

# Pao Pereira Monograph

**NB:** This monograph is designed to provide historical background and an overview of past and current scientific research. This information should not be interpreted as medical advice.

Consult with a qualified healthcare provider regarding therapies, diagnosis and possible treatment.

#### **Related Terms**

Alkaloid; Flavopereirine; Geissospermine; PB 100; Beta-Carboline; Produit Beljanski; a Beljanski Product

# **Background**

On December 7, 1848, Ezequiel Correa Dos Santos presented his thesis "Monographia do Geissospermum vellosii vulgo Pao Pereira" at the Faculty of Medicine of Rio de Janeiro. This document has come to be regarded as the first official monography on the benefits of Pao pereira.

In 1879 the journal Medical Times (Vol. X p. 276 – Philadelphia) published a two-page article devoted to Pao pereira. After a description of the method for extracting the alkaloid pereirina, Dr. Torres Homem, Professor of Clinical Medicine at the Academy of Rio de Janeiro state, "There is not a doctor in Brazil who has not obtained good results from the use of this bark ....".

# Reference

Monographia Do Geissospermum Vellosii Vulgo Pao Pereira

Ezequiel C. Dos Santos

Typographia do Archivo Medico Brasiliero, Faculdade de Medicina do Rio de Janeiro, sustentada em 7 de dezembro de 1848.

# **Scientific Name and Taxonomy**

Geissospermum vellosii Allemão (Apocynacae)

Synonyms: Geissospermum laeve (Vell.) Miers, Geissospermum martianum Miers, Tabernaemontana laevis Vell., pao pereira, pau pereira, quinarana.

## Reference

TPL – The Plant List. Version 1.1. Published on the Internet URL: <a href="www.theplantlist.org/">www.theplantlist.org/</a>; Retrieved Sept. 18th, 2015.

### **Botanical Description**

A leafy tree, reaching a height of 22m. The trunk is 25cm to 50cm, ranging from light brown to yellow in color. The bark peels off continuously. Lorenzi (2002) reports that this genus produces latex in the fruit and in the extremities of the branches. Numerous bright flowers appear at the apex of these branches. The fruits are elongated berries, fleshy pulp, bitter taste, containing from 5 to 15 seeds.

### References



# Arnivores Brasilieras: Manual De Identificação E Cultivo De Plantas Arbóreas Do Brasil.

Lorenzi, H.

Vol 2, 4. ed. Nova Odessa, 2002 SP: Instituto Plantarum. V. 2.

# Catalogo de plantas e fungos do Brasil.

Forzza, R. C. (Org.).

Rio de Janeiro: Andrea Jakobsson, Est.dio: Instituto de Pesquisa do Jardim Botânico do Rio de Janeiro, 2010. v. 1.

## A Description Of G.Laeve Bark Is Found In The First Edition Of The Brazilian Pharmacopeia.

Associação de Amigos do Jardim Botanico

N° 35-(2) Albino R (1926). Pharmacopeia of the United States of Brazil - 2013.

 $\underline{http://www.amigosjb.org.br/wp-content/uploads/2013/09/Flora\%C3\%A7\%C3\%A3o-Setembro-Outubro-20130.pdf}$ 

### Geolocalization

Pao pereira is native to Bolivia, Brazil, French Guyana, Guyana, and Suriname.

## References

TPL – The Plant List. Version 1.1. Published on the Internet URL: <a href="www.theplantlist.org/">www.theplantlist.org/</a>; Retrieved Sept. 18th, 2015.

WCSP. 2014. World Checklist of Selected Plant Families. Facilitated by the Royal Botanic Gardens, Kew. Published on the Internet; wcsp/Retrieved Sept. 18th, 2015.

Torpicos® Botanical Garden Database. Published in the Internet. URL <a href="http://www.tropicos.org/Name/1802715?tab=distribution">http://www.tropicos.org/Name/1802715?tab=distribution</a>; Retrieved Sept. 18th, 2015.

### **Management and Harvesting**

Pao pereira is a perene specie, which grows spontaneously <sup>(1)</sup>. The seedlings can be obtained directly from seed, requiring no treatment. The shoots emerge from between 30 and 50 days and should be kept in half light, the germination rate is generally above 50 %. <sup>(2)</sup>. The bark naturally sheds and constantly regenerates <sup>(3)</sup>, therefore there is no need to cut the tree to collect the bark.

### References

(1) <u>Incidência De Pragas E Doenças Em Agroecossistemas De Café Orgânico De Agricultores Familiars Em Poço Fundo-Mg.</u>

P. Martins. M. et al.

Ciênc. agrotec., Lavras, v. 28, n. 6, p. 1306-1313, nov./dez., 2004 - page 1308

(2) Arnivores brasilieras: manual de identificação e cultivo de plantas arbóreas do Brasil.

H. Lorenzi

Vol 2, 4. ed. Nova Odessa, 2002, SP: Instituto Plantarum. V. 2.



# (3) A description of G.laeve bark is found in the first edition of the Brazilian Pharmacopeia.

# Associação de Amigos do Jardim Botanico

N° 35-(2) R. Albino (1926). Pharmacopeia of the United States of Brazil, 2013.

http://www.amigosjb.org.br/wp-content/uploads/2013/09/Flora%C3%A7%C3%A3o-Setembro-Outubro-20130.pdf

### Traditional Use

Considered one of the 10 most useful Brazilian trees in phytomedicine.<sup>(1)</sup> This plant is part of Brazil's history of natural products because the first alkaloid in the country was isolated from its bark by Ezequiel Corrêa dos Santos, the patron of Brazilian pharmacists.<sup>(2)</sup> In South America, the bark of *Geissospermum laeve (Vell.) Miers* either in powder or splinter form, is sold in markets, newsstands and herbal stores as febrifuge to relieve indigestion and stimulate appetite.<sup>(3)</sup> It is also used as an alternative treatment for malaria.<sup>(4)</sup>

#### References

(1) The ten most useful trees genuinely Brazilian medicine

Peckolt G

Rev. Flora Med., 1942, 9: 453-470.

(2) Pereirina: The first alkaloid isolated in Brazil?

MR Almeida; Lima JA, Santos NP, Pinto AC

Braz. J. Pharmacogn., 2009, 19: 942-952.

(3) Dictionary of useful plants from Brazil and exotic crops.

Pio Corrêa M

Brasilia: Brazilian Institute for Forestry Development - 1984

(4) Antimalarial Remedies In French Guiana: A Knowledge Attitudes And Practices Study.

M. Vigneron, X. Deparis, E. Deharo, G. Bourdy.

Journal of Ethnopharmacology, Volume 98, Issue 3, 26 April 2005, Pages 351–360.

### **Modern Use**

In Europe, it has been recommended as a tonic and a febrifuge since 1933.<sup>(1)</sup> In South America, it is used preventively to reinforce the immune system.<sup>(2)</sup> In the USA it is distributed as a dietary supplement by Maison Beljanski and statements of nutritional support have been filed with the FDA.<sup>(3)</sup> There is also recent interest in a possible improvement of memory deficit<sup>(4)</sup> as well as antiF cancer activity<sup>(5)</sup> and antiF viral properties.<sup>6</sup>

#### References

(1) Medicamenta, Guida Teorico-pratica per Sanitari

Dizionario dei Medicamenti 1933, p. 2389.

(2) A Search For Natural Bioactive Compounds In Bolivia Through A Multidisciplinary Approach.

V. Munoz, M. Sauvain, G. Bourdy, J Callapa, et al.



Journal of Ethnopharmacology, 2000;69(2):127-137.

# (3) U.S. Food and Drug Administration

(2003) http://www.fda.gov/ohrms/dockets/dailys/03/Nov03/110403/97s-0162-let11462-vol88.pdf.

(4) <u>Geissospermum Vellosii Stembark Anticholinesterase Activity And Improvement Of Scopolamine-</u>Induced Memory Deficits.

Lima J. A. et al.

Pharmacology, Biochemistry and Behavior. 2009, Vol. 92, 508-513.

(5) The Plant Extract Of Pao Pereira Potentiates Carboplatin Effects Against Ovarian Cancer.

Yu J, Chen Q.

Pharm Biol. 2014 Jan;52(1):36-43. doi: 10.3109/13880209.2013.808232. Epub 2013 Sep 13. http://www.ncbi.nlm.nih.gov/pubmed/24033267

(6) Tolerance and Feasibility of a 12-Month Therapy Using the Antiretroviral Agent PB 100 in AIDS-Related. D. Complex Patients

D. Donadio, et al.

Dtsch. Zschr. Onkol. 26(6):145-149, 1994.

# **Toxicity**

The bark of Geissospermum contains numerous alkaloids<sup>(1)</sup>, and the extraction process is key to the safety of the extract.<sup>(2)</sup> The most important alkaloid isolated from G. laeve is geissospermine. Isolated for the first time by O. Hesse in 1877.<sup>(3)</sup> Geissopermine was subjected to acid hydrolysis and yielded cleavage products geissoschizine, apogeissoschizine and geissoschizoline. Geissospermine is considered poisonous by subcutaneous, intravenous, and intraperitoneal routes. Moderately toxic by ingestion.<sup>(4)</sup> Geissospermine rich extracts have been used as one of the ingredients of Indian arrow-poisons by native Indian tribes in Brazil.<sup>(5)</sup> M. Beljanski was first to extract Flavopereirine from G. Laeve bark.<sup>(6)</sup> Beljanski's Flavopereirine-rich extract has a good safety record. Toxicity studies were submitted to the FDA by Natural Source International (Viva) as part of a New Dietary Ingredient notification<sup>(7)</sup> and the good tolerance of the product was also demonstrated in preclinical studies<sup>(8)</sup>, as well as in humans, including immunodeficients.<sup>(9)</sup> No public data available from other suppliers.

# References

(1) <u>Isolation And Structural Elucidation Of Indole Alkaloids From Geissospermum Vellosii By Mass Spectrometry</u>

Flaubert Mbeunkui and al.

Journal of chromatography. B, Analytical technologies in the biomedical and life sciences(Impact Factor: 2.69). 02/2012; 885-886:83-9. DOI: 10.1016/j.jchromb.2011.12.018

(2) <u>Alkaloids Of Geissospermum Vellosii. Further Studies On Geissospermine And The Structures Of The Indolic Cleavage Products, Geissoschizine And Apogeissoschizine.</u>

Henry Rapoport, Richard J. Windgassen Jr., Neil A. Hughes, Thomas P. Onak J. Am. Chem. Soc., 1960, 82 (16), pp 4404–4414



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Annales Pharmaceutiques Françaises, 1959, v. 17, p. 626-633.

(4) Lookchem®, Professional Database Of Chemicals And Molécules,

Retrieved in 2015 form: http://www.lookchem.com/Geissospermine/

(5) Bulletin of the New York Botanical Garden,

Volumes 11-12 New York Botanical Garden 1921 – Botany, P 123.

(6) Flavopereirine-Based Pharmaceutical Composition For Treatment Of HIV Infection.

Beljanski, M.

W09402146 A1, February 3, 1994.

(7) U.S. Food and Drug Administration

Retrieved form: http://www.fda.gov/ohrms/dockets/dockets/95s0316/rpt0005\_02.pdf

(8) The Plant Extract Of Pao Pereira Potentiates Carboplatin Effects Against Ovarian Cancer.

Yu J, Chen Q.

Pharm Biol. 2014 Jan;52(1):36-43. doi: 10.3109/13880209.2013.808232. Epub 2013 Sept 13. http://www.ncbi.nlm.nih.gov/pubmed/24033267

(9) <u>Tolerance and Feasibility of a 12-Month Therapy Using the Antiretroviral Agent PB 100 in AIDS-Related. D. Complex Patients</u>

D. Donadio, et al.

Dtsch. Zschr. Onkol. 26(6):145-149, 1994.

### **Mechanism of Action**

*Pao pereira* exerts three different mechanisms of action:

- It selectively induces apoptosis in destabilized cells.<sup>1</sup>
- It also seems able to reduce inflammation.<sup>2</sup>
- It has anti-viral activity.3

### References

(1) B-Carboline Alkaloid-Enriched Extract from the Amazonian Rain Forest Tree Pao Pereira Suppresses Prostate Cancer Cells

Debra L. Bemis, PhD; Jillian L. Capodice, LAc, MS; Manisha Desai, PhD; Aaron E. Katz, MD; Ralph Buttyan, PhD

Journal of the Society for Integrative Oncology, 2009, Vol 7, No2.

<sup>(2)</sup> Pao Pereira Extract Suppresses Castration- Resistant Prostate Cancer Cell Growth, Survival And Invasion Through Inhibition Of Nfkb Signaling



Cunjie Chang, BS; Wei Zhao, MS, Bingxian Xie, BS,;Yongming Deng, BS, Tao Han, BM; Yangyan Cui, BS, Yundong Dai, BS; Zhen Zhang, BS; Jimin Gao, MD, PhD; Hongqian Guo, MD, PhD; and Jun Yan, PhD. Integrative Cancer Therapies 2013, Vol XX(X) 1-10.

(3) <u>Tolerance and Feasibility of a 12 Month Therapy Using the Antiretroviral Agent PB100 in AIDS-Related Complex Patients</u>

D. Donadio, G. Pontello, T Nawrocki, J. E. Causse. Journal of Oncology, 1994, Vol 26, No.6 (145-149).

#### Possible Interactions

There are no reports of adverse effects in humans in current literature.

High doses (200 mg/kg) of *Pao pereira* extracts have anticholinergic activity and caused convulsions and death in animals. (1)

### References

(1) <u>Geissospermum Vellosii Stembark: Anticholinesterase Activity And Improvement Of Scopolamine-Induced Memory Deficits</u>

Lima JA, Costa RS, Epifanio RA, et al.

Pharmacol Biochem Behav. May 2009;92(3):508-513.

# **Side Effects/Contraindication**

- Side Effects: none known
- Contraindications: none known
- Interactions:
  - o Interactions with Herbs & Supplements: none known
  - o Interactions with Drugs: *Pao pereira* offers a synergistic effect that may enhance the effect of chemotherapy and allow for reduced toxicity. (1,2)
  - o Interactions with Lab Tests: none known

#### References

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(2) <u>Inhibition of Pancreatic Cancer and Potentiation of Gemcitabine Effects by the Extract of Pao Pereira</u> Jun Yu, PhD., Jeanne Drisko, PhD. and Qi Chen, PhD. Oncology Reports" (vol.30 n°1, pp 149-156, July 2013 – Doi: 10.3892/or.2013.2461)

# **Allergies and Warnings**

Avoid with known allergy or hypersensitivity to *Pao pereira*, its constituents, or other members of the Apocynaceae family



Interaction with food, other drugs or other dietetic products No known interactions

Statement of the manufacturer that there are no GMO or BSE/TSE issues: No GMO/BSE/TSE with PAO  $\,$  V® or PAO V "FM"®

# **Dosage/Administration**

Protocols have been published. (1)

# Reference

(1) Morton Walker, D.P.M. (2012) Cancer's Cause, Cancer's Cure. Austin, TX: Hugo House Publishing;

### **Author Information**

This information is based on a systematic review of scientific literature edited and peer-reviewed by contributors to The Beljanski Foundation.