical traits, artificial intelligence (AI) can analyze large datasets of plant samples to pinpoint possible endophytic species (73). It can assist in standardizing the process of isolation and maintaining culture conditions for endophytes to ensure their viability and growth (82). It is capable of assessing the metabolic profiles of endophytes to find bioactive substances with potential medicinal applications (75). Artificial Intelligence can aid in the analysis of genetic and biochemical data generated by endophytic research to identify novel drug development targets (83). Artificial Intelligence can be used in the design and optimization of drugs based on endophytic compounds, resulting in the creation of novel medicines (84). In addition, AI also analyses clinical trials for endophyte-derived pharmaceuticals, thereby enhancing their efficacy and safety. Apart from this, AI can assist in the commercialization of endophytic research by identifying potential markets, developing marketing strategies, and optimizing supply chains (85).

Conclusion

Endophytes existing as eco-friendly bioagents help to achieve a sustainable environment in the future. Bacterial and fungal endophytes aid in the greater development of medicinal plants by increasing the rate of plant hormones. Correspondingly, they increase medicinal properties by improving the seed germination stage and nutrient content. Besides, focus can be given to various techniques like regeneration, genetic modification, and electroporation which give a high yield of targeted bioactive compounds which gives numerous benefits to medicinal plants. Furthermore, the advancement of technologies such as AI has been incorporated to revolutionize the field of endophytic research in medicinal plants. The capability of AI to analyze large datasets of genomic and metabolomic data can help identify suitable endophytes with pharmaceutical potential and aid in the development of new drugs.

Indeed, the research of endophytes on medicinal plants has shown AI to be of enormous value to human society. Overall, the study of endophytes on medicinal plants in conjunction with artificial intelligence has enormous potential to advance drug discovery, develop more potent therapies, and advance human health. Researchers can speed up the discovery and development of novel medicinal compounds from these natural sources by utilizing AI.

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Authors' contributions

Saloni Kunwar and Aditya Joshi: Writing-original draft and Data curation. Prateek Gururani and Deepa Pandey: Conceptualization and Investigation. Neha Pandey: Supervision, Resources. All authors read and approved the final manuscript.

Compliance with ethical standards

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