

HIGH PINOCEMBRIN, PINOSTROBIN, AND PANDURATIN A WITH NOTABLE ANTIOXIDANT ACTIVITY IN FINGERROOT POWDER SOLD THROUGH ONLINE STORES

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Abstract

Fingerroot (*Boesenbergia rotunda* (L.) Mansf.) is a plant known for its effective antioxidant properties, attributed primarily to its flavonoid content. Despite its increasing availability as a powdered product sold through online platforms, information regarding its flavonoid content and antioxidant activity remains limited. This study presents the first comparative analysis of 40 commercial fingerroot powder products, focusing on the quantification of three major flavonoids - pinocembrin (PC), pinostrobin (PS), and panduratin A (PA) - and their antioxidant activity. High-performance liquid chromatography was employed to quantify PC, PS, and PA, while antioxidant activity was assessed using the DPPH radical scavenging assay. The results revealed that PS was the predominant flavonoid, with content ranging from 0.33% to 4.65% (mean: 2.88%; median: 3.06%). PC content ranged from 0.74% to 1.94% (mean: 1.27%; median: 1.25%), and PA content ranged from 0.04% to 1.48% (mean: 0.81%; median: 0.88%). The DPPH radical scavenging activity, expressed as percent inhibition, ranged from 60.67% to 77.37% (mean: 69.86%; median: 69.70%). Considerable variability in flavonoid contents and antioxidant activity was observed among samples. These results provide new benchmark data for evaluating the chemical quality of fingerroot powders available online and underscore their practical potential as functional food or dietary supplement ingredients with strong antioxidant efficacy.

Keywords: Panduratin A; Pinocembrin; Pinostrobin; DPPH radical

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Introduction

The dried root and rhizome of *Boesenbergia rotunda* (L.) Mansf., commonly known as fingerroot, are widely recognized for their biological and medicinal properties. Fingerroot contains a variety of bioactive compounds, including flavonoids such as pinocembrin (PC) and pinostrobin (PS), as well as boesenbergin A and panduratin A (PA) (Department of Medical Sciences Ministry of Public Health, 2022). Due to its high flavonoid content, this plant is known for its potent antioxidant properties (Hop & Son, 2023; Saah *et al.*, 2021). Moreover, several studies highlight its broad pharmacological activities, including anti-inflammatory, antiparasitic, antibacterial, aphrodisiac, gastroprotective, hepatoprotective, neuroprotective, renoprotective, wound-healing, anti-allergic, anticancer, and antidiabetic effects (Eng-Chong *et al.*, 2012; Hop & Son, 2023; Jitvaropas *et al.*, 2012; Ongwisetpaiboon & Jiraungkoorskul, 2017). In addition to its traditional uses in food, herbal supplements, and herbal medicine, fingerroot has gained attention for its potential in modern nutraceuticals and functional foods due to its ability to provide health benefits beyond basic nutrition. These applications have fueled interest in its bioactive compounds and their mechanisms of action.

The increasing prevalence of oxidative stress-related diseases has prompted significant interest in the role of antioxidants, particularly flavonoids, in mitigating oxidative damage. Flavonoids, a diverse group of polyphenolic compounds found in various plants, have been studied extensively for their antioxidant properties and mechanisms of action in reducing oxidative stress. These compounds, including PC, PS, and PA, exhibit potent antioxidant activities that can counteract the harmful effects of reactive oxygen species (ROS) and other oxidative agents (Kongsui *et al.*, 2023). Oxidative stress, resulting from an imbalance between ROS production and the body's ability to neutralize these reactive molecules, is linked to the development of numerous chronic diseases, such as cardiovascular disorders, diabetes, neurodegenerative diseases, and certain forms of cancer (Sharifi-Rad *et al.*, 2020). Antioxidants like flavonoids play a crucial role in mitigating these risks by scavenging ROS, chelating metal ions, and modulating antioxidant enzyme systems (Zahra *et al.*, 2024). Moreover, the physicochemical properties of PC, PS, and PA comply with

Lipinski's Rule of Five, indicating favorable drug-likeness (Daina *et al.*, 2017), while their solubility-permeability characteristics correspond to BCS class II, reflecting low aqueous solubility but high membrane permeability (Kongratanasert *et al.*, 2024; Muharrami *et al.*, 2024).

Among the key flavonoids, PC and PS have shown promising results in various studies, demonstrating their capacity to enhance antioxidant enzyme activities and reduce oxidative stress markers. Their efficacy has been demonstrated not only in *in vitro* studies but also in animal models, where they have shown the ability to protect against oxidative damage in key organs, such as the liver, brain, and kidneys (Atun *et al.*, 2017; González *et al.*, 2022; Spiegel, 2023; Yang *et al.*, 2018; Zhao *et al.*, 2023). Panduratin A, another significant flavonoid, has been reported to exert protective effects against oxidative damage in different biological models, highlighting its potential as a functional food ingredient (Thongnuanjan *et al.*, 2021). The commercial availability of fingerroot powder, which is rich in these flavonoids, has increased, particularly through online platforms, making it more accessible to consumers seeking functional foods that promote health and well-being.

Despite the growing interest in flavonoids and their health benefits, there remains a notable gap in the literature regarding the flavonoid composition of commercially available fingerroot powders. Limited data exist on the specific contents of PC, PS, and PA in these products, as well as their antioxidant activities when sold through online stores. The variation in flavonoid content and antioxidant activity may result from several factors, including the source of raw materials, cultivation and post-harvest conditions, processing techniques, storage duration, and product formulation. However, benchmark or reference values for these parameters in commercial fingerroot powders have not yet been established, making quality evaluation and standardization difficult. Therefore, this study aims to address these gaps by systematically quantifying the major flavonoids (PC, PS, and PA) and evaluating the antioxidant activity of commercial fingerroot powders from different online sources. The findings are expected to provide benchmark data that can serve as a reference for product quality assessment and future standard development in industries focusing on functional foods and dietary supplements.

Materials and Methods

Materials

PC (purity 99.5%) and PS (purity 99.9%) standards were purchased from Chengdu Biopurify Phytochemicals Ltd., Sichuan, China, while the panduratin A standard was obtained from the Faculty of Science, Mahidol University, Thailand. 2,2-diphenyl-1-picrylhydrazyl (DPPH) was purchased from Sigma-Aldrich, MO, USA. All solvents used were high-performance liquid chromatography (HPLC) and analytical reagent (AR) grades.

Quantitative analysis of PC, PS, and PA contents in fingerroot powders

Forty fingerroot powder samples were purchased from various online sources in December 2024. Only products without additives were included in the study. Using a method described in previous studies (Monton *et al.*, 2025), the concentrations of PC, PS, and PA were examined using HPLC. With a few slight modifications, the Thai Herbal Pharmacopoeia (THP) (Department of Medical Sciences Ministry of Public Health, 2022) was followed to prepare the samples for chemical analysis. Before extraction, all samples were sieved through a 40-mesh stainless steel sieve to obtain a uniform particle size. Subsequently, 50 mg of accurately weighed fingerroot powder was macerated for 24 h in 10 mL of methanol ($n = 3$). After maceration, the mixture was mixed thoroughly to ensure homogeneity and then allowed to stand for 10 min to allow sedimentation before filtration. After passing through a 0.45- μm nylon syringe filter into an amber vial, the supernatant was subjected to HPLC analysis.

An Agilent 1260 Infinity II system (Agilent Technologies, Inc., CA, USA) with a photodiode array detector and autosampler was used for the analysis. A guard column of the same material (4.6×5 mm, 4 μm particle size) and a Poroshell 120 EC-C18 column (4.6×250 mm, 4 μm particle size) (Agilent Technologies, Inc., CA, USA) were used to achieve separation. The temperature of the column was kept at 25°C. Water and acetonitrile made up the mobile phase, which had a gradient flow rate of 1 mL/min: 50:50 at 0 min, 0:100 at 15 min, and 50:50 between 16 and 18 min. A wavelength of 288 nm was used for detection, and the injection volume was 10 μL .

The analysis began by preparing 1 mg/mL of each standard in methanol, followed by the preparation of a mixed standard solution for the three flavonoids with the following

concentration ranges: 0.78125–100 $\mu\text{g/mL}$ for PC, 1.5625–200 $\mu\text{g/mL}$ for PS, and 0.78125–100 $\mu\text{g/mL}$ for PA. The solutions were filtered before HPLC analysis. Calibration curves were constructed, and the contents of PC, PS, and PA in the samples were calculated from the respective calibration curves. In addition, the validation of this HPLC technique was previously conducted in accordance with the International Council for Harmonisation guidance (ICH Expert Working Group, 2022). The prior study included a full description of the method validation data (Monton *et al.*, 2025).

DPPH radical scavenging assay

The procedure described in a prior study was modified slightly for the DPPH radical scavenging experiment (Sithisarn *et al.*, 2015). A 100 μL sample solution obtained from maceration mentioned earlier and an equivalent volume of a 0.2 mM DPPH methanolic solution were put into a 96-well plate ($n = 3$). After fully mixing the mixture, it was incubated for 30 min at room temperature in the dark. After that, a microplate reader (Bio-Rad Laboratories, Inc., CA, USA) was used to measure the absorbance at 517 nm. The percentage of DPPH scavenging was used to express antioxidant activity (Equation 1). The approach was validated using L-ascorbic acid (10 $\mu\text{g/mL}$) as a positive control.

$$\text{DPPH radical scavenging (\%)} = \left(\frac{\text{Abs}_{\text{control}} - \text{Abs}_{\text{sample}}}{\text{Abs}_{\text{control}}} \right) \times 100 \quad (1)$$

Where $\text{Abs}_{\text{control}}$ and $\text{Abs}_{\text{sample}}$ are the absorbance of the control and sample, respectively.

Clustering and heat map analysis

The clustered heat map was generated using data on PC content, PS content, PA content, and percent DPPH radical scavenging. Average linkage clustering was employed as the clustering method, and Euclidean distance was used as the distance measurement method. The analysis and visualization were performed using the Heatmapper tool (<http://www.heatmapper.ca/expression/>).

Statistical analysis

Data are presented as the mean, median, and standard deviation (SD) of three independent measurements ($n = 3$).

Results

The 40 fingerroot powder samples obtained from various online sources were analyzed for flavonoid contents - PC, PS, and PA - using HPLC. The contents of each flavonoid are shown in Figure 1. It was found that PS was the major flavonoid, followed by PC and PA, respectively. The average and SD of PS, PC, and PA were $2.88 \pm 0.78\%$, $1.27 \pm 0.25\%$, and $0.81 \pm 0.35\%$, respectively. Samples 19, 13, and 39 exhibited the highest PS, PC, and PA contents, respectively. While Sample 22 had the lowest PS and PA contents, Sample 32 had the lowest PC content.

Figure 2 shows a box-and-whisker plot of the PC, PS, and PA contents in fingerroot powders. It demonstrates that PS was the most abundant compound. The PC content exhibited the lowest variability compared to the PS and PA contents. Outliers were observed in the PC and PS contents, with one outlier for PC and four outliers for PS. The median values and ranges (minimum to maximum) of the PC, PS, and PA contents were 1.25% (ranging from 0.74% to 1.94%), 3.06% (ranging from 0.33% to 4.65%), and 0.88% (ranging from 0.04% to 1.48%), respectively.

The antioxidant activity of fingerroot powders, measured in terms of DPPH radical scavenging activity, is shown in Figure 3. The

extract solutions used in this assay were the same as those prepared for HPLC analysis. All extract solutions were obtained by extracting 50 mg of fingerroot powder in 10 mL of methanol. The results showed that all samples exhibited good antioxidant activity. The DPPH radical scavenging activity of all samples was above 60%, with an average value and SD of $69.86 \pm 3.90\%$, ranging from 60.67% to 77.37%.

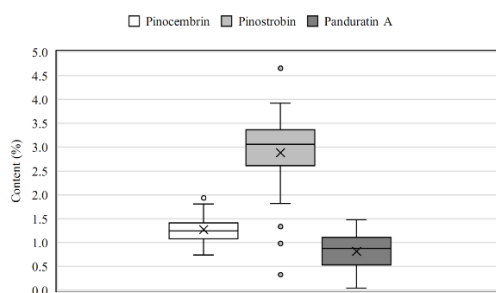


Figure 2. Box-and-whisker plot showing the contents of PC, PS, and PA in fingerroot powders obtained from various online stores. PC, PS, and PA refer to pinocembrin, pinostrobin, and panduratin A, respectively

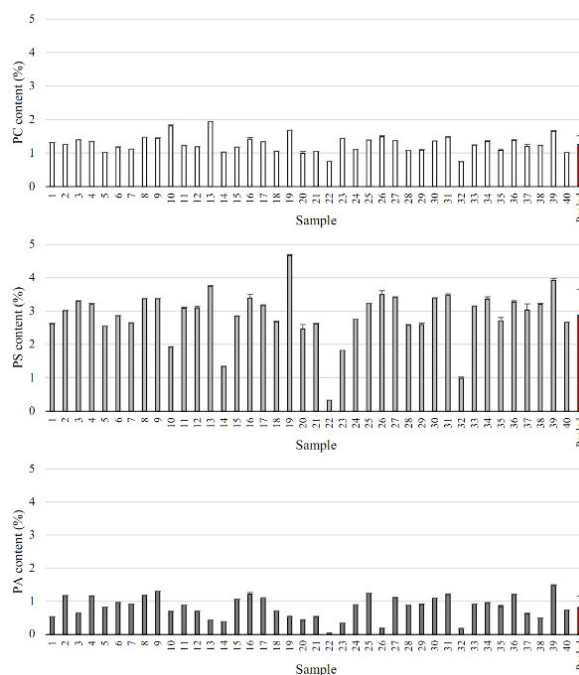


Figure 1. Contents of PC (top), PS (middle), and PA (bottom) in fingerroot powders obtained from various online sources. PC, PS, and PA refer to pinocembrin, pinostrobin, and panduratin A, respectively

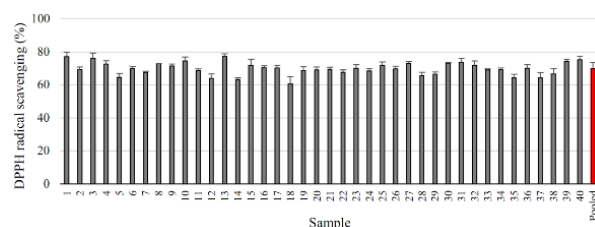


Figure 3. Antioxidant activity of fingerroot powders obtained from various online sources, measured in terms of DPPH radical scavenging activity and presented as percent inhibition

A clustered heat map of fingerroot powders, based on the contents of PC, PS, PA, and DPPH radical scavenging activity, is shown in Figure 4. The fingerroot powder samples were clustered into two groups: Group I and Group II. Independent sample t-test analysis revealed that Group I had significantly higher levels of PC, PS, and PA, as well as significantly higher DPPH radical scavenging activity, compared to Group II.

statistically significant), and significantly higher DPPH radical scavenging activity. Similarly, a comparison between subgroups IIA and IIB within Group II, revealed that subgroup IIA had slightly higher PC content (not statistically significant), slightly lower PS content (not statistically significant), slightly higher PA content (not statistically significant), and significantly higher DPPH radical scavenging activity.

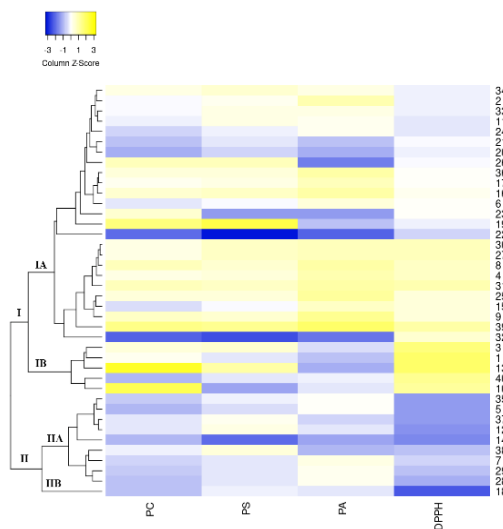


Figure 4. Clustered heat map of fingerroot powders obtained from various online sources, based on the contents of PC, PS, PA, and DPPH radical scavenging activity. PC refers to pinocembrin, PS to pinostrobin, PA to panduratin A, and DPPH to 2,2-diphenyl-1-picrylhydrazyl. The clustered heat map was generated using the Heatmapper tool (<http://www.heatmapper.ca/expression/>)

Within Group I, a comparison between subgroups IA and IB showed that Group IB had slightly higher PC content (not statistically significant), slightly lower PS and PA content (not

Discussion

Flavonoids have been identified as bioactive compounds in fingerroot and are known to exhibit antioxidant activity (Monton *et al.*, 2025). A higher flavonoid content appears to correlate with greater antioxidant activity. In the present study, almost all fingerroot powder samples contained PC, PS, and PA concentrations of $1.27 \pm 0.25\%$, $2.88 \pm 0.78\%$, and $0.81 \pm 0.35\%$, respectively. Previous research reported pooled data from 32 fingerroot root samples with average levels and SDs of PC, PS, and PA at $0.62 \pm 0.16\%$, $1.49 \pm 0.68\%$, and $0.55 \pm 0.25\%$, respectively. For rhizome samples, the reported values were $0.98 \pm 0.19\%$, $1.90 \pm 0.77\%$, and $0.77 \pm 0.33\%$, respectively (Monton *et al.*, 2025). The findings from the present study revealed that the flavonoid content (PC, PS, and PA) in the fingerroot powder samples analyzed is higher than the levels reported in the previous study (Monton *et al.*, 2025). The THP specifies that fingerroot should contain no less than 2.0% w/w of PS (Department of Medical Sciences Ministry of Public Health, 2022). Previous research indicated that only 6 out of 32 fingerroot root samples and 14 out of 32 fingerroot rhizome samples met the THP standards (Monton *et al.*, 2025). However, 35 out of 40 samples (87.5%) in the present study met the THP standards, suggesting that the fingerroot powders sold through online sources exhibit high quality in terms of chemical constituents.

The findings of the present study concerning the flavonoid content of fingerroot powders available through online platforms align with

previous research on the curcuminoid content of Zingiberaceous plant rhizomes, especially turmeric (*Curcuma longa*), sold online. Both studies highlight the increasing commercial availability of these plants while emphasizing concerns regarding their chemical quality. In a previous study, curcuminoid profiling of *Curcuma* species demonstrated substantial variation in bioactive compound levels, with *C. longa* exhibiting the highest curcuminoid content, followed by *C. aromatica*, *C. zedoaria*, *Z. montanum*, and *C. wananhueanga*. Notably, some *C. longa* samples failed to meet the THP standard, indicating inconsistencies in the quality of online herbal products (Monton *et al.*, 2024). Similarly, this study found variations in the flavonoid content (PC, PS, and PA) of fingerroot powder samples, but a significantly higher proportion (87.5%) met the THP requirement for PS ($\geq 2.0\%$ w/w). This suggests that fingerroot products available online may exhibit greater compliance with quality standards compared to some *Curcuma* samples analyzed in the previous study. Furthermore, the previous study demonstrated that species and cultivation locations influenced curcuminoid composition, as evidenced by cluster analysis (Monton *et al.*, 2024). While the current study did not specifically assess geographical variations, the higher flavonoid content in the analyzed fingerroot samples compared to previously reported values suggests potential differences due to cultivation practices, processing methods, or storage conditions. This highlights the need for further research to determine the factors affecting the chemical profiles of fingerroot and other Zingiberaceous plants sold online.

Interestingly, Samples 22 and 32 exhibited antioxidant activity comparable to that of other samples, despite their low flavonoid content. This may be attributed to the potent antioxidant properties of certain bioactive compounds, such as flavonoids. However, a previous study reported that among individual flavonoids, PC and PS demonstrated relatively low DPPH radical scavenging activity, whereas PA exhibited the highest activity, with an IC_{50} value of $76.56 \mu\text{g/mL}$. This can be explained by the fact that flavanones, including PC and PS, are generally weaker radical scavengers compared to PA (Elbatreek *et al.*, 2023). However, a preliminary test examining the correlation between each flavonoid and antioxidant activity showed no significant relationship. The authors suggested that antioxidant activity results from the combined effects of multiple compounds rather than being attributed solely to flavonoids or a single specific flavonoid (Doan *et al.*, 2024; Wilczyńska & Żak, 2024).

The molecular characteristics of PC, PS, and PA also demonstrate conformity with Lipinski's Rule of Five, as reflected by their respective parameters: PC (4 hydrogen-bond acceptors, 2 hydrogen-bond donors, molecular weight 256.25 g/mol, log P 2.26), PS (4 hydrogen-bond acceptors, 1 hydrogen-bond donor, molecular weight 270.28 g/mol, log P 2.66), and PA (4 hydrogen-bond acceptors, 2 hydrogen-bond donors, molecular weight 406.51 g/mol, log P 4.77) (Daina *et al.*, 2017). These physicochemical features indicate favorable oral drug-likeness and reflect their lipophilic profiles. Correspondingly, their limited aqueous solubility and relatively high permeability place these compounds within BCS class II, characteristics inherent to their chemical nature (Kongratanapasert *et al.*, 2024; Muharrami *et al.*, 2024). Such information can be useful beyond pharmacological considerations, providing a basis for evaluating the bioactive compound content and potential antioxidant contributions in applications such as functional foods and dietary supplements. Understanding these properties could help guide formulation strategies and quality assessment in product development, ensuring consistency in the functional and health-promoting attributes of fingerroot-derived products.

The results of the clustering analysis revealed distinct differences between Group I and Group II, with Group I exhibiting significantly higher levels of PC, PS, PA, and DPPH radical scavenging activity. Within Group I, further subdivision into subgroups IA and IB highlighted additional variations. While both IA and IB demonstrated high flavonoid content and antioxidant activity, IB outperformed IA in terms of bioactive compound concentration and efficacy. Specifically, IB had slightly higher PC content, slightly lower PS and PA content (though not statistically significant), and significantly higher DPPH radical scavenging activity. This suggests that IB represents a superior quality subset within Group I, emphasizing its potential as a high-performance functional food ingredient. Therefore, consumers should prioritize products from Group IB when selecting a store to purchase fingerroot powder to ensure higher quality and greater antioxidant efficacy. The findings underscore the importance of improving standards across the production and supply chain to ensure the consistent quality and efficacy of fingerroot powder products.

Given the significant role of environmental and agronomic factors, farmers need to adopt Good Agricultural Practices (GAP) to ensure high-quality fingerroot production. GAP involves optimizing agricultural techniques such as soil management, water use, pest control, and crop rotation, which

help to maintain the health of the plants and improve the consistency of bioactive compound levels (Srivastava *et al.*, 2024). Additionally, promoting organic farming practices can enhance the environmental sustainability of fingerroot cultivation while avoiding the use of synthetic chemicals that may interfere with flavonoid synthesis. Organic practices, such as the use of natural fertilizers and pest control methods, can improve both the quality and environmental footprint of the product (Gamage *et al.*, 2023; Rani *et al.*, 2023). To further enhance the quality of fingerroot products, proper packaging is crucial. Packaging that protects the product from environmental stressors such as light, moisture, and temperature fluctuations will help maintain the stability and integrity of flavonoids during storage and transportation. Furthermore, the packaging should not only preserve the bioactive compounds but also improve the product's appearance, making it more appealing to consumers. The aesthetic value of packaging plays a significant role in consumer preference and trust in the product (Duarte *et al.*, 2024). Additionally, obtaining FDA registration and certification for fingerroot products will help ensure compliance with regulatory standards for consumption, thereby building consumer confidence and promoting market consistency (Dominguez Díaz *et al.*, 2020; Intravook *et al.*, 2024). Understanding and addressing these factors is crucial for optimizing fingerroot cultivation and ensuring high flavonoid yield and quality. Standardizing agricultural practices, improving soil management, and refining harvesting and storage methods could help maintain consistency in flavonoid content. Given the substantial influence of environmental, agronomic, and regulatory factors on flavonoid biosynthesis, future research should focus on developing best practices for cultivation and processing to enhance the efficacy and quality of fingerroot products in the market. However, this study is limited by the lack of detailed information regarding the commercial fingerroot powder samples, including product origin, cultivar, cultivation region, harvest maturity, processing method, and storage duration. Such data were largely unavailable from product labels, which restricts the ability to link specific product attributes to the observed variations in PC, PS, and PA contents and DPPH radical scavenging activity. Additionally, the current analysis focused on three major flavonoids, but other bioactive compounds present in fingerroot may also contribute to antioxidant activity, though they were not assessed in this study. The study also did not investigate the effects of geographical or seasonal variations on flavonoid profiles, which may influence the

chemical composition of commercially available powders. Finally, antioxidant activity was only measured using the DPPH assay; therefore, additional assays may be required to fully capture the contribution of flavonoids to overall antioxidant potential.

Previous studies have emphasized that geographic and environmental factors substantially affect the production of secondary metabolites in medicinal plants, including fingerroot. Altitude, local climate, and sunlight exposure can alter the biosynthesis of bioactive compounds, while temperature, rainfall, and seasonal variations impact plant growth and the accumulation of flavonoids (Li *et al.*, 2020; Pant *et al.*, 2021). Soil characteristics, such as pH, nutrient content, organic matter, and drainage, further modulate the uptake of nutrients and synthesis of secondary metabolites (Aqeel *et al.*, 2024; Karimi *et al.*, 2020; Lotfi *et al.*, 2024; Pacheco-Hernández *et al.*, 2021). Although these factors are known to influence flavonoid content, the current study could not control for them because the fingerroot powders were obtained from online sources rather than directly from specific cultivation sites. Consequently, while environmental and agronomic conditions are important determinants of flavonoid levels, the commercial nature of the samples limited the ability to assess their direct effects. Furthermore, flavonoid levels can vary over time due to differences in harvest periods and plant maturity (Monton *et al.*, 2024; Wunnakup *et al.*, 2025). The current study analyzed commercially available powders at a single point in time, so it cannot capture temporal variations that may exist in fresh fingerroot rhizomes. Comprehensive sampling throughout the year would be needed to fully understand the seasonal fluctuations of PC, PS, and PA in fingerroot.

Conclusions

This study highlights that fingerroot, increasingly marketed in powdered form through online platforms, contains considerable levels of bioactive flavonoids, which are key contributors to its well-documented antioxidant properties. Among the three major flavonoids analyzed-PC, PS, and PA-PS emerged as the predominant compound, with notably higher concentrations compared to the other flavonoids. The antioxidant activity of the fingerroot powders, as measured by the DPPH radical scavenging assay, further supports their functional potential, demonstrating strong free radical inhibition across all samples. These findings underscore the promise of fingerroot powder as

a functional food ingredient with health-promoting properties. The high flavonoid content, combined with notable antioxidant activity, positions it as a valuable natural supplement that could support oxidative stress management and overall health. However, the variability observed in flavonoid content and antioxidant activity across products suggests the need for standardized production and quality control measures to ensure consistent efficacy and consumer confidence.

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Author Contributions

Conceptualization: C.M., J.S., W.R.; Methodology: C.M.; Investigation: C.M., J.S.; Data Curation: C.M., J.S., W.R.; Writing – Original Draft: C.M., J.S., W.R.; Writing – Review & Editing: C.M., J.S., W.R.; Supervision: C.M. All authors have read and agreed to the published version of the manuscript.

Ethics Statement

Ethical approval was not required for this study because it did not involve human participants, animals, identifiable personal data, or materials requiring institutional ethical review.

Declaration of Generative AI Use

During the preparation of this manuscript, the authors used ChatGPT (GPT-4o mini, OpenAI) and DeepSeek-V3 (DeepSeek) to assist with proofreading and correcting grammatical errors during the manuscript writing process. These tools were used solely for language editing purposes. All AI-assisted outputs were critically reviewed, verified, and revised by the authors, who accept full responsibility for the content of this manuscript.

Conflict of Interest

The authors declare that they have no conflicts of interest related to this work.

Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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