References on Guacatonga (*Casearia sylvestris*) from Part 3 of Fighting Cancer with Plants from the Rainforest By Leslie Taylor

The published research referenced in the book which is shown below will include the initials **HS**, **IVT**, **IVA**, **REV**, **INS**, **REV** and **NEW**. HS refers to research conducted in humans; IVT refers to *in vitro* research conducted inside of test tubes; IVA refers to *in vivo* research conducted in animals; REV refers to a review article that evaluated and summarizes multiple studies on the subject; INS refers to *in silico* research (newer computer modeling including molecular docking studies) and NEW refers new biological research methods which determine genes and signaling pathways, and molecular pathways of actions which were developed during and after the Human Genome Project discussed in chapter 4.

This research below was last updated in August 2025. To view research published after that time, follow these links to the National Institute of Health's National Library of Medicine on **Guacatonga**.

Cancer Research on Guacatonga

Review Articles:

Carvalho, F., et al. "Casearia essential oil: An updated review on the chemistry and pharmacological activities." *Chem. Biodivers.* 2023 Sep; 20(9): e202300492.

Martínez-Casares, R., et al. "Anti-inflammatory and cytotoxic activities of clerodane-type diterpenes." *Molecules*. 2023 Jun; 28(12): 4744.

Michalak, I., et al. "Look into my onco-forest - Review of plant natural products with anticancer activity." *Curr. Top. Med. Chem.* 2022; 22(11): 922-938.

Konrath, E., et al. "The potential of Brazilian native plant species used in the therapy for snakebites: A literature review." *Toxicon*. 2022 Oct; 217: 17-40.

Acquaviva R., et al. "Advances on natural abietane, labdane and clerodane diterpenes as anti-cancer agents: Sources and mechanisms of action." *Molecules*. 2022 Jul; 27(15): 4791.

Cortelo P., et al. "A molecular networking strategy: high-throughput screening and chemical analysis of Brazilian Cerrado plant extracts against cancer cells. *Cells*. 2021 Mar; 10(3): 691.

Ferreira, P., et al. "Folk uses and pharmacological properties of *Casearia sylvestris*: a medicinal review." *An Acad Bras Cienc.* 2011 Dec; 83(4): 1373-84.

Saleem, M. "Lupeol, a novel anti-inflammatory and anti-cancer dietary triterpene." *Cancer Lett.* 2009; 285(2): 109-15.

Guil-Guerrero, J., et al. "Cytotoxicity screening of endemic plants from Guayana highlands." *Trop. Biomed.* 2009 Aug; 26(2): 149-54.

Test Tube Studies on Multiple Cancer Cell Lines:

Yang, M., et al. "Potential function of loliolide as a novel blocker of epithelial-mesenchymal transition in colorectal and breast cancer cells." *Cell Signal.* 2023 May; 105: 110610. (**IVT**)

Park, S., et al. "Oxidative stress-protective and anti-melanogenic effects of loliolide and ethanol extract from fresh water green algae, *Prasiola japonica*." *Int. J. Mol. Sci.* 2018 Sep; 19(9): 2825. (**IVT**)

Ferreira-Silva, G., et al. "Casearin D inhibits ERK phosphorylation and induces downregulation of cyclin D1 in HepG2 cells." *Toxicol. In Vitro.* 2017 Feb; 38: 27-32. (**IVT**)
Ferreira, P., et al. "Preclinical anticancer effectiveness of a fraction from *Casearia sylvestris* and its component casearin X: In vivo and ex vivo methods and microscopy examinations." *J. Ethnopharmacol*. 2016; 186: 270–279. **(IVT, IVA**).
Bou, D., et al. "Dinor Casearin X, a new cytotoxic clerodane diterpene from *Casearia sylvestris*." *J. Braz. Chem. Soc.* 2015; 26(8): 1725-1729, 2015. (**IVT**)
Ferreira-Silva, G., et al. "Morphological and biochemical alterations activated by antitumor clerodane diterpenes." *Chem. Biol. Interact.* 2014 Oct; 222: 112-25. (**IVT**)
Bou, D., et al. "Chemical composition and cytotoxicity evaluation of essential oil from leaves of *Casearia sylvestris*, its main compound α-zingiberene and derivatives." *Molecules*. 2013 Aug; 18(8): 9477-87. (**IVT**)
Ismail, M., et al. "Anticancer properties and phenolic contents of sequentially prepared extracts from different parts of selected medicinal plants indigenous to Malaysia." *Molecules*. 2012 May; 17(5): 5745-56. (**IVT**)
Vieira-Júnior, G., et al. "Cytotoxic clerodane diterpenes from *Casearia rupestris*." *J. Nat. Prod.* 2011 Apr; 74(4): 776-81. (**IVT**)
dos Santos, A., et al. "Casearin X, its degradation product and other clerodane diterpenes from leaves of *Casearia sylvestris*: evaluation of cytotoxicity against normal and tumor human cells." *Chem. Biodivers.* 2010 Jan; 7(1): 205-15. (**IVT**)
de Mesquita, M., et al. "Cytotoxic activity of Brazilian Cerrado plants used in traditional medicine against cancer cell lines." *J. Ethnopharmacol.* 2009 Jun; 123(3): 439-45. (**IVT**)
Vieira, G., et al. "Cytotoxic clerodane diterpenoids from *Casearia obliqua*." *J Nat Prod.* 2009 Oct; 72(10): 1847-50. (**IVT**)
Guil-Guerrero, J., and Campra, P. "Cytotoxicity screening of endemic plants from Guayana highlands." *Trop. Biomed.* 2009 Aug; 26(2): 149-54. (**IVT**)
Balunas, M., et al. "Relationships between inhibitory activity against a cancer cell line panel, profiles of plants collected, and compound classes isolated in an anticancer drug discovery project." *Chem. Biodivers.* 2006; 3(8): 897-915. (**IVT**)
Shen, Y., et al. "Cytotoxic clerodane diterpenoids from *Casearia membranacea*." *J. Nat. Prod.* 2005; 68(11): 1665-8. (**IVT**)
Maistro, E., et al. "Evaluation of the genotoxic potential of the *Casearia sylvestris* extract on HTC and V79 cells by the comet assay." *Toxicol. In Vitro*. 2004 Jun; 18(3): 337-42. (**IVT**)
Oberlies, N., et al. "Novel bioactive clerodane diterpenoids from the leaves and twigs of *Casearia sylvestris.*" *J. Nat. Prod*. 2002; 65(2): 95-99. (**IVT**)
Almeida, A. "Antitumor and anti-inflammatory effects of extract from *Casearia sylvestris*: comparative study with Piroxicam and Meloxicam." Instituto de Ciencias Biomedicas, University of Sao Paulo (Dissertation, 4/02/99). (**IVT**)
Itokawa, H., et al. "Antitumor substances from South American plants." *J. Pharmacobio. Dyn.* 1992; 15(1): S-2. (**IVT**)

Animal Studies on Anti-Tumorous Actions of Multiple Chemicals or Multiple Cancers (breast, colon, glioblastoma, sarcoma, melanoma cancers):

Francesa, M., et al "[Effect of *Casearia sylvestris* treatment on angiogenesis induced by Ehrlich tumor cells]." *Revista Eletrônica Acervo Saúde* 2021 Feb; 13(2): e5640. (**IVA**)

Ferreira, P., et al. “Preclinical anticancer effectiveness of a fraction from *Casearia sylvestris* and its component casearin X: *In vivo* and *ex vivo* methods and microscopy examinations.” *J. Ethnopharmacol*. 2016; 186: 270–279. **(IVT, IVA**).
Felipe, K., et al. “Inhibition of tumor proliferation associated with cell cycle arrest caused by extract and fraction from *Casearia sylvestris* (Salicaceae).” *J. Ethnopharmacol.* 2014 Sep; 155(3): 1492-9. (**IVA, IVT**)
Da Silva, S., et al. "Chemotherapeutic potential of two gallic acid derivative compounds from leaves of *Casearia sylvestris* Sw (Flacourtiaceae)." *Eur. J. Pharmacol.* 2009 Apr; 608(1-3): 76-83. (**IVA**)
Morita, H., et al. "Structures and cytotoxic activity relationship of casearins, new clerodane diterpenes from *Casearia sylvestris* Sw." *Chem. Pharm. Bull*. (Tokyo) 1991 Dec; 39(3): 693-97. (**IVA, IVT**)
Itokawa, H., et al. "New antitumor principles, casearins A-F, for *Casearia sylvestris* Sw. (Flacourtiaceae)." *Chem. Pharm. Bull*. (Tokyo) 1990; 38(12): 3384-88. (**IVA, IVT**)
Itokawa, H., et al. "Antitumor principles from *Casearia sylvestris* Sw. (Flacourtiaceae), structure elucidation of new clerodane diterpenes by 2-D NMR spectroscopy." *Chem. Pharm. Bull*. (Tokyo) 1988 March; 36(4): 1585-88. (**IVA**)

Breast Cancer:
Felipe, K., et al. "Inhibition of tumor proliferation associated with cell cycle arrest caused by extract and fraction from *Casearia sylvestris* (Salicaceae)." *J. Ethnopharmacol.* 2014 Sep; 155(3): 1492-9. (**IVT, IVA, NEW**)
Dupuy, L., et al. "[*In vitro* effect of lupeol and casearin G on peripheral blood mononuclear and tumor cells]." *Rev. Med. Chil.* 2013 Sep; 141(9): 1150-7. (**IVT**)

Brain Cancer:
Ferreira, P., et al. “Preclinical anticancer effectiveness of a fraction from *Casearia sylvestris* and its component Casearin X: *in vivo* and *ex vivo* methods and microscopy examinations.” *J. Ethnopharmacol.* 2016 Jun; 186: 270-279. (**IVT, IVA**)

Colorectal Cancer:
Silva, J., et al. “Promising effects of casearins in tumor-bearing mice and antinociceptive action against oncologic pain: molecular docking and *in vivo* findings.” *Pharmaceuticals* (Basel). 2024 May; 17(5): 633. (**IVT, IVA, INS**)
Ferreira, P., et al. “Preclinical anticancer effectiveness of a fraction from *Casearia sylvestris* and its component Casearin X: *in vivo* and *ex vivo* methods and microscopy examinations.” *J. Ethnopharmacol.* 2016 Jun; 186: 270-279. (**IVT, IVA**)

Leukemia:
De Ford, C., et al. "The clerodane diterpene casearin J induces apoptosis of T-ALL cells through SERCA inhibition, oxidative stress, and interference with Notch1 signaling." *Cell Death Dis.* 2016; 7: e2070.
Bou, D., et al. “Dinor Casearin X, a new cytotoxic clerodane diterpene from *Casearia sylvestris*.” *J. Braz. Chem. Soc.*, 2015; 26(8): 1725-1729, 2015. (**IVT**)
Ferreira, P., et al. "Casearin X exhibits cytotoxic effects in leukemia cells triggered by apoptosis." *Chem. Biol. Interact.* 2010 Dec; 188(3): 497-504. (**IVT**)
Moreira da Silva, R., et al. "Characterization of casearin X metabolism by rat and human liver microsomes." *Planta Med.* 2019 Mar; 85(4): 282-291. (**IVT, IVA**)

Lung Cancer:

Da Silva, S., et al. "Chemotherapeutic potential of two gallic acid derivative compounds from leaves of *Casearia sylvestris* Sw (Flacourtiaceae)." *Eur. J. Pharmacol.* 2009 Apr; 608(1-3): 76-83. (**IVA**)

de Oliveira, A., et al. "Ethanolic extract of *Casearia sylvestris* and its clerodane diterpene (caseargrewiin F) protect against DNA damage at low concentrations and cause DNA damage at high concentrations in mice's blood cells." *Mutagenesis*. 2009 Oct; 24(6): 501-6. (**IVT, IVA**)

Prostate Cancer:

Dupuy, L., et al. "[In vitro effect of lupeol and casearin G on peripheral blood mononuclear and tumor cells]." *Rev. Med. Chil.* 2013 Sep; 141(9): 1150-7. (**IVT**)

Sarcoma:

Silva, J., et al. "Promising effects of casearins in tumor-bearing mice and antinociceptive action against oncologic pain: Molecular docking and *in vivo* findings." *Pharmaceuticals* (Basel). 2024 May; 17(5): 633.

Itokawa, H., et al. "Antitumor principles from *Casearia sylvestris* Sw. (Flacourtiaceae), structure elucidation of new clerodane diterpenes by 2-D NMR spectroscopy." *Chem. Pharm. Bull*. (Tokyo) 1988 March; 36(4): 1585-88. (**IVT, IVA**)

Itokawa, H., et al. "Isolation of diterpenes as antitumor agents from plants." Patent—Japan Kokai Tokyo Koho-01 1989; 149, 779: 6pp. (**IVT, IVA**)

Cancer Pathways and Mechanism of Actions:

Vecchi, L., et al. "Phospholipase A2 drives tumorigenesis and cancer aggressiveness through its interaction with annexin A1." *Cells*. 2021 Jun; 10(6): 1472. (**REV**)

Peng, Z., et al. "Phospholipase A2 superfamily in cancer." *Cancer Lett*. 2021 Jan; 497:165-177. (**REV***)*

Felipe, K., et al. "Inhibition of tumor proliferation associated with cell cycle arrest caused by extract and fraction from *Casearia sylvestris* (Salicaceae)." *J. Ethnopharmacol.* 2014 Sep; 155(3): 1492-9. (**IVA, IVT**)

Faiella, L., et al. "A chemical proteomics approach reveals Hsp27 as a target for proapoptotic clerodane diterpenes." *Mol. Biosyst.* 2012 Oct; 8(10): 2637-44. (**IVT, INS, NEW**)

Da Silva, S., et al. "Chemotherapeutic potential of two gallic acid derivative compounds from leaves of *Casearia sylvestris* Sw (Flacourtiaceae)." *Eur. J. Pharmacol.* 2009 Apr; 608(1-3): 76-83. (**IVA, IVT**)

Cancer Preventative Actions:

Prieto, A., et al. "Assessment of the chemopreventive effect of casearin B, a clerodane diterpene extracted from *Casearia sylvestris* (Salicaceae)." *Food Chem Toxicol*. 2013 Mar; 53: 153-9. (**IVA, IVT, NEW**)

de Oliveira, A., et al. "Ethanolic extract of *Casearia sylvestris* and its clerodane diterpene (caseargrewiin F) protect against DNA damage at low concentrations and cause DNA damage at high concentrations in mice's blood cells." *Mutagenesis*. 2009 Nov; 24(6): 501-6. (**IVA, IVT**)

Cancer Research on Guacatonga's Polyphenols:

Caffeic Acid: https://pubmed.ncbi.nlm.nih.gov/?term=caffeic+acid+AND+cancer

P-coumaric Acid: https://pubmed.ncbi.nlm.nih.gov/?term=p-coumaric+acid+and+cancer

Ellagic Acid: https://pubmed.ncbi.nlm.nih.gov/?term=ellagic+acid+AND+cancer

Ferulic Acid: https://pubmed.ncbi.nlm.nih.gov/?term=ferulic+acid+AND+cancer
Icaridside II: https://pubmed.ncbi.nlm.nih.gov/?term=icariside+II+and+cancer
Quercetin: https://pubmed.ncbi.nlm.nih.gov/?term=quercetin+AND+cancer
Rutin: https://pubmed.ncbi.nlm.nih.gov/?term=Rutin+AND+cancer
Syringic Acid: https://pubmed.ncbi.nlm.nih.gov/?term=syringic+acid+AND+cancer

Toxicity/Safety Studies:

Nagaoka, L., et al. "Maternal-fetal safety evaluation of an aqueous extract of *Casearia sylvestris* leaves in rats." *Birth Defects Res.* 2023 Dec; 115(20): 1899-1911. **(IVA, IVT)**

Mazzari, A., et al. "*In vitro* effects of European and Latin-American medicinal plants in CYP3A4 gene expression, glutathione levels, and P-glycoprotein activity." *Front. Pharmacol.* 2022 Oct; 13: 826395. (**IVT**)

Ferreira, P., et al. "Toxicological findings about an anticancer fraction with casearins described by traditional and alternative techniques as support to the Brazilian Unified Health System (SUS)." *J. Ethnopharmacol*. 2019; 15: 241–112004. (**IVA, IVT**)

Tirloni, C., et al. "Short-term carcinogenesis evaluation of *Casearia sylvestris*." *Revista Brasileira de Farmacognosia* 2017; 27(5): 05.009 (**IVA**)

Ameni, A., et al. "Toxicity study about a medicinal plant *Casearia sylvestris*: A contribution to the Brazilian Unified Health System (SUS)." *J. Ethnopharmacol.* 2015 Dec; 175: 9-13. (**IVA, IVT)**

Return to the Rain-Tree Tropical Plant Database File on Guacatonga