

Pharmacological Properties and Bioactive Compounds of *Araucaria angustifolia*: A Comprehensive Review

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Araucaria angustifolia (Bertol.) Steud, a member of the Araucariaceae family, is originally found in the southeastern and southern regions of Brazil, extending to Misiones in Argentina. This evergreen tree is predominantly found in the subtropical biome, this tree is valued for its ecological benefits, medicinal properties, and use as a food source. Extensive research has been conducted on its chemical composition, alongside its biological and pharmacological attributes. Findings indicate that various components of the tree, including its bark, knots, needles (or leaves), seeds, and bracts (which are sterile seeds), are rich in active compounds and demonstrate a variety of biological effects. These include strong antioxidant, antiviral, hepatoprotectivity, wound healing activity, anti-inflammatory and antidiabetic properties, along with neuroprotective effects. Historically, different parts of *A. angustifolia* have been utilized in traditional medicine to address numerous health issues, like shingles, respiratory illnesses, and diseases transmitted via sexual contact and various types of wounds. *Araucaria angustifolia* is gaining attention in industries like cosmetics, pharmaceuticals, food, and sustainable materials. In cosmetics, its skin-healing and anti-aging properties are being used in skincare products. The seeds are also being incorporated into functional foods, while the tree's wood is valued in eco-friendly construction and bio-based materials. In light of this context, this review intends to summarize the existing knowledge regarding the chemical and biological properties of *A. angustifolia*, while also offering new insights and valuable information to guide future research on this extraordinary plant.

Keywords: *Araucaria angustifolia*; Araucariaceae; Pharmacological activity; Chemical composition; Traditional medicine.

Araucaria is a remarkable tree belonging to the Araucariaceae family, celebrated for its impressive lifespan and the cones it produces. This tree thrives naturally from the southeastern

and southern parts of Brazil all the way down to the Misiones region in Argentina.¹ South America is home to two remarkable species: *Araucaria angustifolia* and *Araucaria araucana*.

A. angustifolia primarily grows in the southern and southeastern regions of Brazil and also occurs in northeastern Argentina.² In contrast, *A. Araucana* is found exclusively in the mountainous areas of southern Argentina and Chile.³ Among these, *Araucaria angustifolia* (Bert.) O. Kuntze, also known as Brazilian pine, sometimes known as Paraná pine or simply “Araucaria,” is the sole indigenous gymnosperm found in Brazil’s Atlantic Forest.

This species is very important to the community, economy, and culture.⁴ Historically, the native woodlands of *A. angustifolia* once spanned approximately 185,000 km² in Brazil.⁵⁻⁶ However, due to extensive timber harvesting, the population has been severely reduced, with only about 2–4% of the original forests remaining.⁷⁻⁸ Currently, most stands of *A. angustifolia* are found in the southern Brazilian states of Paraná, Santa Catarina, and Rio Grande do Sul, with smaller groups located in the southeastern states of São Paulo, Minas Gerais, and Rio de Janeiro.

Currently, *A. angustifolia* is listed as vulnerable to extinction under Brazilian law.⁹ This status has led to increased efforts from government and environmental agencies to promote the cultivation and conservation of the species.¹⁰

The consumable seed of *A. angustifolia* is a crucial food source for both humans and various animal species, particularly rodents. Historically, the indigenous peoples of Southern Brazil, including the Caiçara and Caingang, have relied on seed as a staple food, especially during the winter months. When prepared as a cooked dish or in flour form, it often becomes a key survival food due to its high nutritional content.¹¹

Morphology

Araucaria, a large genus, comprises evergreen coniferous trees with an average height of 98-260 feet (30-80 meters), having a massive and erect stem. This genus is characterized by horizontally growing and whorled branches, which are covered with needle-like and leathery leaves. Two types of leaves are present in these species. Initially, lanceolate and narrow leaves barely overlap each other, and later develop extremely broad and flat leaves that widely overlap each other. These species’ trees are typically dioecious, having a female (seed) and male (pollen) cones found on separate trees, however, some trees are monoecious

as well as change sex with time. The globose female cones enclose several large edible seeds on the top of the tree, the size can vary from species to species, i.e., 2.8 to 9.8 inches (7-25 centimeters) in diameter. Furthermore, the male cones are smaller in size, i.e., 1.6 to 3.9 inches (4-10 centimeters), with a long and narrow to a broad cylindrical shape, 0.6-to-2.0 inches (1.5 to 5.0 centimeters) broad.¹²

Significance

Angustifolia plays a significant role in indigenous Brazilian healing practices. Various components of the tree are used for their therapeutic properties. For instance, tinctures made from the tree’s nodes are traditionally utilized to treat rheumatism, both orally and topically. Infusions of these nodes are also used to address Sexually transmitted infections and kidney disorders. The bark is prepared in infusions to help relieve muscle tension and varicose veins, while a syrup made from the resin is employed to treat infections of the respiratory system. Additionally, Infusions of leaves serve as emollients and antiseptics and are employed to combat Infections of the lungs, rheumatism, tiredness, and anemia.¹³ Dyes from the tree are used for treating wounds and herpes.¹⁴⁻¹⁵ The resin of *Araucaria araucana* has been employed traditionally for the cure of ulcers, and contusions, in addition, to healing cicatrization and skin wounds by the peoples of Amerindian Mapuche situated in Southern Chile and Argentina.¹⁶⁻¹⁷ The seeds of *A. angustifolia* can be utilized in cuisine and culinary products, while the husk can be used in local handmade crafts.¹⁸⁻¹⁹

Bioactivities

Researchers have successfully isolated several compounds from this resin, including (+)-pinoresinol and its monomethyl and dimethyl ethers (notably, pinoresinol monomethyl ether is a newly identified natural product). Additionally, (+)-isolariciresinol, (-)-secoisolariciresinol, and hinokiresinol were isolated. The resin also contains minor quantities of fatty acids, esters, and various sterols such as free sitosterol and campesterol.²⁰ A study in Japan identified two lignans from *A. angustifolia*, 2,3-bis-(p-hydroxyphenyl)-2-cyclopentene-1-one, cryptoresinol along with 4-42-dihydroxychalcone.²¹ Furthermore, a polypeptide named 327 has been identified as a vicilin-like storage protein in *A. angustifolia*.²² The seeds of this plant store starch as their primary storage

compound.²³ Notable bioflavonoids isolated from *A. angustifolia* include bilobetin (4), II-7-O-methylrobustaf flavone and cupressuflavone.²⁴

Researchers discovered two naturally occurring afzelechin derivatives in *A. angustifolia*'s dead bark: epiafzelechin and protocatechuic acid and p-hydroxybenzoate. Both compounds have demonstrated significant antioxidant properties.²⁵ Research has shown that a leaf extract from *A. angustifolia*, rich in biflavonoids, can effectively shield DNA from damage induced by ultraviolet radiation and prevent lipid peroxidation.²⁶⁻²⁷ The leaf of *A. angustifolia* contains six key biflavonoids, including amentoflavone, ginkgetin, di-O-methylated amentoflavone, tri-O-methylated amentoflavone, and tetra-O-methylated amentoflavone.

Lariciresinol-4-methyl ether and Secoisolariciresinol monomethyl ether were obtained from the wood knots of fallen *Araucaria angustifolia* trees. Spectral analysis allowed for the precise determination of the hydroxyl group's position in these compounds. Additionally, The ¹³C nuclear magnetic resonance (NMR) spectra for several phenyltetralin lignans, including galcadin, galbulin, cyclogalgravin and isogalcadin were identified. The assignments of these peaks were on basis of methyl shifts noticed in cyclogalgravin.²⁸

Additionally, the diterpene trans-communic acid was extracted from the roots of young seedlings. In the adult stems, a range of compounds was found, including benzaldehydes such as vanillin, p-hydroxybenzaldehyde and coniferaldehyde; lignans like eudesmin, eudesmin lariciresinol, and pinoresinol and isoflavones including cabrevine and irisolidone.²⁹

The proximal composition of *A. angustifolia* seeds includes 43.70% moisture, 1.50% ash, 3.42% crude protein, 1.67% total lipids, 1.29% total fibres, and 48.42% other sugars. The subcritical n-propane extraction method produced elevated levels of essential fatty acids and total tocopherols and total phytosterols, with yields and compositions comparable to those obtained using the Soxhlet method. However, the Soxhlet-extracted oil was less stable against lipid oxidation. The key fatty acids identified were linoleic, oleic, and palmitic acids, and the Sovová model provided a good fit for the experimental data.³⁰ The proteins

AaTI-1 (36.955 kDa) and AaTI-2 (35.450 kDa) from *Araucaria angustifolia* seeds were identified as trypsin inhibitors. They specifically inhibit plasmin (Kiapp 7.0 iM) and trypsin (Kiapp 85 nM) without affecting chymotrypsin or other coagulation enzymes.³¹

Pharmacological activities

Gastroprotective and Cytotoxicity

The resin of the *Araucaria araucana* tree, native to southern Chile and Argentina, has been traditionally used by the Mapuche people as a natural remedy to treat ulcers. This resin has demonstrated protective effects on the stomach lining in animal studies. To explore these properties further, researchers isolated and identified various compounds from the resin and tested their effectiveness in protecting the stomach and their potential toxicity. Chile sample was collected from resin, and eleven diterpenes were isolated, including ten labdane-type diterpenes and one pimarane. Additionally, the labdane analogs 15,19-diacetoxylabd-8(17)-en and 15-acetoxylabd-8(17)-en-19-ol were identified as natural products for the first time.³²

Additionally, six diterpenes previously found in other plants were newly mentioned from the *A. araucana* resin. The structures of all these compounds were determined using spectroscopy. To evaluate their gastroprotective effects,²⁴ diterpenes each isolated or synthesized in quantities exceeding 10 mg, were tested in a mouse model with ulcers induced by ethanol and hydrochloric acid, at a dosage of 100 mg/kg. The compounds 15-acetoxylabd-8(17)-en-19-oic acid methyl ester, 15-hydroxyimbricatolal, 15-acetoxylimbricatolal and 15-acetoxy-19-labdanoic acid showed the highest levels of gastroprotection, matching the efficacy of 20 mg/kg of the standard drug lansoprazole.³³

In terms of cytotoxicity, 30 diterpenes and lansoprazole were tested using the neutral red uptake assay against human lung fibroblasts (MRC-5) and the human gastric epithelial cell line AGS. The results showed that cell viability was inhibited in a concentration-dependent fashion values of IC₅₀ values ranging from 27 to over 1000 iM. The study also explored how the cytotoxicity of these compounds correlates with their lipophilicity.³⁴

Antidepressant activity

The impact of the lectin extracted from

A. angustifolia on the central nervous system in mice was explored, specifically examining potential impacts on seizures and locomotor behavior. The experiment involved male Swiss mice that were administered various treatments through intraperitoneal injection, including saline (as a control), three different doses of diazepam (1 mg/kg), flumazenil (1 mg/kg), and lectin (0.1, 1, and 10 mg/kg). The effects of these substances were evaluated using seizure models induced by pentylentetrazole and strychnine, as well as an assessment of locomotor activity using the open field test. At the highest dosage of lectin, there was a significant increase in the time until death in mice subjected to both pentylentetrazole and strychnine in comparison to the control group.

However, the impact was not observed in the pilocarpine seizure model. Locomotor activity was reduced at all lectin dosages. Notably, these reductions in movement were reversed upon pretreatment with flumazenil. The findings suggest that the lectin from *A. angustifolia* exhibits protective effects against seizures induced by pentylentetrazole and strychnine, indicating a possible interaction with the GABAergic and glycinergic neurotransmitter systems. Furthermore, the reduction in locomotor activity points to a central depressant effect, likely mediated through GABAergic mechanisms, which could be reversed with flumazenil³⁵

Antiviral activity

The traditional use of *A. angustifolia* for treating herpes is substantiated by recent research investigating its antiherpes activity. Researchers extracted a hydroethanolic extract (HE) from the leaves and performed subsequent liquid-liquid extractions using different polarity solvents. The cytotoxicity of the HE and its fractions was evaluated, along with their antiviral efficacy against Herpes Simplex Virus type 1 (HSV-1) using the MTT assay. The n-butanol (NB) and ethyl acetate (EA) fractions demonstrated particularly significant antiviral effects. Further fractionation of these fractions yielded 22 subfractions, 14 of which displayed notable activity, with the most effective being subfraction NB1-4. This subfraction exhibited a high selectivity index and was rich in bioactive compounds like biflavonoids and proanthocyanidins including II-7-O-methyl-robusaflavone, bilobetin and cypressuflavone

which are associated with various health benefits. The study's findings lend credible support to the therapeutic potential of *A. angustifolia*, highlighting its promise as a natural antiviral agent and reaffirming the importance of integrating traditional knowledge with scientific inquiry to explore new avenues for herbal medicine.³⁶

Wound-healing activity

An eco-friendly method was explored to utilize the coat of *Araucaria angustifolia* by transforming it into a nanosuspension. This nanosuspension of the seed coat (PCN) was integrated into a Lanette base at 0.5%, 1.0%, 1.5%, and 2.0% concentrations. The study evaluated formulations along with their physicochemical properties, including pH, rheological properties, spreadability, cytotoxic effects, and wound healing capabilities. The findings indicated that adding PCN resulted in a Milky and light brown appearance and lowered the pH while improving spreadability in comparison to formulations that serve as controls. Analysis of its rheology revealed that the PCN Lotions exhibited pseudoplastic characteristics.

Typical of strong gels, the formulations maintained stability during thermomechanical testing. Additionally, cytotoxicity assessments indicated that the formulations were non-toxic at concentrations below 0.05 mg/mL. Regarding wound healing, *in vitro* assays showed that the formulations with 1.5% and 2.0% PCN achieved complete wound closure within 72 hours.³⁷

Antioxidant activity

Two methods for extracting bioactive substances found in the seed coat of *Araucaria angustifolia* specifically using infusion and a shaker method, were investigated, while comparing both to the Soxhlet extraction technique. The primary objective was to evaluate their potential applications in dairy products and to provide a feasible option for small and medium-sized agribusinesses. The results indicated that the shaker method was more efficient than infusion but less effective than Soxhlet regarding extraction yield. Notably, the extract obtained via the shaker method exhibited lower toxicity in *Artemia salina* testing compared to the other methods. Consequently, this extract was chosen for incorporation into yogurt. The addition of the extract significantly enhanced the phenolic content by 100%, increased

flavonoid levels by 19%, and boosted antioxidant activity, as evidenced by the ABTS assay (17%) and DPPH assay (116%). Furthermore, the yogurt demonstrated good stability throughout 30 days of shelf-life testing and maintained low toxicity levels. Interestingly, simulated *in vitro* digestion improved the bioavailability of key bioactive compounds, including phenolics and flavonoids. These findings suggest that the bioactive extract can be effectively utilized as a functional ingredient in dairy products without altering their taste. This approach also promotes a sustainable use of what is typically considered a waste product while adding nutritional value.³⁸

The antioxidant properties of the crude extract, its major components, and isolated substances from the dead bark of *A. angustifolia* have been studied. This tree species, part of the endangered Mixed Ombrophile Forest, naturally sheds its dead bark, showing protective effects against oxidative stress caused by hydrogen peroxide in cell cultures. Our research delves into the antioxidant activity of the hydroalcoholic extract, with particular emphasis on several chemicals identified in the ethyl acetate fraction. Notably, we report, for the first time, the extraction of two afzelechin derivatives from this extract. Among the compounds analyzed, epiafzelechin protocatechuate exhibited exceptionally strong antioxidant activity, achieving an IC₅₀ value of 0.7 μ M in a DPPH assay. Furthermore, in assays evaluating lipid peroxidation caused by UV and ascorbate free radicals, this compound showed IC₅₀ values of 35 μ M and 21 μ M, respectively. Quercetin, a widely recognized antioxidant, also demonstrated significant activity, underscoring the considerable antioxidant potential of the extract and its isolated compounds.³⁹

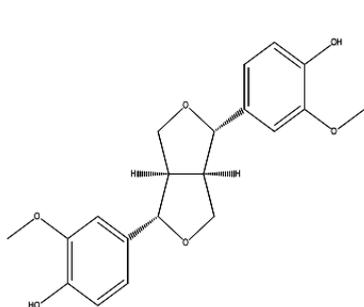
Angustifolia (Bertol.) Kuntze seed is traditionally cooked before consumption, leading to the discarding of seed coatings. However, both the coatings and the cooking water contain phenolic substances that can potentially enhance the mechanical properties and antioxidant qualities of films. This study aimed to extract these polyphenolic compounds from *Angustifolia* seed coats and apply them to zein films. The extracts' composition, extraction yield, and antioxidant properties were evaluated using ABTS, DPPH, and FRAP assays. Results indicated that the

hydroethanolic extract was rich in (+)-catechin and an epicatechin dimer, while protocatechuic acid was dominant in both the cooking water and the ethanolic extracts. Interestingly, the glass transition temperature of zein remained unaffected by the incorporation of the extracts. Furthermore, the presence of extracts contributed to smoother film surfaces and significantly improved the mechanical properties of the zein films. Notably, there was a three-fold enhancement in tensile strength, increasing from 5.80 MPa to 17.65 MPa, alongside a two-fold improvement in elongation at break.⁴⁰

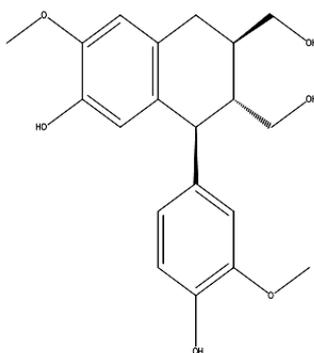
The potential of using extract of seeds from *A. angustifolia* to create biodegradable packaging materials enriched with natural antioxidants was studied. Using HPLC-DAD-ESI/MSⁿ, eight phenolic compounds were identified in the extract, with (+)-catechin and (-)-epicatechin being the most prominent. The extract was incorporated into TPS/PBAT films through a blown extrusion process, and various properties were assessed. The study found that the phenolic compounds from the extract reduced the crystallinity of the films and increased the starch glass transition temperature from 52.5°C to 58.2°C. The film's opacity increased from 0.50 to 0.75, and the water solubility rose from 5.2% to 8.4%. While the film's water vapor permeability remained unchanged, the incorporation of the extract altered the contact angles with water and diiodomethane, indicating changes in surface properties. Most notably, the "free radical scavenging capacity of the films was significantly enhanced by the seed extract. The DPPH assay revealed that the films containing the extract had an inhibition rate of 85%, compared to 50% for films without the extract. These results underscore the extract's effectiveness in improving



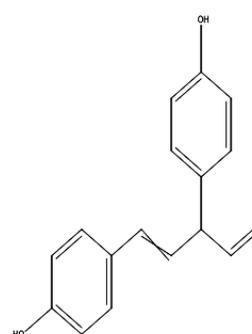
Fig. 1. *Araucaria Angustifolia*



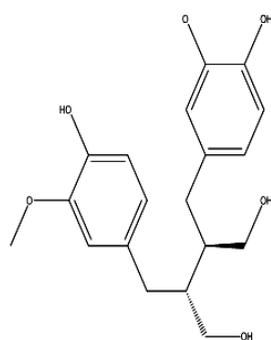
Pinoresinol



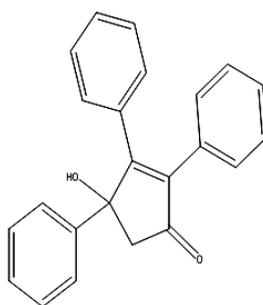
Isolariciresinol



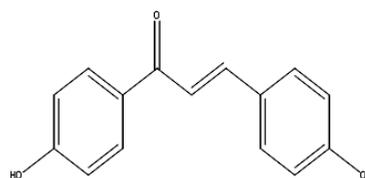
Hinokiresinol



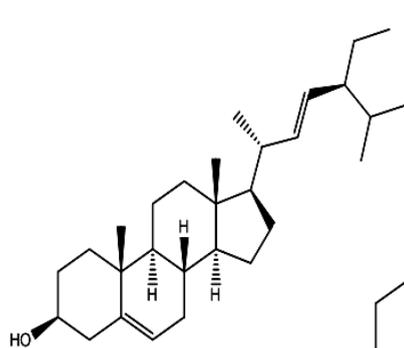
Secoisolariciresinol



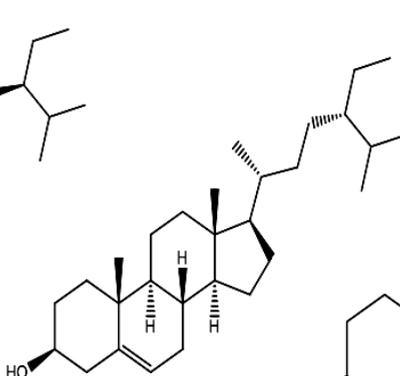
4-Hydroxy-2,3,4-triphenylcyclopent-2-en-1-one



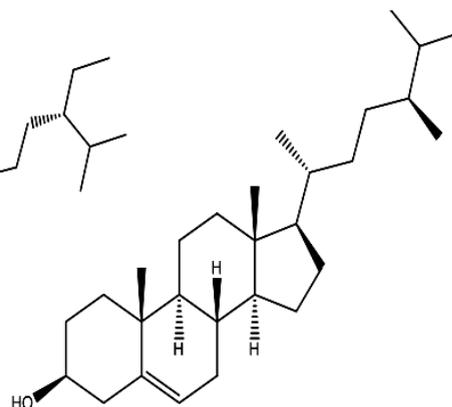
(E)-1,3-Bis(4-hydroxyphenyl)prop-2-en-1-one



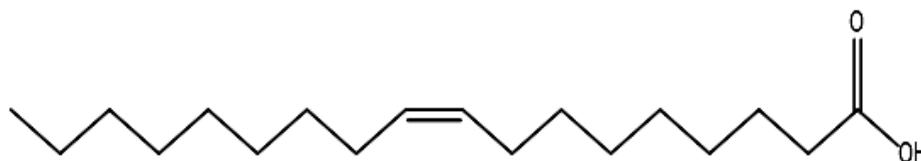
Stigmasterol



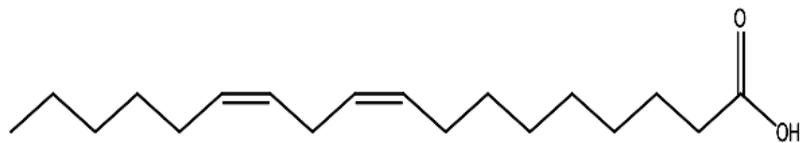
Sitosterol



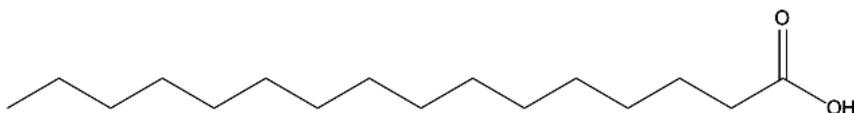
Campesterol



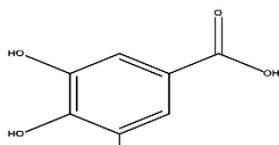
Oleic acid



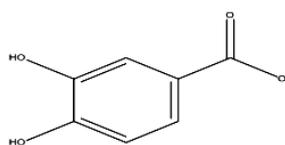
Linoleic acid



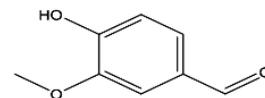
Palmitic acid



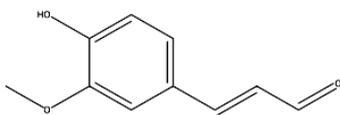
Gallic acid



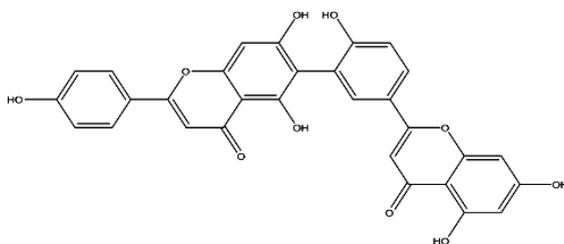
Protocatechuic acid



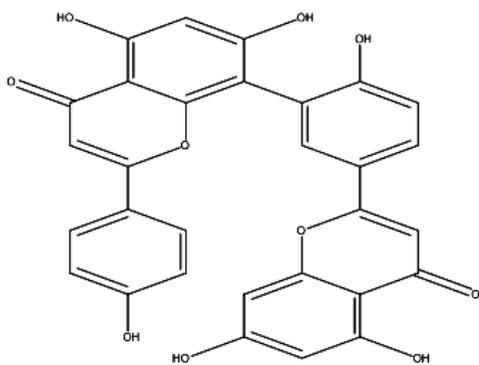
4-hydroxy-3-methoxybenzaldehyde



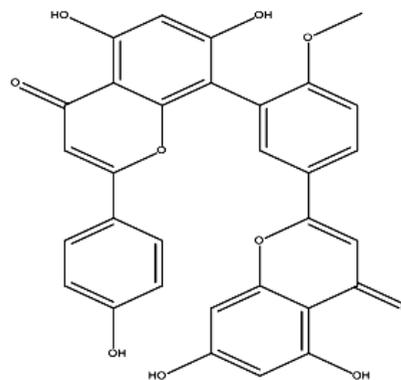
Coniferyl aldehyde



Robustaflavone



Amentoflavone



Bilobetin

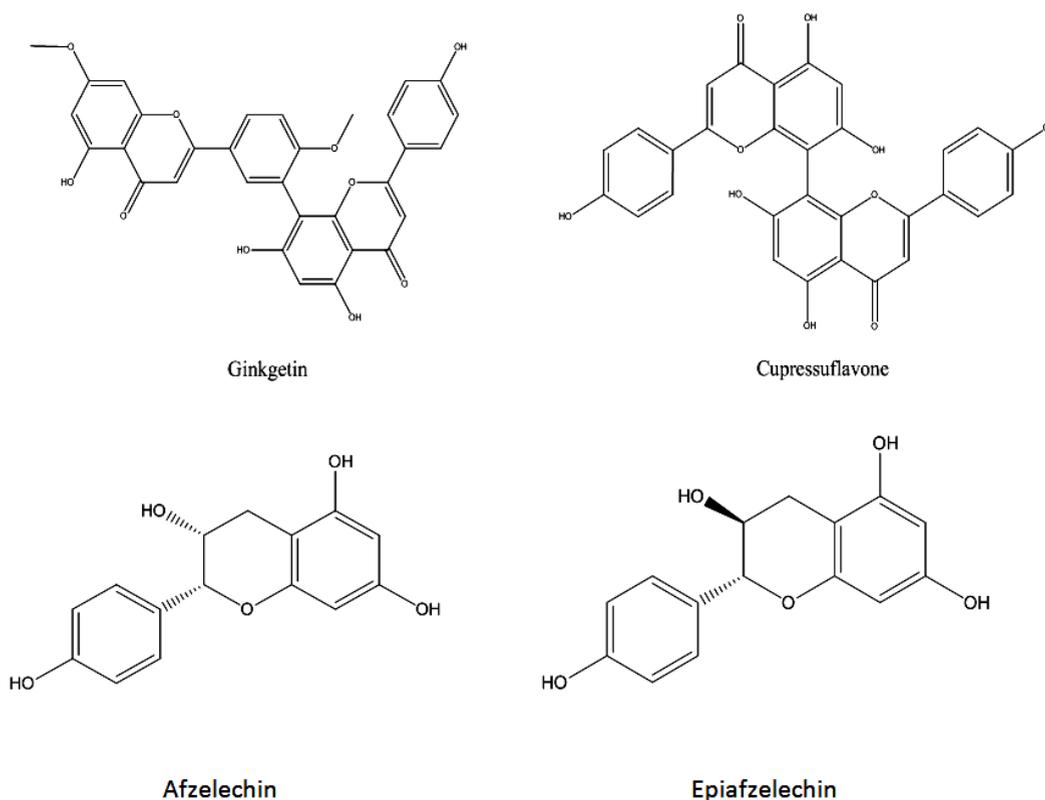


Fig. 2. Bioactive constituents of *Araucaria angustifolia*

the antioxidant properties of the films, highlighting their potential as active packaging materials⁴¹

Antioxidant Potential of Discarded Parts of *Araucaria angustifolia*

This study examines the antioxidant capabilities of the non-edible components of *Araucaria angustifolia*, including its trunk bark, seed coat, and spikes. Extracts were obtained using water, methanol, and acetone and then evaluated for their antioxidant activities through DPPH and ORAC assays. Methanol emerged as the most effective solvent, producing extracts with the highest phenolic content and strongest antioxidant performance. Major phenolic compounds such as gallic acid, chlorogenic acid, and quercetin were especially abundant in the trunk bark extracts. These extracts also significantly enhanced oxidative stability in food systems like buttermilk and soybean oil. Spectroscopic and statistical analyses confirmed that methanolic extracts were particularly rich in phenolics and flavonoids. The antioxidant potential of *A. angustifolia* was found

to be on par with other well-known conifers, indicating its promise as a sustainable source of natural antioxidants for use in food, health, and cosmetic applications.⁴²

Encapsulation of Antioxidant Compounds Using Modified Starch-Based Hydrogel

Dorneles *et al.* (2024) delved into the encapsulation of bioactive compounds extracted from the bracts of *Araucaria angustifolia*, using calcium alginate hydrogel beads enhanced with modified pinhão starch, which was created through hydrodynamic electrospray ionization jetting. By incorporating starch, they were able to enhance the rheological properties of the dispersion, resulting in increased viscosity and structural stability, as evidenced by lower compliance values and greater rupture strength. Spectroscopic analysis (ATR-FTIR) showed that the encapsulation process was based purely on physical interactions, with no new chemical bonds being formed. The starch-enhanced beads also demonstrated improved thermal stability and a higher encapsulation

efficiency, reaching up to 66.99% at a 6% starch content. Impressively, the antioxidant activity remained strong after encapsulation, ranging from 81.08% to 96.04%. Furthermore, *in vitro* digestion simulations revealed that the release of total phenolic compounds primarily occurred during the intestinal phase (60.72%–63.50%), underscoring the effective protection and targeted delivery of antioxidants.⁴³

Antioxidant Activity and SEM Analysis of Encapsulated *Araucaria angustifolia* Bract Extracts

The anticancer properties of bioactive substances derived from the bracts of *A. angustifolia* are typically discarded as waste. The researchers first used microwave-assisted extraction with water to obtain an aqueous extract rich in

phenolic compounds. These compounds were then encapsulated using freeze-drying and spray-drying techniques, with wall materials Polydextrose/partially hydrolyzed guar gum (PD-PHGG) and pectin/hydrolyzed collagen (PEC-HC).

To evaluate the anticancer properties of encapsulated powders, the researchers used several key parameters. They measured the retention rates of total phenolic compounds, with powders encapsulated in PD-PHGG achieving 80.57% retention through spray-drying and 89.94% through freeze-drying. Solubility rates were also assessed, with PD-PHGG encapsulated powders showing high solubility at 98.00 g/100 g for spray-drying and 97.69 g/100 g for freeze-drying. In terms of antioxidant activity, which is often linked to anticancer effects, the study found

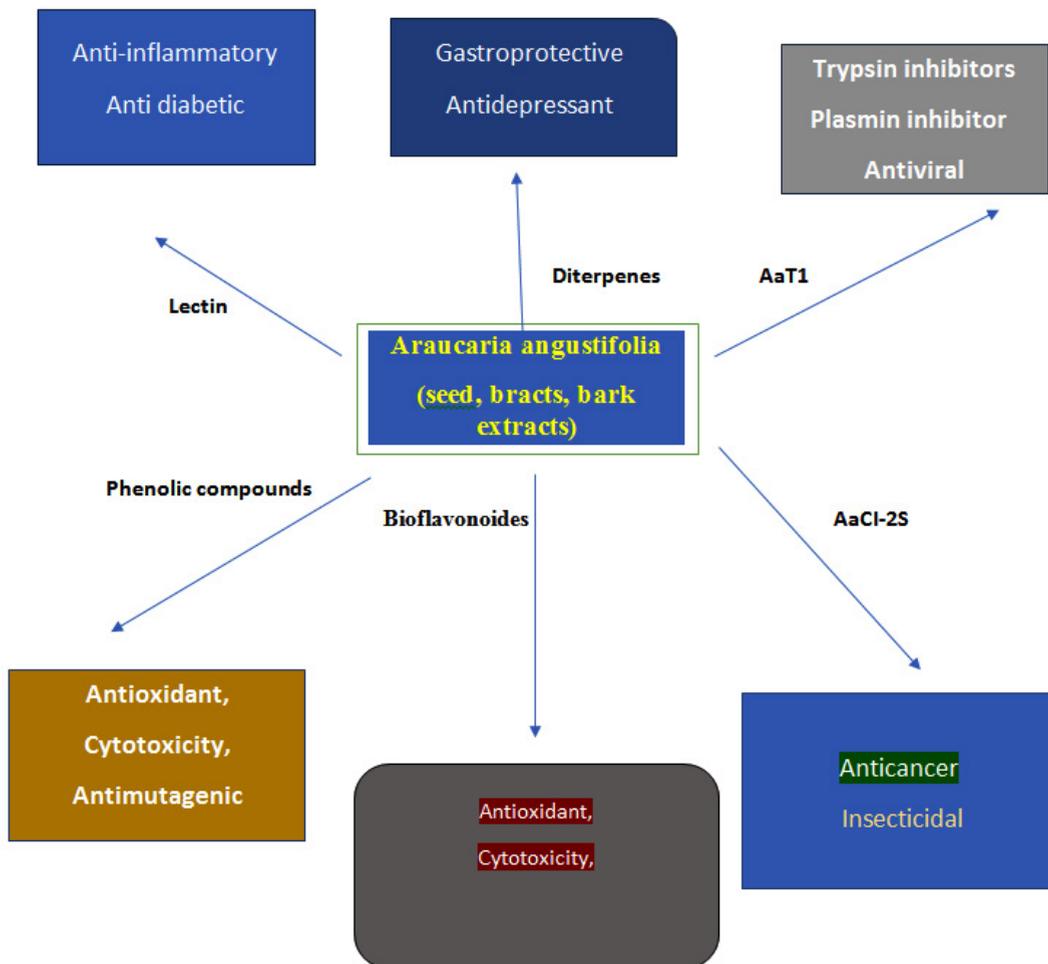


Fig. 3. Flow chart of Bioactive Compounds and Biological Activities of *Araucaria angustifolia*

Table 1. Summary of Bioactive Compounds, Their Biological Activities, and References

Compounds	Molecular Formula	Biological Activity	Observed Effects	References
Catechin	C ₁₅ H ₁₄ O ₆	Antioxidant, Antidiabetic	Protects DNA, inhibits α -amylase, strong radical scavenging	40,41
Epicatechin	C ₁₅ H ₁₄ O ₆	Antioxidant, Anticancer	Cytotoxic to cancer cells, inhibits lipid peroxidation	40,41
Rutin	C ₂₇ H ₃₀ O ₁₆	Antioxidant and antimutagenic activities	Inhibits inflammation, protects against oxidative stress	45
Quercetin	C ₁₅ H ₁₀ O ₇	Antioxidant, Anticancer	ROS scavenger, supports PACAP protein binding in cancer inhibition	39
Gallic Acid	C ₇ H ₆ O ₅	Antioxidant, Antimicrobial	Lipid peroxidation inhibitor,	42
Lectin (AaL)	Protein	Anti-inflammatory, Neuroprotective	Reduces edema, Reduced seizure mortality	53,54,35
Biflavonoids	C ₃₀ H ₁₈ O ₁₀	Antidepressant		
AaCI-2S	2S albumin-like protein	Antiviral	Inhibit HSV-1 replication, high selectivity index	36,24
Epiatzelechin	C ₉ H ₁₀ O ₄	Anticancer, Insecticidal	Targets cancer and termite digestive proteases	48
Protocatechuic acid	C ₁₅ H ₁₄ O ₅	Antioxidant	The hydroalcoholic extract of shows strong antioxidant activity in DPPH, lipid peroxidation, and free radical assays.	25,39
Diterpenes, AaT1 and AaT2	C ₂₀ H ₃₂ Protein	Gastroprotective, anticancer	Inhibit tumour cells dose-dependently, protect gastric lining	32, 33, 34
		Trypsin and plasmin inhibitor	AaT1-1 and AaT1-2 inhibit trypsin and plasmin, affecting digestion and clot resolution.,	30
Bilobetin	C ₃₁ H ₂₀ O ₁₀	Metabolic Regulation	Lowered postprandial glucose; α -amylase inhibition	32,36
Cupressus flavone	C ₃₀ H ₁₈ O ₁₀	Antiviral activity	comparable to acarbose.	

that the freeze-dried powders with PD-PHGG retained higher antioxidant capacity compared to other formulations. The DPPH assay results indicated that these powders maintained significant antioxidant activity even after accelerated storage tests. This suggests that the encapsulated phenolic compounds were effective in preserving their bioactivity, which is crucial for potential anticancer applications.

Additionally, scanning electron microscopy (SEM) revealed that spray-dried powders had a spherical shape, while freeze-dried powders were more irregular. FTIR analysis confirmed that encapsulation occurred through physical interactions, and PEC-HC powders showed enhanced heat stability, according to thermogravimetric analysis. These factors contribute to the stability and effectiveness of the encapsulated compounds. Overall, the study highlights the potential of using *Araucaria angustifolia* bracts as a source of natural antioxidants with possible anti-cancer benefits. By transforming a waste product into a valuable ingredient, the research underscores a sustainable approach to enhancing food formulations and exploring new therapeutic options.⁴⁴

Antioxidant and antimutagenic activities

The tree species *A. angustifolia*, commonly known as Brazilian pine, belongs to the Araucariaceae family. The female strobilus of this tree contains seeds, which are the edible part, along with bracts that comprise around 80% of the strobilus and are largely nonfunctional. Recent discussions have highlighted the potential benefits of antioxidant-rich diets in reducing the risks associated with various diseases linked to oxidative stress, including neurological diseases, atherosclerosis, and cancer. This research focused on examining the phenolic composition of the aqueous extract derived from the bracts of *A. angustifolia*, as well as its antioxidant, mutagenic, and antimutagenic properties. The findings indicated that the extract possesses significant antioxidant capabilities *in vivo* as well as *in vitro*. Furthermore, it was noticed that at lower concentrations, the extract did not exhibit mutagenic effects and effectively mitigated Hydrogen peroxide damage to the DNA of yeast cells. In these extracts, the main phenolic chemicals found were catechin, epicatechin, and rutin. These

findings suggest promising applications for natural compounds in the nutraceutical industry and indicate that utilizing these bracts can contribute positively to environmental sustainability.⁴⁵

Cytotoxicity

The extraction of phenolic compounds from the sterile bracts of *A. angustifolia* was investigated, with the pinecones, which make up about 80% of the cone, being known to be rich in these bioactive compounds. The aim was to optimize the extraction process using the response surface method and to evaluate the bioactivity of the extracts. The study investigated how varying ethanol concentrations, solute-to-solvent ratios, and extraction temperatures affected the yield and antioxidant properties of the phenolic compounds. HPLC was used to identify and quantify specific phenolics, including quercetin, epicatechin, gallic acid, kaempferol, and catechin. The optimal extraction conditions were found to be 60% ethanol, a solute-to-solvent ratio of 1:38 (w/v), and a temperature of 80°C. Under these conditions, the extract demonstrated strong antioxidant activity and significant concentrations of phenolic compounds.

Additionally, the extract exhibited significant antibacterial properties, inhibiting pathogenic bacteria by about 80% at a concentration of 10,000 µg/mL, and inhibiting lactic acid bacteria by 27.9% at 15,000 µg/mL. The extract showed an α-glucosidase inhibitory action that was approximately 10 times lower than acarbose, indicating its potential for antidiabetic applications. While the extract did not show notable antioxidant or cellular activity to decrease inflammation, it demonstrated high antiproliferative and antitumor cytotoxicity effects on cancer cells. Overall, the phenolic extract from *Araucaria angustifolia* bracts demonstrates promising potential for combating diseases related to oxidative stress. Future work should focus on assessing the safety and bioavailability of the extract to determine effective and safe application concentrations.⁴⁶

Anticancer activity

The recycling of agricultural and industrial waste, focusing on the seed of *A. angustifolia*, indigenous to Argentina, Paraguay, and southern Brazil was studied. The outer coat of this seed, a byproduct, has a high concentration of phenolic compounds. The research explored transforming

this residue into mechanical defibrillation of nanocellulose and assessed the properties of films and gels made from this material when combined with polyvinyl alcohol (PVA). The research evaluated how incorporating microfibrillated cellulose (MFC) from pinhão affected the physical and regenerative properties of gels and films. The study found that adding MFC to PVA increased the modulus of elasticity of the material. Biocompatibility was assessed by testing the cytotoxicity of the films and gels using an MTT test on Schwann cancer cells and 3T3 fibroblasts. Additionally, a scratch test migration experiment on HaCat keratinocyte cells showed that samples with lower concentrations of the films and gels achieved complete closure of the scratch within 72 hours. Molecular docking studies revealed that quercetin had favorable interaction scores with the PACAP protein, indicating a promising interaction for enhancing Schwann cell protein synthesis. The compound demonstrated notable stability and compactness after 14 nanoseconds of simulation. Overall, this research highlights the potential of using pinhão seed coats as a valuable resource for creating advanced materials with enhanced physical properties and regenerative capabilities.⁴⁷

Anticancer and Insecticidal activity

The anti-cancer and insecticidal activities of *A. angustifolia* seed extracts, which are consumable by both humans and animals, were investigated. Their research demonstrated that these extracts exhibit significant insecticidal properties, particularly against termites like *Nasutitermes corniger*, a prevalent species in tropical regions. This effect is attributed to the extracts' ability to inhibit cysteine protease activities, which are essential for the digestive processes of these insects. The study further identified and purified a specific cysteine protease inhibitor, AaCI-2S, through reversed-phase, size-exclusion, and ion exchange chromatography. "Spectroscopic analyses and circular dichroism studies showed the functional and structural stability of AaCI-2S, establishing its inhibitory activity across a range of temperatures and pH conditions. Besides targeting cysteine proteases in *Callosobruchus maculatus*, AaCI-2S also inhibited other proteases such as cathepsin L, ficin, papain, and bromelain" Remarkably, it reduced the proliferation of prostate and gastric

cancer cell lines, indicating its potential as a bioactive compound for cancer therapy.⁴⁸

Extraction of Bioactive Compounds Using Microwave-Assisted Extraction

In this study, researchers explored the use of microwave-assisted extraction to isolate phenolic compounds found in the bracts of *Araucaria angustifolia*. "They tested different extraction conditions by varying microwave power (700, 800, and 1,000 watts) and extraction times (10, 15, and 20 minutes), using water as the extracting medium. The results showed that the yield of phenolic compounds, tannins, and radical scavenging activity was significantly affected by the power level and extraction time." The ideal conditions for extraction were determined to be 1,000 watts for 20 minutes, resulting in the highest concentrations of condensed tannins (779.95 mg/g), total tannins (27.09 mg/g), and total phenolic compounds (47.61 mg/g). Additionally, the radical scavenging capacities, measured by ABTS·⁺, were 427.28 imol/g and 467.79 imol/g for DPPH. These results were comparable to those achieved with complete extraction with acetone acting as a solvent. The colorimetric analysis showed that the extract had a Hue angle of 62.28° and a Chroma value of 31.20. "The predicted optimal conditions from the response surface method confirmed that 1,000 watts and 20 minutes were ideal. From a practical perspective, the study highlights that the bracts of *Angustifolia* are a good source of phenolic compounds particularly Condensed tannins have antibacterial, anticarcinogenic, antimutagenic, and antioxidant qualities, among other health benefits.

"Water is used as a solvent in the microwave-assisted extraction process, as it not only shortens the extraction time but also reduces the thermal degradation of sensitive components." but also minimizes energy consumption. These findings suggest that this method could be effectively scaled up for industrial applications in food formulation.⁴⁹

Antimicrobial activity

An aqueous extract from the solid waste of *A. angustifolia* seeds was studied for its antibacterial properties and its synergistic action with heat against *Listeria monocytogenes*. The research focused on the extract's efficiency at a concentration of 10 kg/m³ against several

microorganisms, including *Staphylococcus aureus* and *Bacillus cereus*, while also exploring its antifungal activities. Their findings showed that *A. angustifolia* seeds' coat extract effectively inhibited the tested bacteria but did not demonstrate antifungal properties. Kinetic modeling indicated that the inactivation of *L. monocytogenes* followed a first-order reaction, with the bacterial death rate proportional to the remaining bacterial concentration. Notably, at a temperature of 55 °C, using the extract increased the inactivation rate constant by 105%, showing a significant enhancing effect on heat treatment. Additionally, the extract continued to improve inactivation rates at higher temperatures of 60 °C and 70 °C, with increases of 58% and 42%, respectively. Overall, These findings imply that extract from pinhão coats might be a valuable tool in food preservation by reducing the stability of *L. monocytogenes* and potentially enhancing food safety and shelf life.⁵⁰

The Neuroprotective Potential of *Araucaria angustifolia* Extract

Neuropsychiatric disorders and dementia are examples of brain disorders that frequently arise from mitochondrial dysfunction and oxidative stress, contributing to neuronal damage. Mitochondrial complex I is particularly significant in the generation of reactive oxygen species (ROS) and is a key factor in the development of these disorders. While strides have been made in treatment modalities, standard medications frequently fail to adequately target the underlying mitochondrial issues and redox imbalances within neurons. *Araucaria angustifolia*, a well-known pine species from South America, has a history of use in traditional medicine. Its extract, especially derived from the bracts, is rich in flavonoids that play a vital role in managing cellular redox processes. This study explores the effects of the extract from *A. angustifolia* (AAE) on mitochondrial complex I impairment caused by rotenone in human dopaminergic SH-SY5Y cells. The results demonstrated that AAE effectively restored both the assembly and function of mitochondrial complex I. This improvement was primarily linked to increased levels of NDUFS7 protein and the NDUFV2 gene. Additionally, treatment with AAE led to reduced neuronal ROS production and decreased lipid peroxidation. These groundbreaking findings indicate that AAE

may offer neuroprotective benefits, presenting a promising avenue for new therapeutic strategies aimed at tackling mitochondrial dysfunction associated with brain disorders.⁵¹

“Morphology of Starch from *Araucaria angustifolia* Seeds: Structural Analysis Using HMT, SEM, AFM, and XRD”

The morphological and structural characteristics of starch derived from *A. angustifolia* seeds were studied. Both native and heat-moisture treated (HMT) starches were examined. The starch was extracted using an aqueous method, and various parameters, including amylose content, moisture, ash, protein, and fat, were assessed following AOAC standards. “The amylose content of the starch extracted from *Araucaria angustifolia* seeds was found to be 26.3%. The moisture content was below 8.5%, and the ash content was less than 1.44%. To analyze the starch granules, Atomic Force Microscopy (AFM) and Scanning Electron Microscopy (SEM) were used for complete morphological observations, while X-ray Powder Diffraction (XRD) provided structural assessment. SEM and AFM imaging revealed that untreated starch granules had the largest average diameters, measuring 10.85 μm and 10.64 μm, respectively. In contrast, starch treated with 10% humidity for 60 and 120 minutes showed smaller granules. AFM measurements indicated that the medium roughness (*r*_a) of the granules increased from 321.68 nm to 470.06 nm with HMT treatment. Additionally, there was a noticeable decrease in the relative crystallinity (*R*_c) of the granules following HMT. The granules generally had round or oval shapes with flat surfaces. Both SEM and AFM provided consistent mean diameter measurements, showing that granule size decreased with higher humidity during the HMT process. The changes in roughness and relative crystallinity were consistent with the HMT conditions, indicating increased roughness and decreased crystallinity as the treatment progressed⁵²

Anti-inflammatory activity

The effects of a lectin (AaL) isolated from *A. angustifolia* seeds on rat paw edema were examined. The researchers evaluated its anti-inflammatory properties, systemic toxicity, inflammatory mediators, pro-inflammatory actions, and the role of sugar residues. When AaL was administered intravenously at doses ranging

from 0.1 to 1 mg/kg, it effectively reduced edema and increased vascular permeability induced in a dose-dependent manner by dextran. This effect was blocked when AaL was combined with N-acetylglucosamine (Glyc-Nac), its binding sugar. Additionally, AaL significantly decreased edema caused by compound 48/80 (33%) and serotonin (18%) but did not affect edema induced by histamine. However, when AaL was injected subcutaneously, it caused paw edema that peaked after 1 hour. This edema was partially reduced either by combining AaL with Glyc-Nac (59%) or by administering the lectin intravenously before the subcutaneous injection (38.8%). The edematogenic effect of AaL was notably suppressed by dexamethasone (51%), pentoxifylline (44.4%), and by depleting mast cells from the rat paw (45.6%). This indicates that the inflammatory response triggered by AaL involves mast cells but does not involve nitric oxide or prostaglandins, as inhibitors of these substances did not affect the edema.

The administration of a single dose of AaL (1 mg/kg, intravenously) over 7 days showed no significant effects on the body weight of the rats, nor did it alter the weights of the liver, kidneys, spleen, or stomach. There were also no changes in blood leukocyte counts or levels of creatinine, urea, or serum transaminases. Systemic toxicity was only observed at substantially higher doses, with a lethal dose 50 (LD50) of 88.3 mg/kg, which is significantly greater than the doses used for anti-inflammatory effects.⁵³

Effects on Metabolism and the Central Nervous System

Araucaria angustifolia seeds play a crucial role in metabolic regulation and neuroprotection, largely due to their high concentration of lectins. These glycoproteins interact with carbohydrates, influencing various biological processes such as cell signaling and enzyme activity. Research suggests that consuming *A. angustifolia* seeds may help regulate blood sugar levels, making them a promising dietary option for managing diabetes. A study by Cordenunsi *et al.* found that eating cooked seeds with their coat led to a 23% lower glycemic response compared to white bread, indicating their potential to stabilize postprandial blood glucose levels.⁵⁴

Silva *et al.* explored the impact of seed coat extracts, which are rich in proanthocyanidins, on glycemic control in animal studies. Their research showed that administering 250 mg/kg of the extract significantly reduced blood sugar levels in rats after starch consumption. Additionally, the extract effectively inhibited both human salivary and porcine pancreatic α -amylase enzymes, highlighting its potential as a natural remedy for controlling postprandial hyperglycemia. These findings suggest that *A. angustifolia* seeds and their extracts could offer valuable therapeutic benefits for individuals with diabetes, warranting further research into their mechanisms.

a Table: Summary of Bioactive Compounds, Their Biological Activities, and References and clinical applications.⁵⁵

Functional and Sustainable Uses of *Angustifolia* Seed

The tree's edible seed, known as the *angustifolia* seed, contains up to 72% starch (on a dry basis), along with dietary fiber, essential fatty acids, and various beneficial minerals. Its starch exhibits a low glycemic response due to the presence of resistant starch, making it an excellent option for gluten-free and diabetic-friendly diets. Additionally, both the seed and its often-overlooked husk and bracts are rich in phenolic compounds with antioxidant, antimicrobial, and anti-inflammatory properties. These bioactive elements show significant potential in the food, pharmaceutical and cosmetic industries, supporting the development of functional foods, edible films, dietary supplements, and skincare products. The article emphasizes the promising opportunities for utilizing the *angustifolia* seed and its byproducts in innovative and sustainable ways that not only promote human health and industrial applications but also contribute to the conservation of *Araucaria* forests and the socio-economic development of local communities.⁵⁶

Bioactive Properties of Phenolic Extracts from *Araucaria angustifolia* Bracts: Antioxidant, Antimicrobial, Antiglycemic, and Antiproliferative Potential

Researchers have explored the bioactive potential of phenolic compounds extracted from the sterile bracts of *Araucaria angustifolia*, which constitute about 80% of the pinecone.

Using response surface methodology, they optimized the extraction process with 60% ethanol, a 1:38 (w/v) solute-to-solvent ratio, and a temperature of 80/ °C. High-performance liquid chromatography identified key phenolics such as gallic acid, catechin, epicatechin, quercetin, and kaempferol. The extract demonstrated strong antioxidant activity and inhibited approximately 80% of pathogenic bacteria at 10,000/ µg/mL, while lactic acid bacteria showed 27.9% inhibition at 15,000/ µg/mL. Notably, the extract's α-glucosidase inhibitory activity was about ten times greater than that of acarbose, indicating significant antiglycemic potential. However, the extract exhibited high cytotoxicity towards non-tumor cells and antiproliferative effects on tumor cells, suggesting potential applications in cancer treatment, albeit with caution regarding dosage and safety.⁵⁷

Therapeutic Efficacy of Brown Propolis from *Araucaria* sp. in Modulating Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic autoimmune disease affecting joints, with a global prevalence of 0.5–1%. While NSAIDs are commonly used, natural alternatives like brown propolis have gained attention for their anti-inflammatory and immune-modulating effects. This study investigated the effects of brown propolis extract from *Araucaria* species using animal models. Pain sensitivity was tested through mechanical and thermal methods, while inflammation was assessed by paw swelling, immune cell migration, and NF-εB expression. In a collagen-induced RA model, joint pain, swelling, weight changes, joint damage, and biochemical markers were also evaluated. Results showed that brown propolis reduced pain, inflammation, and joint damage. It lowered NF-εB levels, prevented joint space loss, and improved overall health markers. Although promising, these findings are from animal studies. Human trials are needed to confirm its effectiveness for RA treatment.⁵⁸

In Vitro Embryogenesis in *Araucaria angustifolia*

This study explored whether exposing *Araucaria angustifolia* somatic embryos to low temperatures in vitro could improve their development through somatic embryogenesis. Immature zygotic embryos were used to induce somatic embryos, which were cultured for 120

days before being subjected to cold treatment at 4.5°C for varying durations: 0, 2, 4, 8, or 16 days. After the cold exposure, the cultures were returned to a standard temperature of 25±2°C for 20 days. Microscopic and cytochemical analyses were then performed. The results showed that the embryogenic cultures, particularly at the PEM III stage, did not progress further in their development. In fact, extended cold exposure negatively impacted the growth of the embryogenic tissue. These findings suggest that cold treatment alone is insufficient to enhance embryogenic development in *A. angustifolia*, and highlight the need for more comprehensive research into the epigenetic mechanisms that regulate embryo development in this species.⁵⁹

Endophytic Fungal Diversity in *Araucaria angustifolia* from Southern Brazil

Araucaria angustifolia, a critically endangered conifer, supports a diverse community of endophytic fungi, though their ecological roles remain underexplored. In a study conducted in a forest fragment in Guarapuava, Paraná, Brazil, researchers collected 90 tissue samples from five individual trees and isolated 61 fungal morphotypes. DNA sequencing of the Internal Transcribed Spacer (ITS) region identified fungi from 37 genera, all belonging to the phylum Ascomycota. These were distributed across three classes—Sordariomycetes, Dothideomycetes, and Eurotiomycetes—encompassing 11 orders and 13 families. Sordariomycetes was the most abundant class, accounting for 40% of the isolates, with *Xylaria* as the most frequent genus (14%), while Eurotiomycetes was the least represented. The findings highlight a rich and varied fungal community that may play an important role in the survival and ecological function of *A. angustifolia*, underscoring the importance of conserving both the species and its associated microbial diversity.⁶⁰

Impact of Mechanical Defibrillation Techniques on seeds of *Araucaria angustifolia*

This study investigated how different mechanical defibrillation techniques influence the characteristics of nanosuspensions derived from various parts of the *Araucaria angustifolia* seed, including the whole seed, its coat, and the almond. The nanosuspensions were assessed for their nutritional content, structural morphology, thermal and rheological behavior, and biological

safety. Findings revealed that the seed coat yielded nanosuspensions rich in fiber (over 63%), while the whole seed and almond fractions were primarily composed of non-fiber carbohydrates, particularly starch. Morphological analysis showed that defibrillation produced nano- and microfibrils in the coat-based suspensions and fine starch granules in almond-based ones. Rheologically, the coat-derived suspensions behaved like gels, whereas almond-based suspensions resembled liquids. Additionally, the coat nanosuspensions were notable for their high levels of flavonoids and phytosterols, suggesting potential health benefits. Importantly, no cytotoxic effects were observed at tested concentrations. Overall, the study highlights the potential of using defibrillation to tailor the functional properties of plant-based nanosuspensions, paving the way for their use in food or pharmaceutical applications.⁶¹

CONCLUSION

This review highlights *Araucaria angustifolia* as a valuable source of starch and bioactive compounds, with antioxidant, anti-inflammatory, antiviral, and wound healing properties found in various plant parts, including the leaves, bark, and pinhão coat. The pinhão almond is also a key ingredient in regional cuisine. Additionally, the plant has been used in traditional medicine, with laboratory studies supporting its biological effects. Also, these activities are attributed to the bioactive compounds in its extracts and essential oils. Its extracts contain flavonoids, tannins, and phenolic acids, contributing to antimicrobial effects against *Staphylococcus aureus* and *Escherichia coli*. The plant also shows neuroprotective potential and anti-inflammatory activity by inhibiting pro-inflammatory cytokines like TNF- α and IL-6.

While *A. angustifolia* shows potential for drug development, further pharmacokinetic, pharmacodynamic, and toxicological studies are needed to confirm its safety and efficacy for clinical use. More research is essential to explore its full potential.

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This research does not involve any clinical trials

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Not Applicable

Authors' Contributions

Sibbala Subramanyam and Surya Prabha Matangi: Plant selection and writing of the paper; Kalaiah Gari Venkata Madhusudhan: Literature Collection; Bharath Rathna Kumar: Bioactivity Study and Structure Analysis; Janapati Pedda Yanadaiah: Review and Editing.

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