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EDITED BY
Sowbiya Muneer,
VIT University, India

REVIEWED BY
Ankita Rajendra Parab,
University of Science Malaysia (USM), Malaysia
Arabi Mohammed Saleh,
VIT University, India

*CORRESPONDENCE
Gusmaini Gusmaini
gusmaini672@gmail.com

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Physio-agronomic characteristics and andrographolide yield of *Andrographis paniculata* in response to endophytic *Bacillus* sp and phosphorus

Gusmaini Gusmaini[1]*, Hera Nurhayati[2], Kartika Kartika[3], Sunjaya Putra[1], Kurnia Dewi Sasmita[1], Rismayani Rismayani[1], Saefudin Saefudin[1], Wahyu Wibawa[1], Dibyo Pranowo[1], Edi Wardiana[1], Yulius Ferry[1], Rossa Yunita[1] and Muhammad Syakir[1]

[1]Research Center for Estate Crops, National Research and Innovation Agency (BRIN), Cibinong, Indonesia, [2]Division of Collaboration and Dissemination of estate crops engineering and modernization, Indonesian Center for Estate Crops Engineering and Modernization, Indonesian Agency for Agricultural Engineering and Modernization, Ministry of Agriculture, Bogor, Indonesia, [3]Research Center for Horticulture, National Research and Innovation Agency (BRIN), Cibinong, Indonesia

Endophytic bacteria can be applied as biofertilizers and plant growth promoters due to their potential to release phytohormones and improve nutrient availability, thereby supporting plant growth and the biosynthesis of bioactive compounds. Effective practical cultivation of medicinal plants, including sambiloto (*Andrographis paniculata*), suggests using biofertilizer, in addition to inorganic fertilizer. Andrographolide, a key compound in *A. paniculata*, is recognized for its therapeutic properties, including anti-inflammatory and antiviral activities, making its enhanced biosynthesis significant in medicinal plant research. Phosphorus is required in andrographolide biosynthesis. The study aimed to determine the physiological and agronomic characteristics, as well as the bioactive compounds of *A. paniculata*, by applying endophytic bacteria and phosphate fertilizer. The trial was arranged in a completely randomized design with six treatments and three replications. The treatments consisted of the following: 1) no treatment (control), 2) 0.675 g P_2O_5 plant^{-1}, 3) 1.35 g P_2O_5 plant^{-1}, 4) endophytic bacteria *Bacillus* sp., 5) endophytic bacteria *Bacillus* sp. + 0.675 g P_2O_5 plant^{-1}, and 6) endophytic bacteria *Bacillus* sp. + 1.35 g P_2O_5 plant^{-1}. Endophytic bacteria *Bacillus* sp. and phosphate fertilizer significantly ($P<0.05$) influenced agronomic characteristics, including growth and fresh and dry biomass production, as well as physiological characteristics, including Net Assimilation Rate (NAR), Relative Growth Rate (RGR), Stem-to-Leaf Ratio (SLR), Leaf Area Index (LAI), and Leaf Area Ratio (LAR). The application of *Bacillus* sp. in combination with 0.675 g P_2O_5 plant^{-1} produced the highest herbage weight and secondary metabolites (andrographolide, 14-deoxy-

11,12-didehydroandrographolide, and neo-andrographolide), and hence could be recommended in *A. paniculata* cultivation. Furthermore, the application of endophytic bacteria *Bacillus* sp. could reduce the use of chemical phosphate fertilizer by 50%, offering significant benefits for farmers and being more environmentally friendly to support sustainable agriculture.

KEYWORDS

endophyte bacteria, bioactive compound, NAR, P fertilizer, productivity, RGR

1 Introduction

The king of bitter plant (*Andrographis paniculata* Nees.), or *sambiloto* in Indonesian, is one of the most widely used plants in pharmaceutical formulations (Irianti et al., 2022). Andrographolide is the primary bioactive compound found in *A. paniculata* and is responsible for the plant's characteristic bitter taste. This diterpenoid lactone and its derivatives (neo-andrographolide, 14-deoxyandrographolide, and 14-deoxy-11,12-didehydro? >andrographolide) possess a wide range of pharmacological properties (Adiguna et al., 2021; Hao et al., 2020). These include anti-inflammatory, antipyretic, antihyperglycemic, antioxidant, antidiabetic (Islam et al., 2018; Liu et al., 2020), antiviral (Adiguna et al., 2021; Jiang et al., 2021; Shi et al., 2020), and gastrointestinal protective activities (Wang et al., 2021). Due to these properties, andrographolide and its biosynthesis have attracted considerable interest in pharmaceutical and agricultural research.

The concentration of andrographolide in *A. paniculata* varies among different plant tissues, with the highest levels found in the leaves (ranging from 2.5% to 4.8%), while only small amounts are detected in the roots, stems, and flowers (Fitriansyah et al., 2024). However, several studies have shown that andrographolide content is also influenced by the plant's age and environmental conditions. For instance, Tajidin et al. (2019) reported that the highest concentration of andrographolide is present when the plants reached 18 WAS (week after sowing).

To improve the biosynthesis of andrographolide and support sustainable cultivation practices, biofertilizers such as endophytic bacteria have emerged as promising alternatives to chemical fertilizers. These bacteria play multiple roles in promoting plant health and productivity. Endophytic bacteria are a type of plant growth-promoting bacteria (PGPB) that can produce phytohormones likeindole acetic acid (IAA), gibberellin (GA3), abscisic acid (ABA), and cytokinin (Egamberdieva et al., 2017). In addition, it fixes nitrogen (N) from the atmosphere (Okamoto et al., 2021), solubilizes phosphate (Li et al., 2017; Alkahtani et al., 2020), and increases the organic matter level released from dead and decomposed bacterial biomass as a biofertilizer (Ali et al., 2022). The endophytic bacteria also generate siderophores (Chen et al., 2016; Maheshwari et al., 2019), which can chelate metals such as Hg, Fe, and Al (Ferreira et al., 2019). These metals, which can hamper plant growth and development, are commonly found in acid soils that dominate the land in Indonesia. Microbes that produce siderophores can also control pathogenic microbes (Kumari et al., 2022), protect plants from environmental stress (Ullah et al., 2019), increase crop productivity, and sustain soil health (Prasad et al., 2020). Endophytic bacteria offer an economical and environmentally friendly approach to increasing plant nutrient supply, reducing chemical fertilizer use, and protecting against abiotic and biotic stresses (Lachu et al., 2022; Prasad et al., 2020).

Recent studies have demonstrated that endophytic microbes can play a significant role in enhancing secondary metabolite production in medicinal plants. For example, Kumari et al. (2023) reported that the bacterial endophyte *Micrococcus luteus* (ASd6) significantly increased both biomass and andrographolide content in *A. paniculata* by 68.01% and 44.16%, respectively. Beyond bacterial endophytes, Nair and Sakuntala (2020) highlighted the role of the root-colonizing mutualistic fungus *Piriformospora indica* as a potent elicitor of andrographolide biosynthesis, achieving a marked increase in andrographolide content up to 58.2 mg/g dry weight compared to 19.5 mg/g in control plants. This improvement was mechanistically associated with the transcriptional upregulation of key genes involved in the mevalonate (MVA) and methylerythritol phosphate (MEP) pathways, including 3-hydroxy-3-methylglutaryl-CoA synthase (HMGS), 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR), 1-deoxy-D-xylulose 5-phosphate synthase (DXS), 1-Deoxy-D-xylulose 5-Phosphate reductoisomerase (DXR), geranylgeranyl pyrophosphate synthase (GGPS), and 1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate reductase (ISPH), all of which contribute to the biosynthesis of andrographolide precursors. These findings underscore the functional significance of plant and endophyte interactions in modulating secondary metabolism and offer a sustainable strategy to boost the production of pharmacologically important compounds.

One of the essential macronutrients for plant growth is phosphorus (P), which is involved in photosynthesis and primary metabolite processes, serving as an energy source to convert ADP into ATP. Glucose, produced from the primary metabolite process, is then used for secondary metabolite formation, including andrographolide, which is synthesized by *A. paniculata*. Andrographolide is a secondary metabolite classified under the diterpenoid group and synthesized through the mevalonate and non-mevalonate acid pathways (Bergman et al., 2019). Phosphorus is required in andrographolide biosynthesis for the production of isopentenyl pyrophosphate/diphosphate (IPP/IDP) and dimethylallyl pyrophosphate/diphosphate (DAMPP/DAMPP) (Bergman et al., 2019; Shailaja et al., 2021).

Given these facts, there is a strong need to explore the combined use of biofertilizers and phosphate fertilizer to maximize *A. paniculata* growth and andrographolide yield. Therefore, this study aimed to determine the most effective combination of endophytic bacteria and phosphate fertilizer dosage by evaluating physiological traits, agronomic performance, and secondary metabolite content. This work supports the application of sustainable cultivation technologies for medicinal plants, as promoted by the Indonesian Ministry of Agriculture.

2 Materials and methods

2.1 Treatments and plant cultivation

The study was conducted at the Cimanggu Research Installation, part of the Indonesian Spices and Medicinal Crops Research Institute. The experimental site was located at 0°41'38.17" N; 127°33'15.18" E, at an elevation of 250 meters above sea level (asl), with Latosol as the predominant soil type.

The field trial was arranged in a completely randomized block design with six treatments and three replications. The treatments were as follows: 1) no treatment (C), 2) 0.675 g P_2O_5 plant^{-1} (P1), 3) 1.35 g P_2O_5 plant^{-1} (P2), 4) *Bacillus* sp. (B1), 5) *Bacillus* sp. + 0.675 g P_2O_5 plant^{-1} (B1+P1), and 6) *Bacillus* sp. + 1.35 g P_2O_5 plant^{-1} (B1+P2). The 1.35 g P_2O_5 plant^{-1} dose represents the recommended phosphorus application for *A. paniculata* cultivation in Indonesia, while the 0.675 g P_2O_5 plant^{-1} dose corresponds to 50% of the recommended rate.

The *A. paniculata* cultivation procedures were as follows: seeds of the Sambina 1 variety were first germinated in a nursery. The germinated seedlings were then transplanted into small polybags filled with a soil-to-manure mixture at a 2:1 ratio and maintained for one month. The experimental site was subsequently cleared and divided into 27 plots, with a 1-meter spacing between blocks.

Each plot measured 2 × 4 m with a plant spacing of 40 × 60 cm. One week before planting, manure was applied at a rate of 250 g plant^{-1}. Phosphorus fertilizer (0.675 and 1.35 g P_2O_5 plant^{-1}) and potassium fertilizer (2.25 g K_2O plant^{-1}) were applied at the time of planting. Nitrogen fertilizer (2.30 g plant^{-1}) was applied in two equal splits at 4 and 8 weeks after planting (WAP).

The endophytic bacteria (*Bacillus* sp.) used in this study were obtained from previous research (Gusmaini et al., 2022) and cultured in Tryptic Soy Broth (TSB) media for 2 × 24 hours. The *Bacillus* sp. suspension, with a population density of 10^8 CFU mL^{-1}, was applied at 3, 5, 7, and 9 WAP at a dose of 100 mL plant^{-1}. The suspension was sprayed onto both the plants and the soil, while the control plants were sprayed with blank media (TSB suspension without bacteria).

2.2 Measurements

The agronomic characteristics, growth parameters including plant height and number of primary branches, were recorded every two weeks (2, 4, 6, 8, 10, 12, and 14 WAP). The yield parameters, such as the fresh and dry biomass weight, were measured at 8, 10, 12, and 14 WAP. The biomass was dried in an oven at 50–60°C to determine the dry weight. Data on physiological characteristics, including net assimilation rate (NAR), relative growth rate (RGR), stem-to-leaf ratio (SLR), and leaf area index (LAI), were also collected. The NAR (Equation 1) and RGR (Equation 2) were calculated according to the formulas below:

$$NAR = \frac{W2 - W1}{t2 - t1} \times \frac{ln\ \ A2 - ln\ \ A1}{A2 - A1} \tag{1}$$

and

$$RGR = \frac{\ln W2 - \ln W1}{t2 - t1} \tag{2}$$

W1 and W2 represent the plant dry weights at times t1 and t2, respectively, while, A1 and A2 denote the corresponding leaf areas at times t1 and t2 (William and Joseph, 1976). The leaf aa index (LAI) was calculated by dividing the maximum leaf area by the land area occupied by the plants. The leaf area ratio (LAR) was determined as the total leaf area divided by the dry biomass weight (Morrison et al., 1999). Leaf area measurements were conducted using a leaf area meter (Li-3000).

Plant tissue nutrient analysis was conducted at 14 WAP. The 0.5 g samples of plant powder we digested using the wet digestion method with sulfuric acid (H_2SO_4) and hydrogen peroxide (H_2O_2). Phosphorus (P) and potassium (K) contents were measured using a spectrophotometer and atomic absorption spectroscopy (AAS), respectively, while nitrogen (N) content was determined using the kjeldahl method (Kjeldahl, 1883). The N, P, K content data are obtained using the formula below:

Nitrogen Content (Equation 3):

$$\text{N content (\%)} = \frac{(\text{V1} - \text{V2}) \times \text{N} \times 14.008 \times \text{fp} \times 100 \times \text{fk}}{\text{W}} \tag{3}$$

where V1 is sample titration volume, V2 is blanko titration volume, N is H_2SO_4 normality, 14.008 is nitrogen atomic weight, fp is dilution correction factor, fk is moisture content correction factor, and W is sample weight.

Phosphorus content (Equation 4):

$$P\ \ content\ \ (\%) = ppm\ \ curve\ \text{x}\ \frac{\text{vol. content of extract in ml}}{1000\ \ ml}\ x\ \frac{100}{sample\ \ weight\ \ in\ \ mg}\ x\ \frac{atomic\ \ weight\ \ of\ \ P}{molecular\ \ weight\ \ of\ \ PO4}\ x\ fk\ x\ fp \tag{4}$$

Potassium content (Equation 5):

$$K\ content\ (\%) = ppm\ curve \times \frac{\text{vol. content of extract in ml}}{1000\ ml} \times \frac{100}{sample\ weight\ in\ mg} \times fk \times fp \quad (5)$$

where fk is moisture correction factor, fp is dilution correction factor.

Andrographolide, neoandrographolide, and 14-deoxy-11,12-didehydroandrographolide were qntified using a TLC Scanner with a mobile phase n-hexane P-ethyl acetate P (2:8). The test solution was prepared by placing 500 mg of simplicia powder into a 10-mL volumetric flask, adding 10 mL of methanol P, and filtering the mixture. The standard solution consisted of 0.1% andrographolide in methanol P. A series of dilutions of the reference solution were prepared until the absorbance values closely matched those of the test solution. Absorbance was measured at the maximum absorption wavelength of 230 nm, and a calibration curve was established.

T andrographolide percentage in the simplicia powder was calculated using the standard curve or the following formula (Equation 3):

$$Andrographolide\ \% = \frac{C\ x\ Au\ x\ V\ x\ fp\ x\ Ap}{W} \times 100 \quad (6)$$

where C is the concentration of the reference solution, Au is the absorbance of the test solution, Ap is the absorbance of the reference solution, V is the volume of the test solution before dilution, fp is the dilution factor of the test solution, and W is the weight of the test material in dry form.

2.3 Data analysis

The effects of treatments on the observed variables were analyzed using analysis of variance. When significant differences were detected, Duncan's Multiple Range Test (DMRT) was applied at a 5% significance level to determine differences among treatment means.

3 Results

3.1 Phosphate status in the field before trial

Information regarding the status and availability of nutrients in the soil was necessary before the application of fertilizers. The total phosphorus (P) content in the soil before the study was found to be very high (0.067%), while the available P was low (4.21 ppm) (Table 1). This result indicated that most of the P was unavailable for plant uptake. The enrichment of the soil with endophytic bacteria could potentially dissolve fixed P, converting it into available P, thereby enhancing the growth and development of *A. paniculata*.

3.2 Agronomic characteristics of *A. paniculata*

Plant height and the number of primary branches are important agronomic traits for the growth of *A. paniculata*. The growth pattern of *A. paniculata* at 2 to 14 WAP showed a steady increase. The application of endophytic bacteria and phosphate fertilizer resulted in a higher plant height compared to the control starting at 4 WAP. Additionally, the number of primary branches also increased from 10 to 14 WAP (Figure 1), and notably, it was significantly higher than the control at 14 WAP (Table 2).

Plant height increased by 6.79% to 13.27%, while the number of primary branches increased by 7.16% to 21.93%, following the application of endophytic bacteria and/or phosphate fertilizer at 14 WAP. The combination of endophytic bacteria *Bacillus* sp. and 0.675 g P_2O_5 plant^{-1} (B1+P1) resulted in the highest increases in both plant height (13.27%) and primary branch number (21.93%) (Table 2).

Fresh and dry herbage yields are key indicators of the success of *A. paniculata* cultivation. Consistent with its growth, the application of endophytic bacteria and phosphate fertilizer enhanced both fresh and dry weight yields from 8 to 14 WAP. The soil in the research site contained low levels of available P; therefore, applying even a small amount of P fertilizer significantly impacted growth and yield, as evidenced by the fresh and dry herbage yields.

The increase in fresh herb production ranged from 12.17-41.74%, while dry herb production ranged from 20.92% to 51.13% at 14 WAP with the application of endophytic bacteria and/or phosphate fertilizer. The combination of endophytic bacteria *Bacillus* sp. and 0.675 g P_2O_5 plant^{-1} (B1+P1) resulted in the highest increase in fresh (41.74%) and dry (51.13%) herb production compared to the control, with no significant difference when 1.35 g P_2O_5 was applied (Tables 3, 4).

Nutrient uptake represents the nutrients absorbed relative to the dry weight of plant biomass. At 14 WAP, N (2.56-2.85 g/plant), P (0.23-0.25 g/plant), and K (2.09-2.34 g/plant) uptake were higher in all treatments compared to the control (Figure 2). Nevertheless, with the application of 1.35 g P_2O_5 plant^{-1} (P2) resulting in the highest uptake of N and magnesium (Mg). Additionally, the combination of endophytic bacteria *Bacillus* sp. and 0.675 g P_2O_5 plant^{-1} (B1+P1) led to the highest uptake of phosphorus (P) and K. In contrast, the application of 0.675 g P_2O_5 plant^{-1} showed the most significant increase in calcium (Ca) nutrient uptake (Figure 2). The effect endophyte and P application on P uptake for all treatments there were no difference.

3.3 Physiological characteristics of *A. paniculata*

A. paniculata fertilized with endophytic bacteria and phosphate showed varying dry-weight production depending on the

TABLE 1 Phosphorus status of the soil before treatments.

Parameters	Value	Note
P total (%)	0.067	Very high
Available P (ppm)	4.210	Very low

harvesting time. As the plants aged, the yield increased. The combination of endophytic bacteria and 0.675 g P_2O_5 plant^{-1} (B1 +P1) resulted in the highest net assimilate rate (NAR) and relative growth rate (RGR) at 12–14 WAP (Figure 3), consistent with the dry weight results (Table 4).

Leaf area index (LAI) and leaf area ratio (LAR) are used to assess plant productivity and calculate the amount of solar radiation absorbed by the leaves for photosynthesis, which directly influences plant biomass production. The LAI trend in *A. paniculata* showed that as the plant aged, the LAI value increased (Figure 4).

This trend aligned with the SLR, which was higher during the vegetative phase than in the generative phase (Table 5). Conversely, the leaf area ratio (LAR) increased as the plant aged. Similar to the dry herb yield, the combination of *Bacillus* sp. and 0.675 g P_2O_5 plant^{-1} (B1+P1) resulted in the highest LAI and LAR at 8–14 WAP (Figure 4).

3.4 Andrographolide and its derivates of *A. paniculata*

Three bioactive compounds of *A. paniculata* measured at 8 and 14 WAP were andrographolide, 14-deoxy-11,12-didehydroandrographolide, and neoandrographolide. Generally, the levels of andrographolide and 14-deoxy11,12-didehydroandrographolide were lower in young plants during the vegetative phase (8 WAP) and increased in older plants during the generative phase (14 WAP) (Figures 5, 6). In contrast, the content of neoandrographolide decreased in older plants, except for the endophytic bacteria *Bacillus* sp. treatment, which showed a slight increase (Figure 5).

Andrographolide is the primary compound in *A. paniculata* that offers numerous benefits as a raw material for herbal medicine. In this study, andrographolide content increased linearly with the harvesting time. At 8 WAP, andrographolide (0.97–1.62%), neoandrographolide (0.30-0.48%), and 14-deoxy-11,12-didehydroandrographolide (0.44-0.75%) content. They did not show significant differences among treatments. However, at 14 WAP, the andrographolide, and 14-deoxy-11,12-didehydroandrographolide content increased to of range of 2.10–3.73% and 0.66-0.99% respectively, indicating significant differences among treatments, but neoandrographolide content (0.26-0.56%), lower than at 8 WAP (Figure 5).

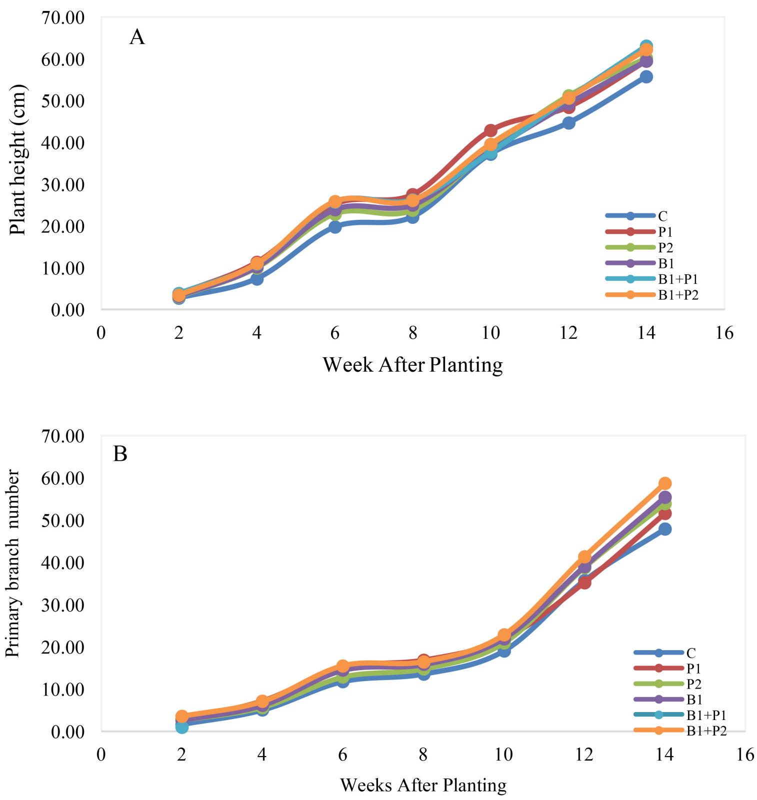

FIGURE 1
Effect of endophytic bacteria and phosphorus application on the growth pattern of *A. paniculata* from 2 to 14 WAP; **(A)** plant height and **(B)** number of primary branches.

TABLE 2 Effect of endophytic bacteria and phosphorus application on the growth of *A. paniculata* at 14 weeks after planting (WAP).

Treatments	Plant height (cm)	Number of primary branches
C	55.69±1.2^{a}	48.06±1.2^{a}
P1	59.47±2.2^{ab}	51.50±1.5^{ab}
P2	60.22±1.5^{ab}	53.84±3.1^{ab}
B1	59.56± 3.1^{ab}	55.37±2.3^{b}
B1+P1	63.08±1.4^{b}	58.60±3.4^{b}
B1+P2	62.22±3.3^{b}	57.63±1.7^{b}

Numbers followed by the same letters within a column are not significantly different at $p < 0.05$ according to Duncan's Multiple Range Test.

The increase in andrographolide content was not directly proportional to its production, as the yield was also influenced by biomass production. As a result, andrographolide yield at 8 WAP (1.24-0.12-0.28 g plant^{-1}) was lower than at 14 WAP (1.98–4.84 g plant^{-1}) across all treatments. Likewise, neoandrograholide (0.04-0.11 to 0.22-0.44 g plant^{-1}), and 14-deoxy-11,12-didehydroandrographolide (0.06-0.14 to 0.76-0.96 g plant^{-1}) (Figure 6). Consequently, both the levels, content and production of total andrographolide at 14 WAP were higher than those at 8 WAP (Figures 5, 6). At 8 WAP, the treatment with *Bacillus* sp. + 1.35 g P_2O_5 plant-^{1} (B1+P2) resulted in higher levels of highest content and yield of andrographolide, neoandrographolide, and 14-deoxy-11,12-didehydroandrographolide (Figure 6). In contrast, at 14 weeks after planting (WAP), plants treated with the combination of *Bacillus* sp. + 0.675 g P_2O_5 plant-^{1} (B1+P1) showed the highest content of these compounds. Meanwhile, plants treated with *Bacillus* sp. (B1) exhibited the highest total andrographolide content (4.93%), while the combination of *Bacillus* sp. + 0.675 g P2O5 plant^{-1} (B1+P1) resulted in the highest total andrographolide yield (6.31 g plant^{-1}) (Figure 6). Overall, the application of endophytic bacteria enhanced the levels of andrographolide and its derivatives in *A. paniculata*.

4 Discussions

The results indicate that the application of endophytic bacteria *Bacillus* sp. and phosphate fertilizer significantly improved plant growth, biomass production, and andrographolide accumulation, supporting the hypothesis that biofertilizers can reduce dependency on chemical inputs while sustaining or even improving yield and compound content. The improvement in agronomic traits such as plant height, branch number, and herbage yield is attributed to the role of *Bacillus* sp. in improving nutrient availability, particularly through phosphorus solubilization, as well as the production of plant growth-promoting phytohormones such as indole acetic acid (IAA) and gibberellic acid (GA3) (Adeleke et al., 2021). Similar findings have been reported in previous studies. For instance, *Bacillus* strains have been shown to positively influence maize growth and increase phosphorus (P) and nitrogen (N) content in the shoots (Alkahtani et al., 2020). Additionally, endophytic bacteria isolated from the medicinal plant *Paris polyphylla* var. *yunnanensis* have been found to enhance its growth (Tao et al., 2022). Likewise, the use of endophytic bacteria improved plant height in tomatoes (Abdallah et al., 2018) and peanuts (Lucero et al., 2021).

Endophytic bacteria not only release phytohormones but also play a crucial role in stimulating plant growth and improving overall plant performance. Previous studies have reported that bacterial endophytes can enhance tryptophan availability and produce substantial amounts of IAA, up to 60 μg mL^{-1} (Alkahtani et al., 2020), and 68 mg L^{-1} (Herlina et al., 2017). These phytohormones stimulated an increase in plant height and the number of primary branches in *A. paniculata*. IAA plays essential roles in regulating various plant cellular mechanisms, including cell orientation, division, organ development, differentiation, and elongation (Asgher et al., 2015; Labeeuw et al., 2016). Meanwhile, GA3 contributes significantly to the formation of lateral shoots (Cai et al., 2022), regulates stomatal behavior, supports metabolic activity under both normal and stress conditions (Zhou et al., 2024) and enhances root number and length (Choudhary et al., 2022).

TABLE 3 Effect of endophytic bacteria and phosphorus on the fresh herbage yield of *A. paniculata*.

Treatments	Fresh herbage yield (g/plant)			
	8	10	12	14
	Harvest time (WAP)			
C	44.88±3.8^{a}	85.08±4.8^{a}	184.23±4.8^{a}	267.97±3.2^{a}
P1	68.34±1.0^{b}	139.11±5.7^{b}	239.66±4.1^{c}	300.59±3.5^{b}
P2	62.30±5.8^{b}	153.74±2.8^{c}	211.48±7.4^{b}	313.18±7.4^{b}
B1	66.22±2.4^{b}	150.74±4.1^{c}	192.16±5.9^{b}	322.00±3.5^{b}
B1+P1	80.51±4.0^{c}	132.04±3.7^{b}	193.90±6.0^{b}	379.82±5.8^{c}
B1+P2	68.06±5.9^{b}	133.65±4.9^{b}	220.15±7.6^{c}	350.97±5.1^{bc}

Numbers followed by the same letters within a column are not significantly different at $p < 0.05$ according to Duncan's Multiple Range Test.

TABLE 4 Effect of endophytic bacteria and phosphorus on the dry herbage yield of *A. paniculata*.

Treatments	Harvesting times (WAP)			
	8	10	12	14
C	10.34±2.1[a]	22.40±1.9[a]	59.83±4.2[a]	85.67±5.4[a]
P1	15.44±1.6[b]	31.94±4.0[b]	65.71±4.3[b]	113.96±5.4[b]
P2	13.59±1.9[b]	34.83±4.8[b]	63.83±3.2[b]	111.30±5.3[b]
B1	15.08±3.2[b]	25.48±4.0[a]	57.32±4.8[a]	103.59±2.3[b]
B1+P1	17.36±2.8[c]	29.25±2.7[a]	56.32±4.2[a]	129.48±2.5[c]
B1+P2	15.57±1.5[b]	31.65±4.2[b]	65.89±3.7[b]	114.85±5.6[bc]

Numbers followed by the same letters within a column are not significantly different at $p < 0.05$ according to Duncan's Multiple Range Test.

Beyond promoting plant growth, endophytic bacteria also improve soil fertility by increasing nutrient availability. Previous studies have demonstrated that endophytic bacteria enhance pepper growth and soil fertility, leading to more efficient nutrient absorption (Gusmaini et al., 2020). In the present study, nutrient uptake patterns varied across treatments, reflecting the differential influence of *Bacillus* sp. and phosphate fertilizer on nutrient availability and transport. For example, the combination treatment (B1+P1) resulted in higher P and K uptake due to microbial phosphate solubilization and improved root architecture, which may enhance potassium mobility (Timofeeva et al., 2022). In contrast, 1.35 g P_2O_5 treatment (P2) led to the highest N and Mg uptake and the 0.675 g P_2O_5 treatment (P1) showed increased calcium uptake, likely because of the higher external availability of nutrients rather than microbial mediation.

These nutrient dynamics translated into higher biomass accumulation. At 14 weeks after planting (WAP), the application of endophytic *Bacillus* sp. and/or phosphate fertilizer led to increases in fresh herb production by 12.17–41.74% and in dry herb production by 20.92–51.13% at 14 WAP. The combined treatment of *Bacillus* sp. and 0.675 g P_2O_5 plant^{-1} (B1+P1) yielded the highest fresh (41.74%) and dry (51.13%) herb production compared to the control and showed no significant difference from the 1.35 g P_2O_5 treatment (Tables 3, 4). This indicates that microbial support may allow for reduced chemical input without compromising productivity. These results are consistent with previous findings where endophytic bacteria increased biomass production by up to 68.01% (Kumari et al., 2023).

In addition to producing phytohormones, *Bacillus* sp. also enhanced nutrient availability through nitrogen fixation and phosphorus solubilization (Lucero et al., 2021). These mechanisms allow nutrients to be utilized more efficiently by plants, thereby supporting their growth. Previous studies have also reported that endophytic bacteria from *Bacillus* strains improved dry biomass and phosphorus use efficiency in wheat cultivars (Wang et al., 2022), as well as enhanced phosphorus uptake in pearl millet under low-phosphorus conditions (Ribeiro et al., 2018).

Enhanced nutrient absorption positively influences plant growth and development, as demonstrated by the increased dry herb yield. The application of phosphate fertilizer, either alone or in combination with endophytic bacteria, significantly improved the uptake of N, P, K, Ca, and Mg, thereby boosting both fresh and dry herb yields (Tables 3, 4). These findings align with previous studies highlighting the role of phosphate-solubilizing endophytic bacteria in enhancing phosphorus uptake.

The net assimilation rate (NAR) describes the relationship between leaf area and dry matter accumulation over time, serving as an indicator of the plant's efficiency in producing dry biomass per unit of leaf area per unit time. A reduction in leaf area adversely

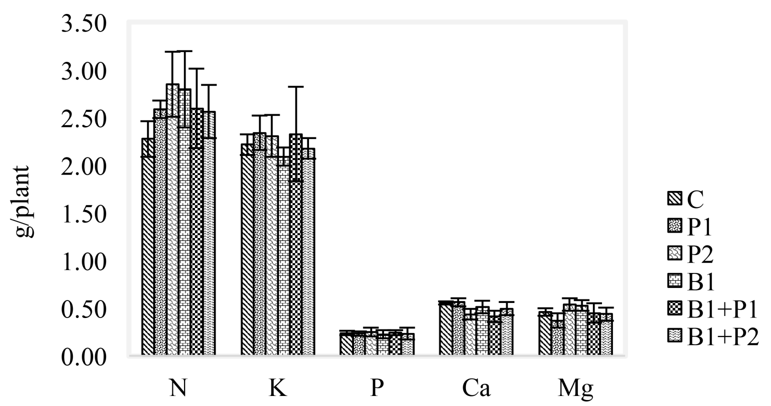

FIGURE 2
Effect of endophytic bacteria and phosphorus application on nutrient uptake of *A. paniculata* at 14 WAP.

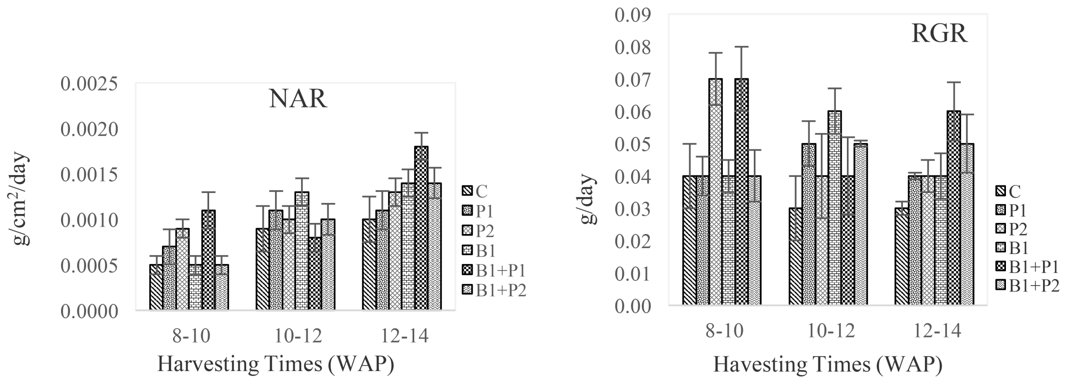

FIGURE 3
Effect of endophytic bacteria and phosphorus on the net assimilation rate (NAR) and relative growth rate (RGR) of *A. paniculata* from 8 to 14 WAP.

impacts dry biomass production. Similarly, the relative growth rate (RGR), which quantifies the rate of dry weight increase over time, is closely influenced by NAR (Lamont et al., 2023).

Endophytic bacteria significantly enhanced the accumulation of andrographolide and its derivatives in *A. paniculata*, with andrographolide content increasing by up to 44.16% following bacterial application (P. Kumari et al., 2023). This enhancement is attributed to the ability of *Bacillus* sp. to produce IAA and GA3, as well as to improve nitrogen and phosphorus acquisition. These factors collectively act as plant growth regulators, thereby promoting biomass production and stimulating the biosynthesis of secondary metabolite (Sales and Rigobelo, 2024).

In this study, the highest total andrographolide yield was observed at 14 weeks after planting (WAP). It is primarily due to two factors, i.e increased biomass and developmental stage. Plant age strongly influences secondary metabolite biosynthesis, with older plants often exhibiting higher metabolite accumulation due to metabolic shifts from growth to defence and storage (Nair and Sakuntala, 2020). Furthermore, enhanced nutrient availability at 14 WAP may have supported the mevalonate (MVA) and methylerythritol phosphate (MEP) pathways involved in andrographolide biosynthesis, especially under *Bacillus* sp. treatment (Kumari et al., 2023; Nair and Sakuntala, 2020).

Additionally, *Bacillus* strains are known to produce a wide range of bioactive compounds, including aromatic compounds, lipopeptides, phytohormones, polysaccharides, and enzymes involved in phenylpropanoid metabolism (Ek-Ramos et al., 2019). These metabolites play critical roles in promoting plant growth and supporting effective crop management strategies. Importantly, the inoculation of endophytic bacteria can influence the biosynthetic pathways of host plants, modulating the production of pharmacologically active compounds while simultaneously supporting vegetative growth (Singh et al., 2017).

Reducing the use of chemical fertilizers is a key priority for sustainable agriculture, particularly in the cultivation of medicinal plants, where minimizing chemical residues is crucial. In tropical

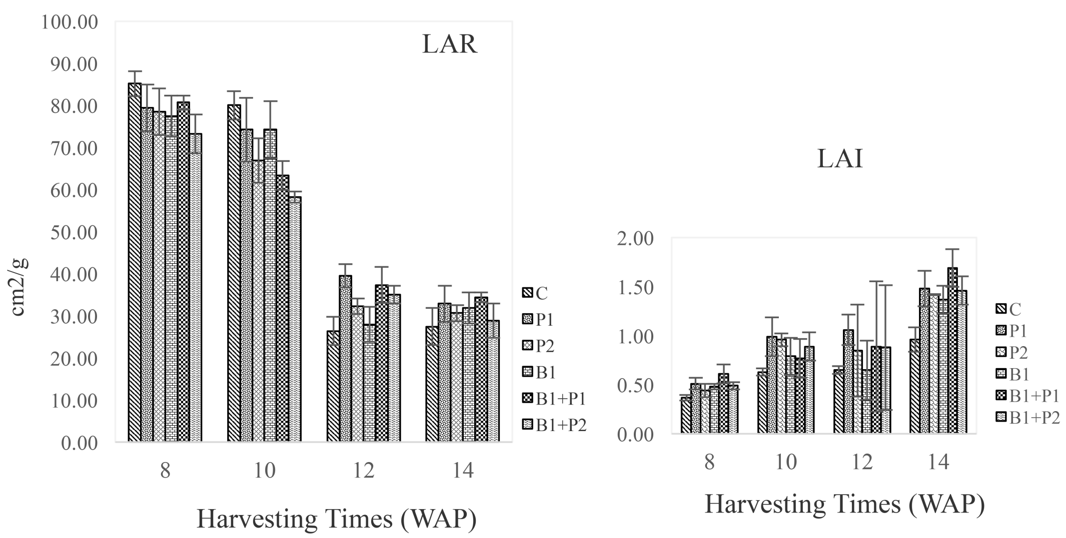

FIGURE 4
Effect of endophytic bacteria and phosphorus on leaf area ratio (LAR) and leaf area index (LAI) of *A. paniculata* from 8 to 14 WAP.

TABLE 5 Effect of endophytic bacteria and phosphorus on the dry stem-to-leaf ratio (SLR) of *A. paniculata*.

Treatments	Harvest Time (WAP)			
	8	10	12	14
C	2.04±0.4 [a]	1.93±0.5 [a]	1.02±0.2 [a]	0.62±0.3[a]
P1	2.52±0.5 [a]	1.92±0.6 [a]	0.89±0.2 [a]	0.51±0.4[a]
P2	2.92±0.3[b]	1.85±0.3 [a]	1.11±0.4 [a]	0.53±0.3[a]
B1	2.69±0.7[ab]	2.16±0.4 [a]	1.02±0.3 [a]	0.65±0.2[a]
B1+P1	2.77±0.4[ab]	2.06±0.5 [a]	1.28±0.1 [a]	0.62±0.2[a]
B1+P2	2.91±0.5[b]	1.86±0.2 [a]	1.09±0.2 [a]	0.60±0.1[a]

Numbers followed by the same letters within a column are not significantly different at $p < 0.05$ according to Duncan's Multiple Range Test.

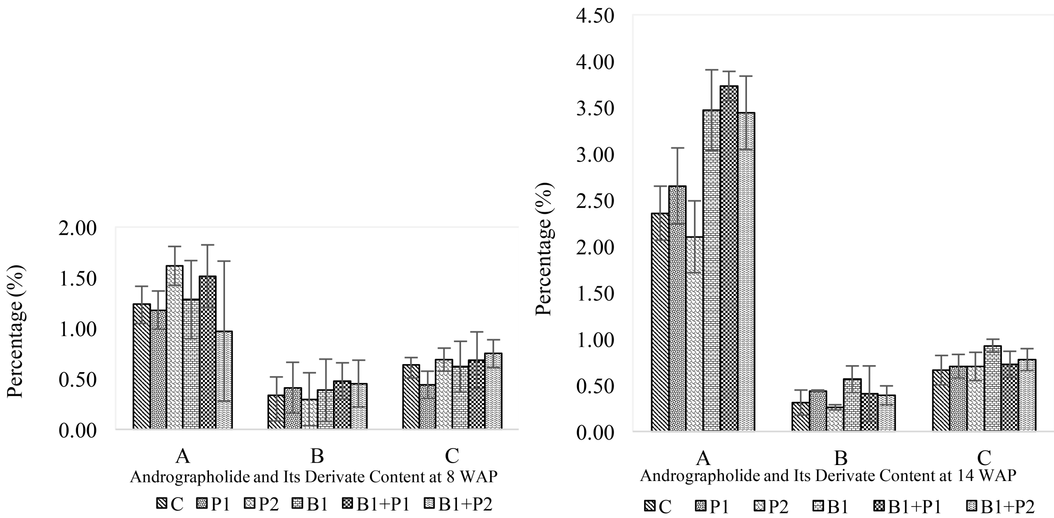

FIGURE 5
Effect of endophytic bacteria and phosphorus on andrographolide and its derivate content at 8 and 14 WAP. **(A)** andrographolide; **(B)** neoandrographolide; and **(C)** 14-deoxy-11,12-didehydroandrographolide.

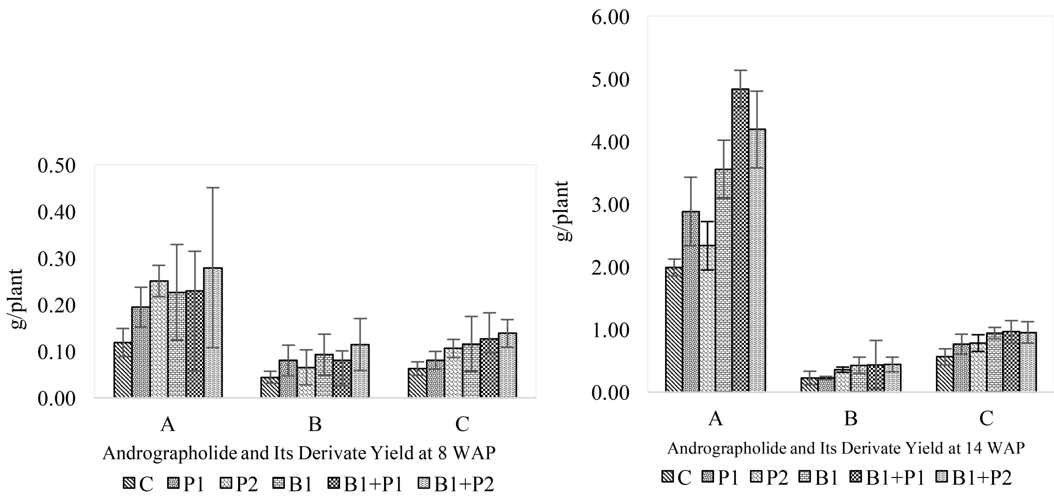

FIGURE 6
Effect of endophytic bacteria and phosphorus on andrographolide and its derivate yield at 8 and 14 WAP. **(A)** andrographolide; **(B)** neoandrographolide; and **(C)** 14-deoxy-11,12-didehydroandrographolide.

soils, chemical phosphorus fertilizers are often inefficient due to their strong fixation by soil particles, which limits their availability to plants. In contrast, microbial biofertilizers such as *Bacillus* sp. offer a more sustainable solution by mobilizing fixed soil nutrients, enhancing root development, and lowering the risk of environmental pollution (Ribeiro et al., 2018; Wang et al., 2022). In this study, *Bacillus* sp. alone or in combination with half-dose phosphate (0.675 g P_2O_5) achieved results comparable to full chemical application (1.35 g P_2O_5), indicating the potential to reduce chemical inputs by up to 50% without compromising plant growth or andrographolide production. These results reinforce the value of microbial biofertilizers as eco-friendly tools to enhance biomass and secondary metabolite production in *A. paniculata*, aligning with broader efforts to promote low input and sustainable medicinal plant cultivation.

5 Conclusions

The agronomic and physiological characteristics, as well as andrographolide yield of *Andrographis paniculata* were significantly improved by applying the endophytic bacteria *Bacillus* sp. and phosphorus fertilizer. The combination of *Bacillus* sp. and 0.675 g P_2O_5 plant^{-1} produced the best agronomic and physiological performance and andrographolide yield, with the best results observed at the flowering stage (14 weeks after planting). This suggests that using *Bacillus* sp. can reduce the use of chemical phosphorus fertilizer by up to 50%, benefiting farmers and contributing to more environmentally friendly practices in support of sustainable agriculture. These results also align with the Ministry of Agriculture's regulation that encourages the use of organic fertilizers as part of Good Agricultural Practice (GAP) for medicinal plants.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

GG: Investigation, Writing – review & editing, Conceptualization, Writing – original draft. HN: Methodology, Data curation, Investigation, Writing – original draft. KK: Visualization, Writing – review & editing, Formal Analysis. SP: Writing – review & editing, Visualization, Formal Analysis. KS: Formal Analysis, Writing – review & editing, Visualization. WW: Writing – review & editing, Formal Analysis, Visualization. RR: Data curation, Methodology, Writing – original draft, Investigation. SS: Data curation, Methodology, Investigation, Writing – original draft. YF: Writing – original draft, Methodology, Investigation, Data curation. DP: Writing – review & editing, Visualization, Supervision. EW: Visualization, Supervision, Writing – review & editing. RY: Visualization, Supervision, Writing – review & editing. MS: Visualization, Writing – review & editing, Supervision.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

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