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Original article [1]

Quantification and biological effects of Podocarpus flavone A in Bolivian *Podocarpus* species, focusing on its antiproliferative and antioxidant properties

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Keys: *Podocarpus oleifolius, Podocarpus ingensis, Podocarpus parlatorei, Podocarpus flavone A, bisflavonoids, antioxidant activity, cytotoxicity on Hela, A549 and CaCo-2 cell lines;*
Claves: *Podocarpus oleifolius, Podocarpus ingensis, Podocarpus parlatorei, Podocarpus flavona A, bisflavonoides, actividad antioxidante, citotoxicidad en Hela, A-549 y CaCo-2 líneas celulares..*

ABSTRACT

This study reports the isolation and analysis of the bisflavonoid Podocarpus flavona A (PFA) from ethanolic extracts of Bolivian Podocarpus species. PFA was obtained from P. oleifolius using column chromatography and HPLC, and its structure was determined by 1D and 2D NMR spectroscopy. HPLC quantification revealed PFA concentrations ranging from 0.37 to 2.20 mg/kg across three species, with detection and quantification limits of 0.098 ppm and 0.327 ppm, respectively. Antioxidant activity was assessed using ABTS and Folin-Ciocalteu assays, showing high antioxidant capacity in both the extracts and pure PFA. Additionally, PFA exhibited cytotoxicity against HeLa and A549 cancer cell lines, without affecting CaCo-2 cells. These findings highlight PFA's potential as a natural therapeutic agent, with selective antioxidant and cytotoxic properties, making it a promising bioactive metabolite found in Bolivian Podocarpus species.

RESUMEN

Este estudio reporta el aislamiento y análisis del bisflavonoide Podocarpus flavona A (PFA) desde extractos etanólicos de especies bolivianas de Podocarpus. La PFA se obtuvo de *P. oleifolius* mediante cromatografía y HPLC, y se caracterizó por espectroscopía RMN. Se detectaron concentraciones de PFA entre 0,37 y 2,20 mg/kg en tres especies, con límites de detección y cuantificación de 0,098 ppm y 0,327 ppm, respectivamente. Los ensayos ABTS y Folin-Ciocalteu revelaron alta actividad antioxidante en los extractos y en el compuesto puro. Además, PFA mostró citotoxicidad contra células HeLa y A549, sin afectar células CaCo-2. Estos hallazgos destacan el potencial terapéutico de PFA como agente natural con propiedades antioxidantes y citotóxicas selectivas, lo que lo convierte en un prometedor metabolito bioactivo presente en especies de *Podocarpus* de Bolivia.

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INTRODUCTION

The Podocarpaceae family is one of the most diverse groups of conifers, both morphologically and ecologically, and is widely distributed across tropical and subtropical forests. Globally, it comprises 20 genera and 219 species, of which 7 genera and 48 species occur in the Americas.[1 2] The genus *Podocarpus* L'Hér. ex Pers. is the largest and most widely distributed genus of the family, with native species present in every continent except Europe.[3] The greatest species diversity is concentrated in tropical and subtropical Asia, South America, and Central America. Many *Podocarpus* species are valued as timber resources, and a considerable number are currently threatened due to deforestation and climate change [3]. In Bolivia are reported eight *Podocarpus* species.[4]

In several regions of the world, *Podocarpus* species are traditionally used in folk medicine.[5]

Different plant parts have been employed to treat ailments such as fevers, asthma, cough, cholera, arthritis, rheumatism, joint pain, and venereal diseases.[6] In some African countries, bark extracts are used as herbal remedies to treat livestock diseases including gall sickness in cattle and distemper in dogs. However, in Bolivia and other areas of South America, the documented use of *Podocarpus* species has been primarily limited to wood for construction and fuel, with little record of traditional medicinal applications [4].

Phytochemical investigations of several *Podocarpus* species have identified nor- and dinorditerpenoid dilactones, along with bisflavonoids of the amentoflavone and hinokiflavone groups, as major constituents and chemotaxonomic markers of the genus.[5 7 8 9 10]

Several bisflavonoids from *Podocarpus* have shown pronounced biological activities. For example, amentoflavone is a potent inhibitor of nucleotide phosphodiesterase and cyclooxygenase and modulates pro-inflammatory gene expression, while 2,3-dihydro-4′,4″-di-O-methylamentoflavone has demonstrated strong tyrosinase inhibitory activity and effects on melanocyte cytotoxicity [11]. Podocarpus flavone A (PFA), another prominent bisflavonoid, has been reported to inhibit STAT3 signaling through JAK2 phosphorylation suppression, resulting in cell cycle arrest and apoptosis in melanoma cells, and is considered a promising inhibitor of melanoma cell proliferation[12].

Additionally, PFA has been identified as an intracellular inhibitor of *Mycobacterium tuberculosis*, showing *in vivo* effectiveness and safety in combination therapies for tuberculosis .[13] PFA has also demonstrated cytotoxic activity against several tumor cell lines (DLD, KB, MCF-7, Hep-2), inducing apoptosis and exhibiting moderate Topoisomerase I inhibitory activity.[14]

Considering that PFA is a bioactive bisflavonoid previously reported in several *Podocarpus* species, this study aimed to investigate its presence in three Bolivian species: *P. oleifolius*, *P. ingensis*, and *P. parlatorei*. Isolating and quantifying PFA from ethanolic leaf extracts and evaluating its antioxidant capacity (ABTS and Folin–Ciocalteu assays) as well as its antiproliferative activity on HeLa, A549, and CaCo-2 cancer cell lines. The results contribute to expanding the chemical and biological knowledge of this relevant bioactive metabolite in native Bolivian *Podocarpus* species.

RESULTS AND DISCUSSION

Isolation and identification of PFA

The leaves of the three Bolivian *Podocarpus* species were extracted by maceration in 96º ethanol for 24 h. A bisflavonoid-enriched extract from *P. oleifolius* was obtained by selective partition of the ethanolic extract with ethyl acetate. Podocarpus flavone A (PFA) was isolated from this enriched fraction by open-column chromatography, followed by preparative HPLC purification of selected fractions. Structural elucidation of the isolated compound was performed using 1D and 2D nuclear magnetic resonance (NMR) spectroscopy. The ^{1}H and ^{13}C NMR spectra (Figure 2) showed predominantly aromatic proton and carbon signals with two carbonyl groups, consistent with a bisflavonoid framework. Signal assignments were confirmed through HSQC and HMBC heteronuclear correlations, and the resulting spectral data were in agreement with previously reported values for PFA [14] confirmed the proposal structure, as shown in Figure 1 and Table 1.

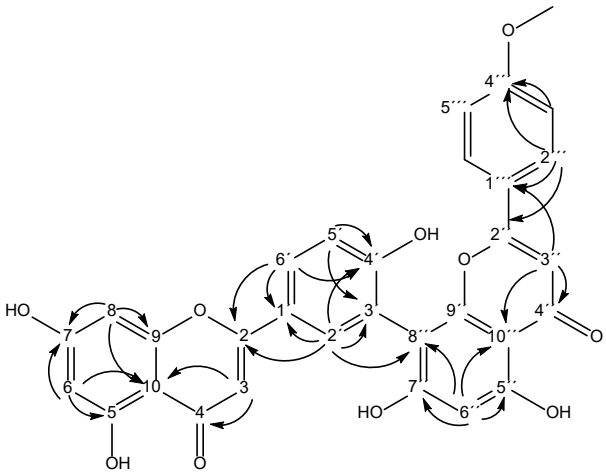

Figure 1. HMBC correlations of Podocarpus flavone A (PFA)

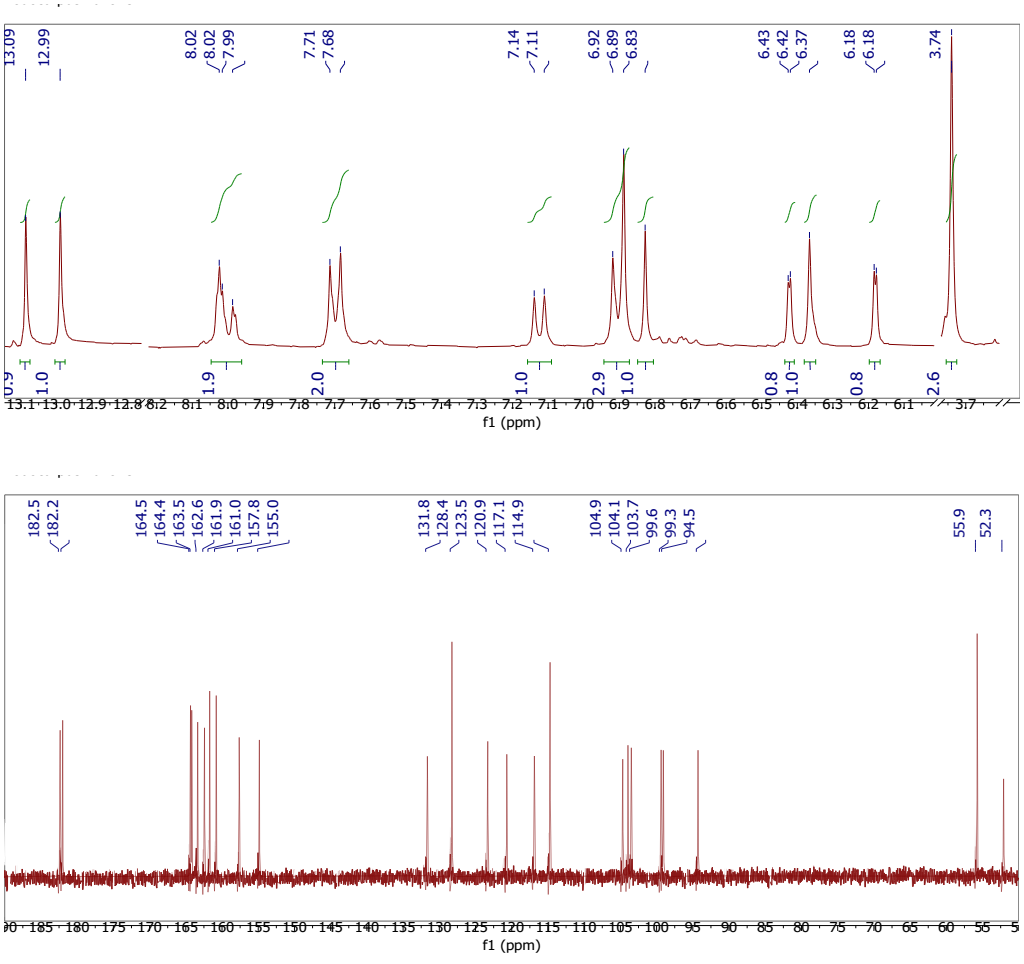

Figure 2. RMN^{1}H and RMN^{13}C spectra of Podocarpus flavone A (PFA)

Table 1. RMN^{1}H and RMN^{13}C data of Podocarpus flavone A (PFA)

No.	δ ^{1}H (*J* in Hz)*	δ ^{13}C Exp*.	δ ^{13}C Bib. [14]
2		164.4 s	164.5 s
3	6.83 s	103.7 d	104.7 d
4		182.2 s	182.6 s
5		162.6 s	162.8 s
6	6.18 *d* (*J* = 1.9)	99.3 d	99.8 d
7		164.5 s	165.6 s
8	6.42 *d* (*J* = 1.9)	94.5 d	94.7 d
9		157.8 s	158.3 s
10		104.9 s	104.8 s
1'		120.9 s	121.5 s
2'	8.02 *d* (*J* = 1.9)	131.8 d	132.4 d
3'		123.5 s	122.2 s
4'		161.9 s	161.1 s
5'	7.13 *d* (*J* = 8.8)	117.1 d	117.0 d
6'	8.00 *dd* (*J* = 8.8, 1.8)	128.4 d	128.1 d
2"		163.5 s	163.9 s
3"	6.89 s	104.1 d	104.0 d
4"		182.5 s	182.9 s
5"		161.9 s	162.1 s
6"	6.36 s	99.6 d	99.7 d
7"		163.5 s	163.7 s
8"		103.7 s	103.9 s
9"		155.0 s	155.6 s
10"		104.9 s	105.2 s
1'"		121.0 s	121.5 s
2'"/6'"	7.70 *d* (*J* = 8.8)	128.4 d	128.2 d
3'"/5'"	6.90 *d* (*J* = 8.3)	114.9 d	114.7 d
4'"		161.0 s	162.6 s
4'"-OCH3	3.59 s	55.9 q	55.2 q

*NMR equipment Bruker 300 MHz ($CDCl_3$)

PFA quantification by HPLC

The quantification results for Podocarpus flavone A (PFA) in the ethanolic extracts of *P. oleifolius*, *P. ingensis*, and *P. parlatorei* was done by an HPLC method where the compound show a peak at t_R = 8.292 min and the typical UV spectrum with two λ_{max} at 270 and 330 nm (Figure 3). The results of quantification are shown in Table 2, which presents the amount of PFA in milligrams per gram of dry plant, showing the biggest content in *P. parlatorei* (2.2 mg/kg dry plant).

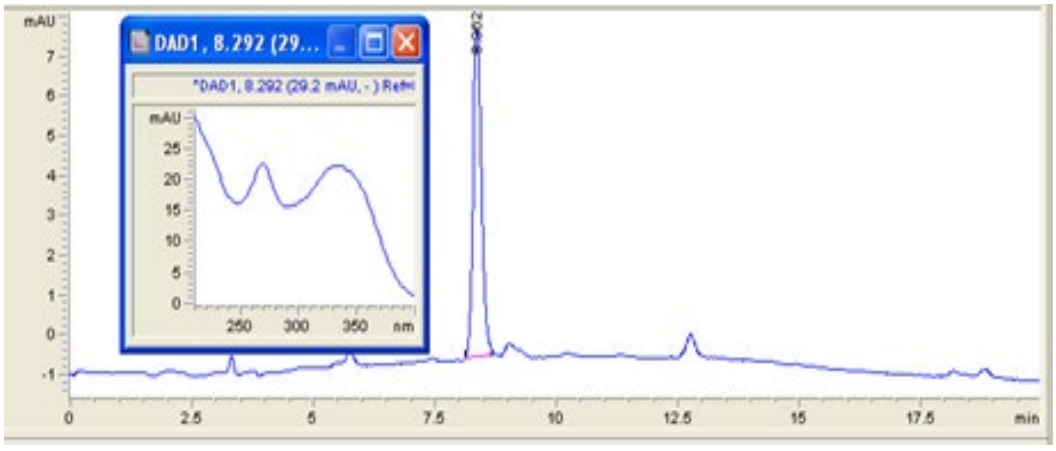

Figure 3. HPLC chromatogram and UV spectrum of Podocarpus flavone A

Table 2. Podocarpus flavone A content in the dry plant of *P. oleifolius*, *P. ingensis*, and *P. parlatorei*

No	Plant species	mg PFA/kg of dry plant
1	*P. oleifolius*	0,58
2	*P. ingensis*	0,37
3	*P. parlatorei*	2,20

Antioxidant activity analysis by ABTS and Folin-Ciocalteau methods

Antioxidant activity determined by the ABTS assay (Table 3) revealed significant differences among samples. Samples 1, 2, and 4 exhibited the highest radical scavenging capacity, indicating a greater abundance of phenolic compounds capable of donating electrons or hydrogen atoms to stabilize the $ABTS^{\bullet+}$ radical. In contrast, sample 3 showed minimal antioxidant response, suggesting a lower presence of active flavonoids or phenolic hydroxyl groups. Dixon's Q-test confirmed the statistical consistency of experimental replicates and validated the reliability of the assay.

Table 3. Results of the ABTS antioxidant capacity in µmol TE/g (Trolox Equivalent per gram of sample)

No	Sample	µmol TE/g of sample Dixon Test
1	EtOH extract of *P. oleifolius*	486,32 ± 0,80
2	EtOH extract of *P. ingensis*	452,94 ± 0,55
3	EtOH extract of *P. parlatorei*	144,34 ± 0,92
4	Podocarpus flavone A	407,87 ± 0,99

Total phenolic content analysis by Folin-Ciocalteau method (Table 4) showed that samples 1, 2, and 4 contained the highest levels of phenolic compounds, reflecting a stronger reducing capacity associated with phenolic hydroxyl groups. Sample 3 displayed a lower phenolic content. The low standard deviations obtained by Dixon test (SD < 1) confirm high precision and reproducibility of the analytical method.

Table 4. Results of Total Phenolic Content by Folin-Ciocalteau analysis in mg GAE/g (Gallic Acid Equivalents per gram of sample)

No	Sample	mg GAE/g of sample Dixon test
1	EtOH extract of *P. oleifolius*	264,23 ± 0,63
2	EtOH extract of *P. ingensis*	212,75 ± 0,43
3	EtOH extract of *P. parlatorei*	77,74 ± 0,234
4	Podocarpus flavone A	210,66 ± 0,86

It is important to note that samples 1 and 2 correspond to ethanolic extracts, whereas sample 4 represents the isolated pure compound. Thus, the antioxidant activity observed in the extracts may be partially attributed to the presence of PFA. However, the comparative values obtained indicate that *P. oleifolius* and *P. ingensis* possess a higher overall content of antioxidant constituents and that PFA is not the primary contributor to the antioxidant capacity of these extracts. This interpretation is supported by the fact that PFA is present at a higher concentration in the ethanolic extract of *P. parlatorei*, yet its extract shows comparatively lower antioxidant activity. Therefore, the antioxidant properties of *P. oleifolius* and *P. ingensis* likely result from a complex mixture of phenolic compounds rather than being driven predominantly by PFA.

Antiproliferative activity evaluation

The evaluation of the antiproliferative capacity of the *Podocarpus oleifolius* EtOH extracts in colon cancer (CaCo-2), cervical cancer (Hela), and lung cancer (A549) cells is shown in Figure 4.

As shown in Figure 4, cervical cancer cells (HeLa) exposed to the *P. oleifolius* ethanolic extract did not exhibit growth inhibition; instead, a dose-dependent increase in cell proliferation was observed beginning at 12.5 µg/mL. In lung cancer cells (A549), the extract did not significantly affect cell proliferation at concentrations between 6.25 and 50 µg/mL, while at 100 µg/mL it induced a slight proliferative response compared to the untreated control. In the case of colon cancer cells (CaCo-2), exposure to the ethanolic extract of *P. oleifolius* did not alter proliferation at

any of the tested concentrations. These results indicate that the ethanolic extract of *P. oleifolius* does not exhibit antiproliferative activity against the evaluated cancer cell lines and, at higher concentrations, may even promote cell growth in HeLa and A549 cells.

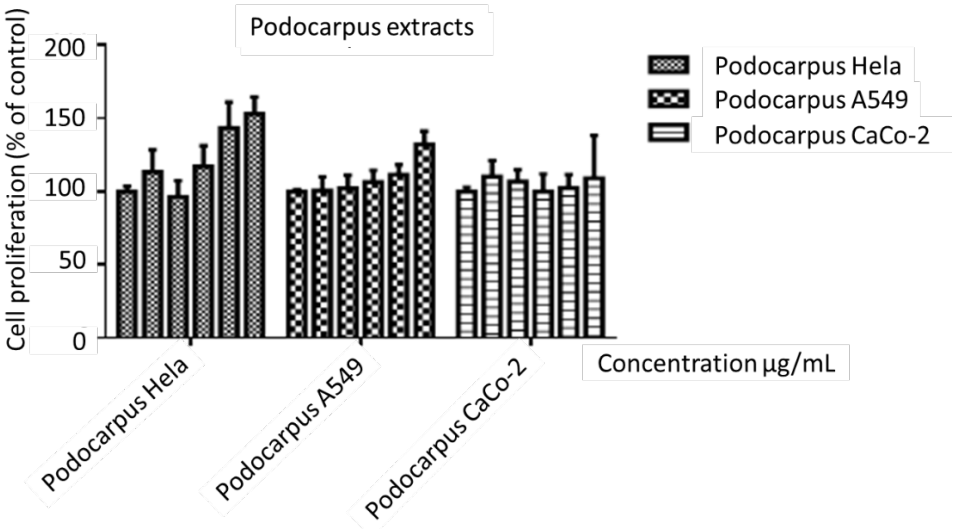

Figure 4. *Cytotoxic activity of Podocarpus oleifolius EtOH extract in three cancer cell lines.*

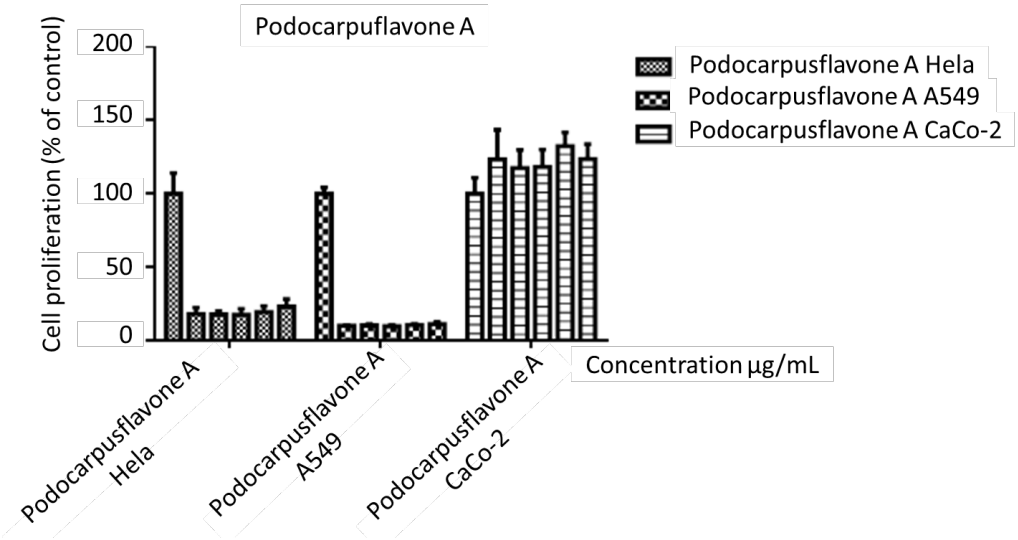

Figure 5. *Cytotoxic activity of Podocarpus flavone A (PFA) in three cancer cell lines.*

As shown in Figure 5, Podocarpus flavone A (PFA) exhibited strong cytotoxic activity against cervical cancer (HeLa) and lung cancer (A549) cells. In both cell lines, the inhibitory response remained consistent across the tested concentrations, indicating a dose-independent effect. In HeLa cells, PFA reduced cell proliferation by 82–77%, while in A549 cells the inhibition ranged from 90–88%, demonstrating a greater cytotoxic effect on lung cancer cells. In contrast, the proliferation of colon cancer cells (CaCo-2) was not significantly affected by PFA at any of the tested concentrations. These results suggest a selective antiproliferative effect of PFA, with higher cytotoxic sensitivity observed in A549 cells compared to HeLa cells, and no evident activity against CaCo-2 cells.

EXPERIMENTAL

Apparatus and chemicals

Nuclear Magnetic Resonance spectra were recorded on NMR equipment, of 300 MHz (Bruker) using $CDCl_3$ and DMSO d6 (Sigma–Aldrich) as solvents. HPLC chromatograms were obtained in Agilent 1100 Series equipment with a quaternary pump, a diode array detector, DAD, and a RP–Silica C18 250 * 4.6 mm E10174 column. All solvents used were HPLC grade and the ultra-pure water was obtained by an ultrafiltration equipment (Satoorius Stedi m brand). The extractions and separations were performed with commercial solvents previously purified by distillation. The fractionations were carried out using absorption chromatography columns on Silica gel 60 (63–200 mesh) and Silica gel 60 G (Merck). The antioxidant assays were carried out using a UV/Vis Bio Tek power wave TM XS2 equipment using Trolox and Gallic Acid (Sigma-Aldrich) as standards.

Plant material

Aerial parts of three Bolivian species from genus *Podocarpus* were collected for this study: *P. oleifolius*, P. *ingensis* and *P. parlatorei*. The first two, *Podocarpus oleifolius* (48°07′09′′S; 54°25′16′′W) and *P. ingensis* (34°27′41′′S, 40°19′37′′W) were collected on Uchumachi hill, located in the Municipality of Coroico, Nor Yungas Province of La Paz, Bolivia, while *Podocarpus parlatorei* was collected on the Sucre-Padilla Highway (20°08′03′′S; 64°21′29′′W). All species were identified by Lic. Arely Palabral, who is part of the National Herbarium of Bolivia LPB, where samples of the collected specimens are located.

Extraction of bisflavonoids

The air-dried and powdered plant material was extracted with 96º EtOH during 24h at room temperature. The obtained EtOH extract was dried by rota-evaporation and then submitted to a selective extraction with EtOAc, for two times, giving a fraction enriched in phenolic compounds, mainly bisflavonoids, controlled by TLC.

Isolation of Podocarpus flavone A

Podocarpus flavone A was isolated from a bisflavonoid-enriched extract of *P. oleifolius* using a fractionation and purification method controlled by TLC. The process included initial separation by column chromatography with silica gel as the stationary phase, followed by purification of the compound by preparative high-performance liquid chromatography (HPLCp). The structural identification of the isolated compound was confirmed by 1D and 2D nuclear magnetic resonance (NMR) techniques (Table 1).

Quantification of Podocarpus flavone A

To quantify Podocarpus flavone A (PFA), an Agilent 1100 Series HPLC system was used at 30°C, employing a solvent gradient system as the mobile phase: Solvent B = Methanol; Solvent A = 0.1% formic acid in water. The gradient used was 75% B and 25% A at 0 minutes, increasing to 100% B after 20 minutes, at a constant flow rate of 0.8 mL/min throughout the gradient. For the quantification of PFA present in the dry material of all collected species, a calibration curve was prepared by preparing concentrations of the compound at 5, 10, 15, and 20 ppm. Measurements were taken at 270 nm, t_R = 8.292 min, yielding the calibration curve equation y = 95.1x + 115.9, which shows a high correlation coefficient R^2 = 0.9985 (Figure 6). From this curve, the PFA concentrations in the different extracts were obtained (Table 2). Additionally, the LOD of 0.098 ppm and the LOQ of 0.327 ppm were determined for the quantification method.

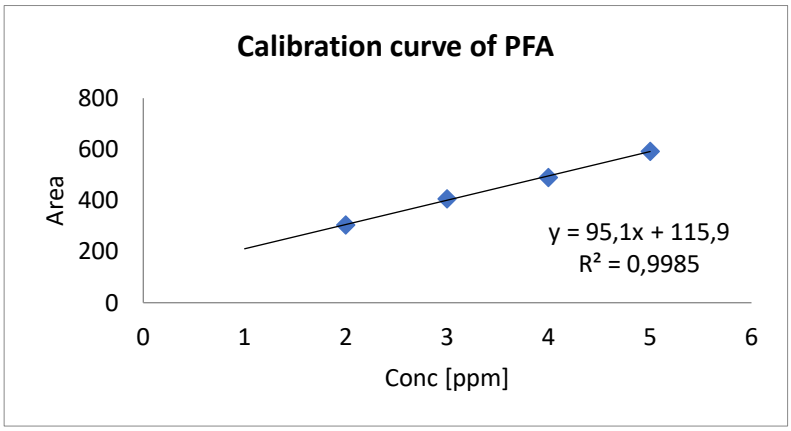

Figure 6. Calibration curve of Podocarpus flavone A (PFA) by HPLC.

Assays of antioxidant activities

ABTS method with respect to TROLOX

The scavenging activity against the $ABTS^{\bullet+}$ cation radical (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) was determined as follows: the $ABTS^{\bullet+}$ cation radical was generated by reacting ABTS (7 mM) with persulfate (2.42 mM) and stored in the dark at room temperature for 12–16 hours. On the day of the analysis, the $ABTS^{\bullet+}$ solution was diluted with ethanol to an absorbance of 0.70 (± 0.02) at 734 nm. Fractions were prepared by dissolving 30.0 mg of each in 5 mL of methanol, and PFA was prepared by dissolving 4.0 mg in 5 mL of methanol. For activity measurement, 100 µL of the sample was vortexed with 1000 µL of $ABTS^{\bullet+}$ solution, and the absorbance was recorded at 734 nm.

For the determination of antioxidant activity based on Trolox, a standard curve of the reference antioxidant, Trolox, was constructed at different concentrations: 0, 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 µM, under the same conditions mentioned above. The generated curve (Figure 7) follows the equation y = 0.8916x – 1.6595 (R^2 = 0.9992); the correlation coefficient indicates good linearity.

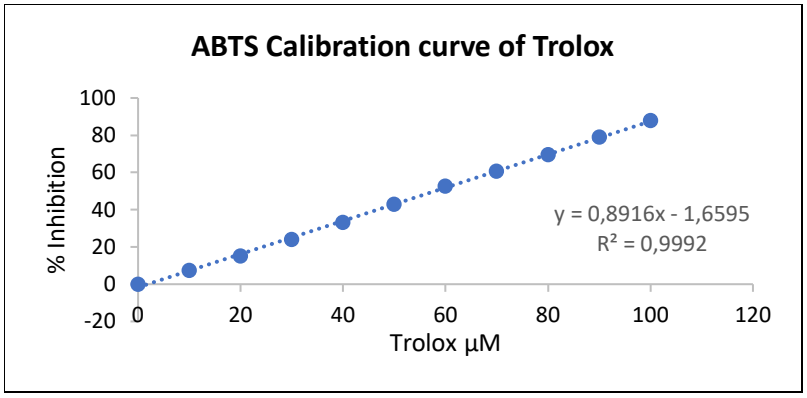

Figure 7. Calibration curve of Trolox for ABTS method.

Quantification of total phenolic compounds by Folin-Ciocalteau relative to gallic acid

The total phenolic content was determined using the Folin–Ciocalteu method, for which 500 µL of Folin–Ciocalteu reagent (1:10 v/v), 400 µL of 7.5% (w/v) sodium carbonate, and 90 µL of distilled water were used. This mixture was vortexed and incubated for 15 min at 45 °C, and the absorbance was measured at 765 nm. The analyzes were performed in triplicate, and the results were expressed as mean values with their standard deviation (SD). For the determination of total phenolic content, a calibration curve was constructed using gallic acid at different concentrations: 10, 20, 30, 40, 50, 60, 70, and 80 mg/mL, under the same conditions mentioned above. The calibration curve (Figure 8) follows the equation y = 0.00121x + 0.0084 (R^2 = 0.9997); the correlation coefficient indicates good linearity.

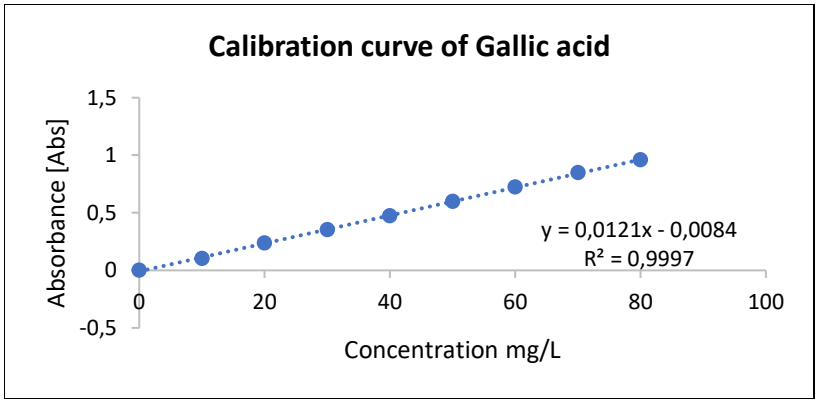

Figure 8. Calibration curve of Gallic acid for Folin-Ciocalteau method.

Assays of antiproliferative activity

For cell culture, the protocol described by Iturri and Rodrigo (2018).[15] was followed, in which the A549, HeLa, and CaCo-2 cell lines were cultured in DMEM supplemented with 10% (v/v) fetal bovine serum, L-glutamine, and antibiotics at 37°C in a humidified atmosphere with 5% CO_2. To obtain a sufficient number of cells, each cell line was cultured to approximately 90% confluency and detached with 0.05% trypsin/0.02% EDTA.

For the MTT assay, 1×10^4 cells per well were seeded into 96-well plates. Twenty-four hours after incubation in CO_2, the compounds were added at the different concentrations under study. The cells were cultured for 48 hours, 20 µL of an MTT solution (5 mg/mL in PBS; Sigma-Aldrich) was added to each well, and the plates were incubated for 1 hour. The formazan produced by the reduction of live cells was dissolved in 100 µL of 100% DMSO. The plate was shaken for 10 min at room temperature to dissolve the precipitate. Absorbance was measured at 540 nm using an ELISA reader. Dose-response curves and % of cell proliferation values were calculated using GraphPad Prism software. The reported values represent the mean of two assays; each performed with three replicates.

CONCLUSIONS

This study enabled the isolation, structural characterization, and biological evaluation of the bisflavonoid Podocarpus flavone A (PFA) from *Podocarpus* species collected in the La Paz and Chuquisaca departments of Bolivia. PFA was isolated from a bisflavonoid-enriched extract, and its structure was confirmed through 1D and 2D NMR analyses, with signal assignments consistent with previously reported data [14].

A sensitive and reproducible HPLC method was developed for the quantification of PFA, with a limit of detection (LOD) of 0.098 ppm and a limit of quantification (LOQ) of 0.327 ppm. Application of this method revealed that PFA is present in varying concentrations across the dry plant material of *P. oleifolius* (0.58 mg/kg), *P. ingensis* (0.37 mg/kg), and *P. parlatorei* (2.20 mg/kg), the latter containing the highest level of the compound.

Antioxidant analyses demonstrated that the ethanolic extracts of *P. oleifolius* and *P. ingensis* exhibited greater antioxidant capacity than the extract of *P. parlatorei*. Although PFA displayed strong antioxidant activity, the comparative results indicate that PFA is not the primary contributor to the antioxidant potential of the extracts. Instead, these activities are likely due to a broader mixture of phenolic constituents present in *P. oleifolius* and *P. ingensis.*

In antiproliferative assays, PFA exhibited marked cytotoxicity against cervical cancer (HeLa) and lung cancer (A549) cell lines, while showing no significant effect on colon cancer (CaCo-2) cells. In contrast, the crude extracts did not display inhibitory activity, indicating that the cytotoxic effect is specifically associated with the purified bisflavonoid.

Overall, these findings confirm that Podocarpus flavone A is a bioactive metabolite with selective cytotoxic and antioxidant properties, and highlight its relevance as a natural compound of pharmacological interest in Bolivian *Podocarpus* species.

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REFERENCES

[1] Page, C.N. 1990. Podocarpaceae. pp. 332-337. En: Kubitzki, K., Kramer, K.U. and Green, P.S. (Editors). The families and genera of vascular plants. Pteridophytes and Gymnosperms. Springer–Verlag, New York.
[2]Khan, R., Hill, R. S., Liu, J., Biffin, E. *Plants*, 2023, **12**, 1171. https://doi.org/10.3390/plants12051171.
[3] Mill, R. R., *Journal of Botany*, 2014, **71**, 309.
[4] Killeen, T. J., Garcia E, E., & Beck, S. G. (1993). Guía de árboles de Bolivia
[5] Abdillahi, H. S., Stafford, G. I., Finnie, J. F., & Van Staden, J., *South African Journal of Botany*, 2010, **76**, 1.
[6] Duke, J. A., & Ayensu, E. S. (1985). Medicinal Plants of China. Algonac, MI: Reference Publications; Riley, M. (1994). Māori Healing and Herbal: New Zealand Ethnobotanical Sourcebook. Paraparaumu, New Zealand: Viking Seven Seas.
[7] Ito, S., & Kodama, M., *Heterocycles*, 1976, **4**, 595–624. doi:10.3987/R-1976-03-0595.

[8] Roy, S. K., Qasim, M. A., Kamil, M., & Ilyas, M. (1987). Bisflavones from the genus *Podocarpus*. *Phytochemistry*, 26, 1985–1987..
[9] Abdillahi, H. S., Stafford, G. I., Finnie, J. F., & Van Staden, J., *South African Journal of Botany*, 2010, **76**, 1.
[10] Kim, C., Le, D., Lee, M., *Molecules*, 2021, **26**, 4326.
[11] Cheng, K.-T., Hsu, F.-L., Chen, S.-H., Hsieh, P.-K., Huang, H.-S., Lee, C.-K., & Lee, M.-H., *Chemical & Pharmaceutical Bulletin*, 2007, **55**, 757.
[12] Meng, H., Pang, Y., Liu, G., Luo, Z., Tan, H., & Liu, X., *Journal of Dermatological Science*, 2020, **100**, 201.
[13] Araujo, M. H. d., Muñoz Sánchez, S., Simão, T. L. B. V., Nowik, N., Antunes, S. S., Pinto, S. C., Sorze, D., Boldrin, F., Manganelli, R., Correia Romeiro, N., Lasunskaia, E. B., Verbeek, F. J., Spaink, H. P., Muzitano, M. F., *Pharmaceuticals*, 2024, **17**, 1560.
[14] Yeh, P.-H., Shieh, Y.-D., Hsu, L.-C., Kuo-Yang, L.-M., Lin, J.-H., Liaw, C.-C., Kuo, Y.-H., *Journal of Traditional and Complementary Medicine*, 2012, **2**, 220.
[15] Iturri, J. P., Rodrigo, G. D., *Revista Boliviana de Química*, 2018, **35**, 6.