

Dalbergiones, dalbergiquinols, and related products are responsible for the dermatitis caused, especially in wood workers, by the various species of Brazilian rosewood: *Dalbergia melanoxylon* Guillemin & Perrotet, *D. retusa* Hemsley, *D. nigra* (Vell. Conc.) Benth., *D. latifolia* Roxb... as well as *Machaerium scleroxylum* Tul. (see quinone-containing drugs).

● **INDIA POON,**
Calophyllum inophyllum L., Clusiaceae

The "beauty-leaf mastwood" tree is found in southeast Asia and from Madagascar to Polynesia. It is used for its oil-rich drupe-like fruit. By expression, this fruit provides a pasty mass, improperly called balsam, rich in triacylglycerols, and containing several 4-arylcoumarin-type derivatives, including calophyllolide, inophyllolide, and *cis*-dihydroinophyllolide. Reputed as a healing and antitumor agent, the balsam was marketed in France for ages as a healing and analgesic agent for the treatment of burns. It is still listed in the product suppliers' catalog, for cosmetic applications.

In 1992, the antiviral properties of calanolides—4-aryl and 4-alkyl coumarins isolated from a variety of *C. lanigerum* Miq. from Sarawak—were shown and this spurred renewed interest in this genus. Like the calanolides, most of the other derivatives in this group (soulattrolide of *C. teysmanii* Miq., costatolide) are reverse transcriptase inhibitors and inhibitors of the cytopathogenicity of HIV-1 *in vitro*, including for strains resistant to AZT. Their unusual mechanism of action, which involves two different sites, makes them the prototypes of a novel class of non-nucleosidic reverse transcriptase inhibitors.

BIBLIOGRAPHY

- Donnelly, D.M.X. and Boland, G. (1994). Neoflavonoids, in "The Flavonoids: Advances in Research since 1986", (Harborne, J.B., Ed.), p. 239-258, Chapman & Hall, London.
- Currens, M.J., Gulakowski, R.J., Mariner, J.M., Moran, R.A., Buckeit, R.W., Gustavson, K.R., McMahon, J.B. and Boyd, M.R. (1996). Antiviral Activity and Mechanism of Action of Calanolide A against the Human Immunodeficiency Virus Type-1, *J. Pharmacol. Exp. Ther.*, **279**, 645-651.
- McKee, T.C., Covington, C.D., Fuller, R.W., Bokesch, H.R., Young, S., Cardellina, J.H., Kadushin, M.R., Soejarto, D.D., Stevens, P.F., Cragg, G.M. and Boyd, M.R. (1998). Pyranocoumarins from Tropical Species of the Genus *Calophyllum*: A Chemotaxonomic Study of Extracts in the National Cancer Institute Collection, *J. Nat. Prod.*, **61**, 1252-1256.
- Zembower, D.E., Liao, S., Flavin, M.T., Xu, Z.-Q., Stup, T.L., Buckheit, R.W., Khilevich, A., Mar, A.A. and Sheinkman, A.K. (1997). Structural Analogues of the Calanolide Anti-HIV Agents. Modification of the *trans*-10,11-Dimethylidihydropyran-12-ol Ring (Ring C), *J. Med. Chem.*, **40**, 1005-1017.

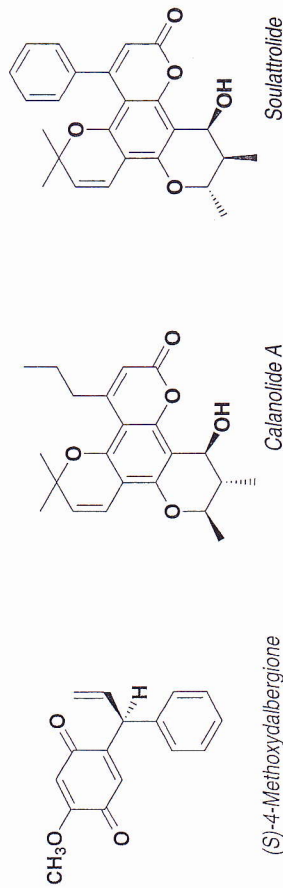
Neoflavonoids

The term neoflavonoid is reserved for C₁₅ compounds of the Ar-C₃-Ar type, structurally related to flavonoids and isoflavonoids and constructed on a 1,1-diphenylpropane skeleton. Like 2- and 3-phenylchromanes, they arise from the condensation of three acetate molecules with one cinnamate molecule, but their mechanism of formation is very different. It is possible (but this is only a hypothesis) that they result from the (SN₂') reaction of a phenol such as phloroglucinol or resorcinol with the α-carbon of the side chain of a phenylpropane unit.

The vast majority of known neoflavonoids has been isolated from the Fabaceae (*Dalbergia*) and Clusiaceae (Lindley = Guttiferae Juss.: *Calophyllum*, *Mammea*, *Mesua*). Some are also found in the Rubiaceae (*Coutarea*) and Asteraceae (*Echinops*).

The group comprises 4-arylcoumarins (4-aryl-2H-1-benzopyran-2-ones), 3,4-dihydro-4-arylcoumarins such as the calomelanols of *Pityrogramma calomelanos* (L.) Link (Pteridaceae)*, neoflavenes, 3-arylbenzo[b]furans, and "open" compounds: dalbergiones, dalbergiquinols, and benzophenones.

The various representatives of the neoflavonoid group have no distinct biological properties. However, we shall cite here the *Calophyllum* "balsam", even though there are apparently no studies to link the healing properties attributed to it to the 4-arylcoumarins that it contains.



* The 3,4-dihydro-4-arylcoumarins described in *Cinchona succirubra* (cinchonans) are viewed more as flavan derivatives—see tannin structure.