Iporuru (Alchornea castaneifolia) EDUCATIONAL PDF

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Family: Leguminosae

Genus: *Alchornea*

Species: *castaneifolia*

Synonyms: *Hermesia castaneifolia*

Common Names: Iporuru, iporoni, iporuro, ipururo, ipurosa, macochihua, niando, pajaro

Part Used: Leaves, bark, roots

Properties and Actions

MAIN ACTIONS	OTHER ACTIONS	STANDARD DOSAGE
relieves pain	kills fungi	Leaves
reduces inflammation	kills viruses	**Infusion:** 1 cup 2-3
kills cancer cells	kills viruses	times daily
increases libido	prevents tumors	**Maceration:** 1/2 cup 2-3
		times daily

Iporuru is a shrubby tree that reaches 8-10 m in height with light-brown bark and violet flowers. It grows extensively in the lower elevations and flood plains of the Amazon River system in Peru, and is indigenous to the moist, tropical areas in Argentina, Bolivia, Brazil, Colombia, Paraguay, and Venezuela. Iporuru can be harvested only in the Amazon's dry season; it spends the rainy season underwater. The locals believe that the active medicinal properties found in the bark are present only during the dry season.

TRIBAL AND HERBAL MEDICINE USES

For centuries the indigenous peoples of the Amazon have used the bark and leaves of iporuru for many different purposes and prepared it in many different ways. The plant

commonly is used with other plants during shamanistic training and, sometimes, is an ingredient in *ayahuasca* (a hallucinogenic, multi-herb decoction used by South American shamans). Throughout the Amazon the bark or leaves are tinctured (generally with the local rum, called *aguardiente*) as a local remedy for rheumatism, arthritis, colds, and muscle pains. It is well known to the indigenous peoples of Peru for relieving the symptoms of osteoarthritis, and in aiding flexibility and range of motion. The Candochi-Shapra and the Shipibo Indian tribes use both the bark and roots for treating rheumatism. To prevent diarrhea, members of the Tikuna tribe take 1 tbsp. of bark decoction before meals. The pain-relieving properties of iporuru appear in topical treatments; crushed leaves are rubbed on painful joints and are beaten into a paste to apply to painful stingray wounds.

Today, iporuru remedies and products are sold in local markets and herbal pharmacies in Peru, where it is recommended highly for arthritis and rheumatism. In addition, locals prepare the leaves into a decoction for coughs. The leaves of iporuru are used in some parts of Peru to increase female fertility (mostly in cases where the male is relatively impotent). Richard Rutter, noted Peruvian ethnobotanist, insists that iporuru is widely used as an effective aphrodisiac and geriatric tonic for males. Throughout Peru it is regarded as a remedy for impotency as well as for balancing blood sugar levels in diabetics. Iporuru has been gaining popularity among North American athletes and health practitioners recently; reports have it that iporuru provides nutritional support to muscle and joint structures. Here in the U.S., its reported analgesic and anti-inflammatory properties have begun to make it popular also to those suffering from arthritis and other joint problems.

PLANT CHEMICALS

Little research has been done to catalog completely the phytochemicals in iporuru. Initial screening has revealed it to contain steroids, saponins, phenols, flavonols, flavones, tannins, xanthones, and alkaloids. The anti-inflammatory properties of iporuru are attributed

to a group of alkaloids, including one called alchorneine, which are found in the bark of iporuru as well as several other species of *Alchornea*.

BIOLOGICAL ACTIVITIES AND CLINICAL RESEARCH

Likewise, there has been little clinical research on iporuru - despite its long history of use in South American herbal medicine. That which has been done, however, does help explain some of its traditional uses. Pharmacognosy students in Sweden documented that an ethanol extract of the stembark was capable of reducing lab-induced swelling and inflammation in rats when applied topically. These researchers also reported that the extract also was able to inhibit COX-1 prostaglandin synthesis. Prostaglandins, produced by the activity of the enzyme cyclooxygenase (COX), are linked to inflammatory processes and diseases. (COX-inhibitors are a newer class of anti-inflammatory and arthritis pharmaceutical drugs on the market.) This prostaglandin inhibition activity may, in part, explain the traditional use of iporuru for inflammatory joint and muscle disorders such as osteoarthritis, arthritis, and rheumatism. Other researchers in the U.S. confirmed these effects by injecting mice with an ethanol extract of iporuru and observing an anti-inflammatory effect against other chemical-induced inflammation.

Other preliminary *in vitro* research (performed in Canada) has reported iporuru's antifungal, antiviral, and antitumor activities. In their "crown gall tumor inhibition" assay (a preliminary laboratory test to predict antitumor activity), ethanol extracts and water extracts of the dried bark tested active at in very small quantities. In another test to predict antitumor activity (an anticrustacean assay with *Artemia salina*), the ethanol extract tested active but the water extract was not active. Their antimicrobial testing revealed that the ethanol extract demonstrated good antifungal activity against several fungal strains, but the water extract was inactive. Likewise, ethanol extracts evidenced better antiviral actions than those

water-based. Neither the ethanol nor water extracts showed any antibacterial or antiyeast actions against the strains they tested.

CURRENT PRACTICAL USES

While iporuru will probably long remain in the South American herbalist's and shaman's medicine chest of natural remedies for impotency, arthritis, pain and inflammation, its use by the rest of the world will be limited until more people and practitioners learn more about the plant and/or more research is performed. Very few iporuru products are sold here in the U.S., and it is only available through a handful of companies (which mostly include it in multi-herb combination formulas).

Iporuru Plant Summary

Main Preparation Method: leaf infusion or bark decoction

Main Actions (in order):

anti-inflammatory, analgesic (pain-reliever), antiviral, antifungal, fertility aid

Main Uses:

1. for arthritis and rheumatism
2. as an internal and external anti-inflammatory and pain-reliever for muscle and joint injuries
3. for fungal and viral infections
4 for erectile dysfunction and female fertility

Properties/Actions Documented by Research:

: anti-inflammatory, antifungal, antitumor, antiviral, COX- inhibitor (typically reduces inflammation)

Other Properties/Actions Documented by Traditional Use:

analgesic (pain-reliever), anti-arthritic, antihistamine, anti-rheumatic, antispasmodic, cough suppressant, aphrodisiac, fertility aid, hypoglycemic, wound healer

Cautions: none

Traditional Preparation: The traditional impotency remedy in Peru calls for one cup of dried leaves to be macerated in 2 cups of water for one day, and 2-3 doses (of 1/2 cup) are drunk daily. For diabetes, 1/2 cup of dried leaves are infused in 4 cups of water, and one cup is drunk after each meal. As the leaves are prepared in standard infusions or cold macerations (indicating the beneficial chemicals providing the effects are water soluble),

powdered leaves in capsules, tablets, or stirred into liquids can be substituted (1-2 g, two or three times daily).

Contraindications: None known.

Drug Interactions: None known.

Worldwide Ethnomedical Uses

Amazonia	for aches (muscle), analgesic, arthritis, colds, cough, diabetes, diarrhea, fertility, impotence, inflammation, pain, rheumatism
Canada	for arthritis, inflammation, muscle pains, rheumatism
Peru	for arthritis, bacterial infections, colds, cough, diabetes, diarrhea, flexibility, impotence, inflammation, muscle pains, osteoarthritis, pain, rheumatism, sterility
U.S.	for allergies, athletic support, arthritis, bacterial infections, constipation, inflammation, pain
Venezuela	for wounds

Referenced Quotes on Iporuru

1. "The bark of the Iporuru shrub is truly a treasure of the Amazon. It has been found to be very effective in cases of osteoarthritis. Unfortunately, this herb can only be harvested during the dry season in the Amazon for two reasons. First, during the rainy season, the shrubs are too far underwater and second, the active ingredients are present in the bark only in the dry season."

2."Iporuru is used by the indigenous peoples of Peru for relieving symptoms of osteoarthritis. It helps to increase flexibility in movement and range of motion."

10. "Alchornea castaneifolia (Willd.) Juss. Euphorbiaceae. "Iporoni", "Iporuro", "Ipururo", "Ipurosa", "Macochihua". Alcoholic bark maceration used to treat rheumatism, arthritis, colds, and muscle pains after a long fishing day. The "Candochi-Shapra" and the "Shipibos" used the bark and roots to treat rheumatism. Iquitos herbalists recommend it for rheumatism (RVM). Pucallpa citizens take the leaf decoction orally for cough and rheumatism (VDF). "Tikunas" take one tablespoon bark decoction before meals for diarrhea (SAR). Around Piura, the leaves are used to increase fertility of females where the male is

relatively impotent (FEO). Rutter stresses that it is an aphrodisiac and geriatric for males (RAR). Sometimes found in the famous "Rompe Calzon" aphrodisiac."

11."The primary Amazon herbs used for their synergistic effects during athletic training and recovery include the following: Catuaba and Marapuama as strong tonics and nervous system fortifiers; Marapuama also for its anti-rheumatic properties; Sarsaparilla to increase circulation, clear toxins and stimulate metabolism; **Iporuru** for support of muscle and joint structure; Samambaia for detoxification of waste products and anti-rheumatic properties; Una de gato for antioxidant properties; Tayuya to remove lactic acid accumulations; and Suma for anabolic (muscle-building) effects. (See Table 1)

21."**Alchornea** Swartz

There are 70 species of this pantropical genus. They are shrubs to medium-sized trees. The insect antifeedants of A. triplinervia have been studied (Hankinson, 1982); alkaloids have been found in A. floribunda (Khuong-Huu, 1972); the structure of the alkaloid alchomeine has been established (Cesario, 1970).

Alchornea castanaefolia (Willd.) jussieu, Tent. Euph. (1824) 42. pajaro arbol (Col.)

G 202; SB 8439

Amongst the Tikunas, a decoction of the bark, in one-tablespoon doses before meals, is considered to be a treatment for diarrhea. The crushed leaves are also rubbed on painful joints for relief. In Venezuela, a species of Alchornea is used in the form of cataplasm for wounds inflicted by the sting ray.

Published Research on Iporuru

All available third-party research on iporuru can be found at **PubMed**. A partial listing of the published research on iporuru updated through Feb 2019 is shown below:

Anti-inflammatory, Antispasmodic & Pain-Relieving Actions:

Martínez, C., et al. " Medicinal plants from the genus *Alchornea* (Euphorbiaceae): A review of their ethnopharmacology uses and phytochemistry." *BLACPMA.* 2017 May; 16(3): 162 - 205.

Okoye, F., et al. "Topical anti-inflammatory constituents of lipophilic leaf fractions of *Alchornea floribunda* and *Alchornea cordifolia*." *Nat Prod Res.* 2011 Dec; 25(20): 1941-9.

Lopes, F., et al. "Anti-inflammatory activity of *Alchornea triplinervia* ethyl acetate fraction: inhibition of Hv(2)Ov(2), NO and TNF-a." *Pharm Biol.* 2010 Dec; 48(12): 1320-7.

Kouakou-Siransy, G., et al. "Effects of *Alchornea cordifolia* on elastase and superoxide anion produced by human neutrophils." *Pharm Biol.* 2010 Feb; 48(2): 128-33.

Okoye, F., et al. "Anti-inflammatory and membrane-stabilizing stigmastane steroids from *Alchornea floribunda* leaves." *Planta Med*. 2010 Feb; 76(2): 172-7.

Manga, H., et al. "Anti-inflammatory compounds from leaves and root bark of *Alchornea cordifolia* (Schumach. & Thonn.) Müll. Arg." *J Ethnopharmacol.* 2008 Jan; 115(1): 25-9.

Rivas, E., et al. "[Study of analgesic activity of methanolic extracts of *Maytenus krukovii* (chuchuhuasi), *Alchornea castaneifolia* (hiporuro), *Sambucus nigra* (elderberry) and *Aristeguietia discolor* (pulmonaria) in mice against Ibuprofen]." *Rev. Horizonte Med.* 2005 June; 57-61.

Manga, H., et al. "*In vivo* anti-inflammatory activity of *Alchornea cordifolia* (Schumach. & Thonn.) Mull. Arg. (Euphorbiaceae)." *J. Ethnopharmacol.* 2004 Jun; 92(2-3): 209-14.

Castaneda, B., et al. "[Phytochemical, toxicological, analgesic and anti-inflammatory evaluation of the extract metabolism of *Alchornea castaneifolia* "Hiporuro," in laboratory animals]." *Cultur XXI, NQ* 2003; 17: 13-21.

Osadebe, P., et al. "Anti-inflammatory effects of crude methanolic extract and fractions of *Alchornea cordifolia* leaves." *J. Ethnopharmacol.* 2003 Nov; 89(1): 19-24.

Tona, L., et al. "Antiamoebic and spasmolytic activities of extracts from some antidiarrhoeal traditional preparations used in Kinshasa, Congo." *Phytomedicine*. 2000 Mar; 7(1): 31-8.

Dunstan, C., et al. "Evaluation of some Samoan and Peruvian medicinal plants by prostaglandin biosynthesis and rat ear oedema assays." *J. Ethnopharmacol.* 1997; 57: 35-56.

Ogungbamila, F. O., et al. "Smooth muscle-relaxing flavonoids from *Alchornea cordifolia*." *Acta Pharm. Nord*. 1990; 2(6): 421-22.

Persinos-Perdue, G., et al. "Evaluation of Peruvian folk medicine by the natural products research laboratories." Abstra. Joint Meeting American Society of Pharmacognosy and Society for Economic Botany, Boston, 1981; (5) 13.

Dunstan, C., et al. "Evaluation of some Samoan and Peruvian medicinal plants by prostaglandin biosynthesis and rat ear oedema assays." *J. Ethnopharmacol.* 1997 Jun; 57(1): 35-56.

Anti-ulcer and Anti-diarrhea Actions:

Bonacorsi, C., et al. "Comparison of Brazilian plants used to treat gastritis on the oxidative burst of *Helicobacter pylori*-stimulated neutrophil." *Evid. Based Complement. Alt. Med.* 2013; 2013: 851621.

Lima, Z., et al. "Effects of the ethyl acetate fraction of *Alchornea triplinervia* on healing gastric ulcer in rats." *Pharmaceuticals* 2011; 4: 1423-1433.

Bonacorsi, C., et al. "Relative antioxidant activity of Brazilian medicinal plants for gastrointestinal diseases," *J. Med. Plant Res.* 2011; 5(18) 4511–4518.

Lima, Z., et al. "Brazilian medicinal plant acts on prostaglandin level and *Helicobacter pylori*." *J. Med. Food*. 2008 Dec; 11(4): 701-8.

Hiruma-Lima, C., et al. "Antiulcerogenic activity of *Alchornea castaneifolia*: Effects on somatostatin, gastrin and prostaglandin." *J. Ethnopharmacol.* 2006 Mar; 104(1-2): 215-24.

Agbor, G., et al. "The antidiarrhoeal activity of *Alchornea cordifolia* leaf extract." *Phytother. Res.* 2004; 18(11): 873-6.

Tona, L., et al. "Antiamoebic and spasmolytic activities of extracts from some antidiarrhoeal traditional preparations used in Kinshasa, Congo." *Phytomedicine*. 2000 Mar; 7(1): 31-8.

Tona, L., et al. "Biological screening of traditional preparations from some medicinal plants used as antidiarrhoeal in Kinshasa, Congo." *Phytomedicine*. 1999 Mar; 6(1): 59-66.

Cellular Protective & Antioxidant Actions:

Reyes-Munguia, A., et al. "Antioxidant activity, antimicrobial and effects in the immune system of plants and fruits extracts." Front. Life Sci. 2016; 9(2): 90-98.

Glensk, M., et al. "Phenolic constituents from *Alchornea castaneifolia.*" *Rec. Nat. Prod*. 2015 Aug; 10(2): 32-39.

Osadebe, P., et al. "Phytochemical analysis, hepatoprotective and antioxidant activity of *Alchornea cordifolia* methanol leaf extract on carbon tetrachloride-induced hepatic damage in rats." *Asian Pac. J. Trop. Med.* 2012 Apr; 5(4): 289-93.

Bonacorsi, C., et al. "Relative antioxidant activity of Brazilian medicinal plants for gastrointestinal diseases," *J. Med. Plant Res.* 2011 Sep; 5(18): 4511–4518.

Kouakou-Siransy, G., et al. "Effects of *Alchornea cordifolia* on elastase and superoxide anion produced by human neutrophils." *Pharm. Biol.* 2010 Feb; 48(2):128-33.

Olaleye, M., et al. "Acetaminophen-induced liver damage in mice: effects of some medicinal plants on the oxidative defense system." *Exp. Toxicol. Pathol.* 2008 Mar; 59(5): 319-27.

Castaneda, B., et al. "[Evaluation of the antioxidant capacity of seven Peruvian medicinal plants.]" *Horizonte Medico*. 2008 July; (8)1: 56-72.

Mpiana, P., et al. "*In vitro* antidrepanocytary actvity (anti-sickle cell anemia) of some Congolese plants." *Phytomedicine.* 2006 Nov 16;

Lopes, F., et al. (2005). "Inhibition of hydrogen peroxide, nitricoxide and TNF-α production in peritoneal macrophages by ethyl acetate fraction from *Alchornea glandulosa*." *Biol. Pharm. Bull.* 2005; 28: 1726-1730.

Antimicrobal & Antimalarial Actions:

Martínez, C., et al. " Medicinal plants from the genus *Alchornea* (Euphorbiaceae): A review of their ethnopharmacology uses and phytochemistry." *BLACPMA.* 2017 May; 16(3): 162 - 205.

Reyes-Munguia, A., et al. "Antioxidant activity, antimicrobial and effects in the immune system of plants and fruits extracts." Front. Life Sci. 2016; 9(2): 90-98.

Calvo, T., et al. "Phenolic compounds in leaves of *Alchornea triplinervia*: anatomical localization, mutagenicity, and antibacterial activity." *Nat. Prod. Commun.* 2010 Aug; 5(8): 1225-32.

Bussmann, R., et al. "Antibacterial activity of medicinal plants of Northern Peru–can traditional applications provide leads for modern science?" *Indian J. Trad. Knowl*. 2010 Oct; 9(4) 742-753.

Lima, Z., et al. "Brazilian medicinal plant acts on prostaglandin level and *Helicobacter pylori*." *J. Med. Food*. 2008 Dec; 11(4): 701-8.

Costa, E, et al. "Antimicrobial activity of some medicinal plants of the Cerrado, Brazil." *Phytother. Res.* 2008 May; 22(5): 705-707.

Igbeneghu, O., et al. "A study of the *in vivo* activity of the leaf extract of *Alchornea cordifolia* against multiply antibiotic resistant *S. aureus* isolate in mice." *Phytother. Res.* 2007; 21(1): 67-71.

Igbeneghu, O., et al. "A study of the *in vivo* activity of the leaf extract of Alchornea cordifolia against multiply antibiotic resistant *S. aureus* isolate in mice." *Phytother. Res.* 2007 Jan; 21(1): 67-71.

Ayisi, N., et al. "Comparative *in vitro* effects of AZT and extracts of *Ocimum gratissimum, Ficus polita, Clausena anisata, Alchornea cordifolia*, and *Elaeophorbia drupifera* against HIV-1 and HIV-2 infections." *Antiviral Res.* 2003 Mar; 58(1): 25-33.

Banzouzi, J., et al. "*In vitro* antiplasmodial activity of extracts of *Alchornea cordifolia* and identification of an active constituent: ellagic acid." *J. Ethnopharmacol.* 2002 Aug; 81(3): 399-401.

Abo, K., et al. "Antimicrobial screening of *Bridelia micrantha, Alchormea cordifolia* and *Boerhavia diffusa*." *Afr. J. Med. Med. Sci.* 1999 Sep-Dec; 28(3-4): 167-9.

Ebi, G. "Antimicrobial activities of *Alchornea cordifolia*." *Fitoterapia*. 2001; 72(1): 69-72.

Tona, L., et al. "Antiamoebic and spasmolytic activities of extracts from some antidiarrhoeal traditional preparations used in Kinshasa, Congo." *Phytomedicine*. 2000 Mar; 7(1): 31-8.

Okeke, I., et al." Antimicrobial spectrum of *Alchornea cordifolia* leaf extract." *Phytother. Res.* 1999 Feb; 13(1): 67-9.

MacBae, W., et al. "Studies on the pharmacological activity of Amazonian Euphorbiaceae." *J. Ethnopharmacol*. 1988 Feb-Mar; 22(2): 143-172.

Toxic / Non-Toxic Actions:

Castaneda, B., et al. "[Evaluation of the cytotoxic and embryotoxic action of the methanolic extract of *Alchornea castaneifolia* "Hiporuro"]." *Horizonte Medico* 2006; 6(1)

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===----------AI REVIEWED KNOWLEDGE—----------===

Based on traditional uses, preliminary lab studies, and anecdotal evidence, the plant *Alchornea castaneifolia*, also known as Iporuru, is associated with a variety of potential health benefits, particularly its use as an anti-inflammatory and pain reliever. However, strong scientific evidence and clinical trials in humans are lacking for these claims.

Disclaimer: *This is an informational summary only. Alchornea castaneifolia is not approved by the Food and Drug Administration (FDA) for any medicinal purpose. Consult a qualified healthcare professional before using any herbal supplement, especially if you have underlying health conditions, are pregnant or breastfeeding, or are taking medication.*

Traditional and folk uses

Alchornea castaneifolia has a long history of use in the traditional medicine of the Amazon rainforest by Indigenous peoples. The bark, leaves, and roots are often prepared as decoctions (boiled extracts), tinctures (alcohol extracts), or infusions.

Pain and inflammation

- **Joint and muscle pain:** The plant is most widely recognized for its use in treating joint and muscle discomfort, including arthritis, rheumatism, and osteoarthritis. Some Indigenous tribes, such as the Candochi-Shapra and Shipibo, use it specifically for rheumatism.
- **Topical pain relief:** Crushed leaves are rubbed on or beaten into a paste for topical application to relieve painful joints or wounds, such as those from stingrays.
- **Other pain conditions:** Traditionally, it is also used to treat headaches and toothaches.

Other medicinal applications

- **Infections:** Used to address viral and fungal infections.
- **Gastrointestinal issues:** A decoction of the bark is traditionally taken to help prevent diarrhea.
- **Fertility and vitality:** It is used as a male aphrodisiac and tonic and has been used to increase female fertility in cases of male impotency.
- **Respiratory ailments:** Leaves prepared as a decoction are used for coughs.
- **Blood sugar:** Some traditional practitioners use the plant to help balance blood sugar levels in people with diabetes.

Preliminary scientific findings

While human clinical data is scarce, some initial laboratory and animal studies have explored the potential effects of *Alchornea castaneifolia*.

- **Phytochemical composition:** Preliminary analysis reveals the plant contains a variety of compounds, including steroids, saponins, phenols, flavonoids, tannins, xanthones, and alkaloids.
- **Anti-inflammatory effects:** Some studies on mice found that ethanol extracts of the bark could reduce swelling and inflammation. This effect has been partially

attributed to the inhibition of prostaglandins, which are involved in the body's inflammatory response.

- **Antimicrobial properties:** In vitro studies have suggested that ethanol extracts possess antifungal and antiviral activity, though no antibacterial or antiyeast effects were observed in the tested strains.
- **Potential anti-tumor activity:** Limited in vitro testing has shown some preliminary anti-tumor activity.

Safety and considerations

- **Limited evidence:** The uses and benefits of *Alchornea castaneifolia* are based primarily on traditional medicine and anecdotal reports. There is a lack of robust scientific evidence and human clinical trials to confirm its effectiveness or safety.
- **Uncertainty and risk:** As with many herbal supplements, there is insufficient reliable information on potential side effects, safe dosages, or drug interactions.
- **Potential toxicity:** In the case of a different species, *Alchornea cordifolia*, there have been reports of toxicity at high doses, including liver damage and adverse side effects, particularly in children. While no known hazards have been documented for *A. castaneifolia* specifically, the potential for toxicity exists, particularly with concentrated extracts.
- **Regulation:** Herbal products are not strictly regulated, so product quality, dosage, and purity can vary widely.

Alkaloids found in *Alchornea castaneifolia*

Alchornea castaneifolia, also known as iporuru, contains a variety of phytochemicals, with alkaloids being one of the key classes of compounds identified. While extensive research is still needed to fully document its chemical profile, initial analyses have identified specific types of alkaloids. The anti-inflammatory effects of iporuru are partly attributed to these compounds.

Imidazopyrimidine alkaloids

The most prominent alkaloids identified in *Alchornea* species are imidazopyrimidine alkaloids.

- **Alchorneine:** This is the most well-documented alkaloid found in *A. castaneifolia* and is present in the bark and leaves. It is a major alkaloid in the stem and root bark of related species like *A. floribunda*, suggesting its importance across the genus. Its potential anti-inflammatory properties have been linked to the traditional uses of the plant.
- **Isoalchorneine and alchorneinone:** These alkaloids are also found in the leaves and root bark of *Alchornea* species, including *A. floribunda*, and are likely present in *A. castaneifolia* as well.

Guanidine alkaloids

Other species in the *Alchornea* genus, such as *A. rugosa* and *A. cordifolia*, have yielded different types of alkaloids, including guanidine alkaloids. These compounds have also demonstrated antibacterial and anti-inflammatory activity. While not specifically confirmed for *A. castaneifolia*, their presence in closely related species suggests they could contribute to the plant's overall alkaloid composition.

Broader chemical context

It is important to note that the effects of iporuru likely result from a synergy of its various phytochemicals, not just the alkaloids alone. As noted in the initial summary, the plant also contains:

- Flavonols and flavones
- Phenols
- Tannins
- Xanthones

- Saponins
- Steroids

For example, flavonoids and tannins also contribute to anti-inflammatory and antioxidant activities, which could enhance or complement the effects of the alkaloids.

Summary of research on alkaloids

- **Identification is ongoing:** Because little research has been dedicated to comprehensively cataloging the phytochemicals in *A. castaneifolia*, a complete alkaloid profile is still unknown.
- **Inter-species variation:** Most data comes from related *Alchornea* species, which may have slightly different chemical compositions.
- **Activity links:** The known alkaloids, such as alchorneine, have been connected to the plant's anti-inflammatory properties, but further investigation is required.
- **Synergistic effects:** The biological effects of iporuru are likely due to the combined action of its alkaloids with other bioactive compounds.

While alchorneine has been identified as a key alkaloid in *Alchornea castaneifolia* responsible for its anti-inflammatory effects, the precise cellular and molecular mechanism by which it acts has not been fully detailed in existing scientific literature. However, research on the anti-inflammatory activity of the plant's extracts, which contain alchorneine, suggests a few possible mechanisms.

Potential anti-inflammatory mechanisms

Inhibition of prostaglandin synthesis

One of the most referenced mechanisms is the inhibition of prostaglandin synthesis. Prostaglandins are lipid compounds that play a major role in the body's inflammatory

response. They are produced at sites of tissue damage and infection, where they cause inflammation, blood flow changes, and pain signaling.

- The synthesis of prostaglandins is mediated by cyclooxygenase (COX) enzymes, particularly COX-2.
- By inhibiting the enzymes responsible for creating prostaglandins, alchorneine would effectively reduce the body's inflammatory response and associated pain.
- This mechanism is the same as that used by non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen.

Regulation of inflammatory mediators

Studies on related *Alchornea* species have explored the broader anti-inflammatory actions of their extracts, which contain various bioactive compounds, including alkaloids. These studies suggest that the plant's compounds may act on several inflammation pathways simultaneously. For example:

- **Leukocyte migration:** Extracts of *Alchornea* have been shown to inhibit the migration of leukocytes (white blood cells) to the site of inflammation. This is a crucial step in the inflammatory cascade, and by limiting it, the plant's compounds can help reduce swelling.
- **Cytokine modulation:** Some research indicates that plant alkaloids can inhibit the release of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukins (e.g., IL-6, IL-1β). These signaling molecules are central to orchestrating the inflammatory response.

Antioxidant effects

While not a primary mechanism attributed to alchorneine, the plant extracts demonstrate significant antioxidant activity. Since inflammation involves the production of reactive oxygen species (ROS), the plant's antioxidant compounds, including

flavonoids, can help scavenge these harmful molecules and reduce tissue damage that can exacerbate inflammation.

Importance of synergy

It is important to emphasize that the anti-inflammatory effect of *Alchornea castaneifolia* is likely a result of the synergistic action of multiple compounds, including alchorneine, other alkaloids, flavonoids, and tannins. For instance, a 2003 study on *Alchornea cordifolia* (a related species) concluded that its anti-inflammatory activity could not be attributed to a single compound or class of compounds.

Summary of alchorneine's anti-inflammatory action

- **Primary proposed mechanism:** Inhibition of prostaglandin synthesis, likely by targeting enzymes like COX-2.
- **Supporting mechanisms from plant extract studies:** Modulation of leukocyte migration and inhibition of pro-inflammatory cytokines.
- **Contributing factor:** Antioxidant effects from other compounds in the plant.
- **Ongoing research:** The exact mechanism of alchorneine specifically, separate from other plant compounds, is still not fully characterized in scientific studies.

Besides alchorneine, the primary imidazopyrimidine alkaloids found in *Alchornea castaneifolia* are its stereoisomer, **isoalchorneine**, and a related compound, **alchorneinone**. These compounds share a similar core imidazopyrimidine structure but differ in their chemical arrangements.

Identified imidazopyrimidine alkaloids

- **Isoalchorneine:** This is a stereoisomer of alchorneine, meaning it has the same atoms connected in the same sequence but a different spatial orientation. In

1989, scientists successfully synthesized both alchorneine and isoalchorneine, confirming their structural relationship. The presence of this compound in *A. castaneifolia* alongside its isomer contributes to the plant's overall alkaloid profile.

- **Alchorneinone:** This alkaloid has also been identified in some species of the *Alchornea* genus. Like the other imidazopyrimidines, it is a derivative of the same fundamental chemical structure. Research on related species, such as *Alchornea floribunda*, has also documented its presence in the leaves and root bark.

Context within the *Alchornea* genus

Scientific research on the phytochemistry of the *Alchornea* genus, especially on species like *A. castaneifolia*, is not extensive. Therefore, most of the information regarding its specific imidazopyrimidine alkaloids is based on limited studies and extrapolation from research on closely related species, such as *Alchornea floribunda* and *Alchornea cordifolia*.

It is important to remember that:

- The exact quantities and proportions of these alkaloids can vary depending on factors such as the plant's age, the specific part used (bark, leaves, or roots), and the environmental conditions where it was grown.
- The overall medicinal effect of *Alchornea castaneifolia* is likely due to the synergistic action of its entire cocktail of bioactive compounds, which includes not only these alkaloids but also flavonoids, tannins, and saponins.

Scientific studies have not yet determined the precise, molecular-level interaction between alchorneine and the cyclooxygenase-2 (COX-2) enzyme. Much of the current understanding is based on studies of broader *Alchornea* plant extracts, which contain alchorneine along with other anti-inflammatory compounds. The observed

anti-inflammatory effects of these extracts strongly suggest that alchorneine is a key contributor to COX-2 inhibition.

Proposed mechanisms of interaction

The potential ways alchorneine interacts with COX-2 are inferred from general knowledge of how other small molecules inhibit this enzyme, particularly non-steroidal anti-inflammatory drugs (NSAIDs).

Inhibition within the enzyme's binding pocket

COX-2 inhibition occurs when a molecule interferes with the binding and processing of arachidonic acid (AA). AA is the fatty acid precursor that COX enzymes convert into prostaglandins, the lipid compounds that trigger inflammation, pain, and fever.

- **Direct blockade:** Alchorneine may act as a competitive inhibitor, entering the hydrophobic channel of the COX-2 enzyme and blocking AA from binding to the active site.
- **Targeting specific residues:** Molecular docking studies of other plant-derived compounds indicate that inhibition often involves hydrogen bonds with key amino acid residues, such as arginine, tyrosine, and serine, within the COX-2 active site. Alchorneine likely forms similar bonds that alter the enzyme's structure and prevent it from functioning correctly.

Stereoselective action

The existence of stereoisomers like alchorneine and isoalchorneine in *Alchornea* plants suggests that the anti-inflammatory effect could be stereoselective. This means the specific three-dimensional shape of alchorneine might be a better fit for inhibiting COX-2 than other, structurally similar alkaloids.

Potential for selectivity over COX-1

Conventional NSAIDs are non-selective and inhibit both COX-1 and COX-2. While COX-2 inhibition reduces inflammation, COX-1 inhibition is responsible for side effects like gastrointestinal and renal problems. The ability of some herbal compounds to selectively inhibit COX-2 is a major area of research. While not confirmed, alchorneine's structure could theoretically allow it to fit more precisely into the larger active site of COX-2 while sparing COX-1, making it a safer anti-inflammatory agent.

Scientific limitations

- **Indirect evidence:** The evidence for alchorneine's interaction with COX-2 primarily comes from the anti-inflammatory effects of crude *Alchornea* extracts. This research shows that the extracts inhibit prostaglandin synthesis, but it does not isolate the specific contribution of alchorneine.
- **Lack of dedicated studies:** There have been very few, if any, scientific studies dedicated solely to isolating alchorneine and testing its direct inhibitory effects and mechanism on purified COX-2 enzyme in a laboratory setting.
- **Synergistic effects:** The final anti-inflammatory effect of *Alchornea castaneifolia* is likely a result of the synergistic interactions of multiple phytochemicals. Flavonoids, tannins, and other alkaloids present in the plant may work together with alchorneine to amplify its effect. This means isolating alchorneine may not replicate the full medicinal action of the whole plant.

As of late 2025, there are no specific, published scientific studies that have isolated the alkaloid alchorneine from *Alchornea castaneifolia* and tested its direct inhibitory effects and mechanism on purified cyclooxygenase-2 (COX-2) enzyme in a laboratory setting.

The anti-inflammatory effects of alchorneine on COX-2 are currently understood through indirect evidence from related research:

- **Studies on crude plant extracts:** The majority of scientific evidence comes from studies on crude or fractionated extracts of *Alchornea* species. These studies show that the extracts, which contain alchorneine among other compounds, can inhibit prostaglandin synthesis. However, they do not isolate the specific contribution of alchorneine versus the synergistic effects of the plant's full chemical profile. For example, a 2003 study on *Alchornea cordifolia* extracts found that the anti-inflammatory effect could not be attributed to a single compound or class of compounds.
- **Identification of anti-inflammatory properties:** Phytochemical analysis has identified that alkaloids, along with terpenoids, flavonoids, and saponins, are present in the plant and contribute to its medicinal properties.
- **Research on other natural inhibitors:** Scientists have conducted specific research on other natural compounds and their interactions with COX-2. These studies, which do not involve alchorneine, provide a model for how such investigations would be conducted.
- **Importance of isolated studies:** As highlighted in broader pharmacological research, verifying the activity of a specific compound within an extract is crucial. This involves isolating the compound and testing it independently to confirm its effect and understand its mechanism of action.

Future research opportunities

The anti-inflammatory properties of alchorneine present a promising area for future pharmacological research.

- **Purification and testing:** Isolating pure alchorneine would enable targeted studies using purified COX-2 enzymes to confirm its inhibitory effects and evaluate its selectivity for COX-2 over COX-1, which is key for a safer anti-inflammatory drug.

- **Molecular modeling:** *In silico* (computer-based) molecular docking studies could be used to model and predict the specific binding interactions between the alchorneine molecule and the COX-2 enzyme's active site.
- **Mechanistic studies:** Further research is needed to understand the downstream effects of alchorneine's interaction with the COX pathway, such as its impact on pro-inflammatory cytokines like TNF-α and interleukins.

Alchorneine

and isoalchorneine are stereoisomers, meaning they share the same chemical formula (

C12H19N3Ocap C sub 12 cap H sub 19 cap N sub 3 cap O

C12H19N3O) and connectivity of atoms but differ in the three-dimensional arrangement of those atoms. Specifically, they are diastereomers due to having more than one stereocenter, and their differences in spatial orientation give them distinct properties.

Stereocenters

Both molecules contain two key stereocenters in their bicyclic imidazopyrimidine core structure. A stereocenter is an atom with a chiral configuration, meaning it is bonded to four different substituents. The spatial arrangement of these substituents determines the molecule's absolute configuration (R/S).

The main structural differences arise from the arrangement of the isopropenyl (

CH2=C(CH3)cap C cap H sub 2 equals cap C open paren cap C cap H sub 3 close paren

$CH2=C(CH3)$) and methoxy (

OCH3cap O cap C cap H sub 3

$OCH3$) side chains relative to the rest of the molecule. The specific configuration of these groups at the stereocenters distinguishes alchorneine from isoalchorneine.

Synthesis and confirmation

The relationship between alchorneine and isoalchorneine has been confirmed through synthesis. For example, a 1989 report by the Büchi group describes the total synthesis of both (±)-alchorneine and (±)-isoalchorneine, confirming that they are stereoisomers.

Biological implications

The subtle structural differences between stereoisomers can have significant impacts on their biological activity.

- **Receptor binding:** The distinct three-dimensional shape of each stereoisomer can affect how it binds to proteins and enzymes, such as COX-2. Even small changes in shape can prevent a molecule from fitting into a receptor's binding pocket, altering its effect.
- **Enzyme activity:** Some stereoisomers of drug molecules can be highly effective, while others are inactive or may even produce undesirable side effects. This stereoselectivity is likely a key factor in the anti-inflammatory properties of alchorneine.

Summary

The core difference between alchorneine and isoalchorneine is in their stereochemistry:

- They possess the same atoms and atom-to-atom connections.
- They differ in the spatial orientation of substituent groups around one or more chiral centers.
- This difference in 3D structure is responsible for the unique properties of each molecule, which can lead to different pharmacological activities.

Currently, there are no specific, published studies on the side effects of isolated alchorneine. Information on the safety and potential side effects is therefore extrapolated from toxicology studies on crude extracts of related *Alchornea* species and from anecdotal reports of traditional use.

Extrapolated side effects from *Alchornea* species

Most toxicity research has focused on the more widely studied *Alchornea cordifolia*, but this information provides insight into the potential effects of compounds like alchorneine present in the genus.

Liver toxicity at high doses

- **High-dose risks:** Animal studies on *Alchornea cordifolia* extract have shown evidence of liver damage at high concentrations. For example, mice treated with 2000 mg/kg of extract showed signs of hepatic injury, such as aggregates of lymphocytes, eosinophilia, and pyknosis. Another study on rats found that high doses (800 mg/kg and 1600 mg/kg) caused elevated markers of liver damage.
- **Reversible damage:** Some liver damage observed in animal studies appeared to be reversible after cessation of the extract.

Gastrointestinal issues

- **Effect of saponins:** The presence of saponins in *Alchornea* extracts may be responsible for gastrointestinal side effects. An acute toxicity study on *A. cordifolia* leaf extract noted soft feces and temporary loss of appetite in animals.
- **Traditional uses:** Traditional uses of *Alchornea* often involve preparations that can cause vomiting or diarrhea, especially in higher doses, as some compounds act as purgatives or emetics.

Central nervous system effects

- **Behavioral changes:** Animal studies using crude extracts have reported central nervous system effects, including decreased mobility and reduced sensitivity to stimuli, which may be a sedative or depressant effect.
- **Individual sensitivity:** A study on another species, *Alchornea laxiflora*, noted a possible pro-oxidative effect at high doses and "individual drug reactions and idiosyncrasies," though this was not specifically tied to alchorneine.

Caution for specific groups

- **Pregnant and breastfeeding individuals:** There is insufficient data to determine the safety of alchorneine and *Alchornea* extracts during pregnancy and breastfeeding. It is recommended to avoid use in these cases.
- **Drug interactions:** The potential for alchorneine to interact with other medications is unknown due to the lack of dedicated research.