Mem. Inst. Oswaldo Cruz, Rio de Janeiro, Vol. *86*, Suppl. II, 5-8, 1991

POTENTIAL SOURCES OF BIODYNAMICALLY ACTIVE NATURAL PRODUCTS IN BRAZIL

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In contrast to China where vegetation is predominantly herbaceous, vegetation in Brazil is commonly arboreous. This fact may explain why Chinese drugs are usually acetate derived, while actual and potential natural therapeutic agents from Brazil are mostly shikimate derived. Only relatively few compounds isolated from Brazilian plants have been submitted to adequate pharmacological testing.

Key words: chemodiversity – bioactivity – chemosystematics – shikimate derivatives – mevalonate derivatives

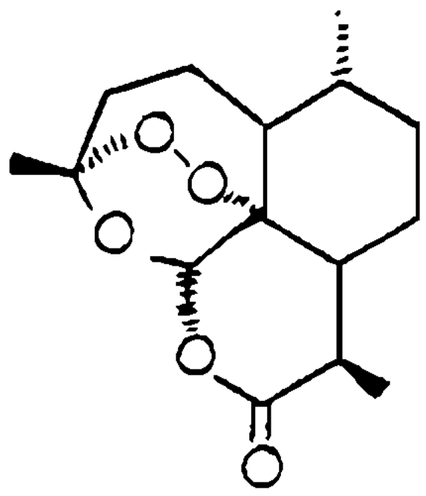
The participation of Chinese and Brazilian investigators in a Symposium which aims to fortify work in chemistry and pharmacology of natural products is not fortuitous. Indeed from the standpoint of potential sources of biodynamically active natural products these vast territories are very diverse, possibly even complementary. In China predominate herbaceous plants in open fields, in Brazil predominate woody plants in closed forests. Brazil with its vast territorial extension (8 500 000 km^2) possesses well over 60,000 species of higher plants, about 10% of the entire Flora, encompassing not less than 75% of all forest species.

It is by now well known that natural products are biosynthetised by a very small number of metabolic routes: the acetate route, the mevalonate route, a route linked to some Krebs cycle derived amino acids, another route linked to sugars of the Calvin cycle and the shikimate route. A clear trend, but of course only a trend, exists which favours the production of secondary metabolites in herbaceous plants by the first three routes and in woody plants by the shikimate route.

RESULTS AND DISCUSSION

In consequence of these concepts there should be a tendency towards the production of terpenoids in plants from China and of lignoids in plants from Brazil, chiefly if their habitat is the Amazon valley. Thus it is not surprising that it was in China where the antimalarial sesquiterpene lactone artemisinin (1) from *Artemisia* species, family Asteraceae, was discovered, while the Amazon forest gave the tryptophane derived quinine (2) from a *Cinchona* species, family Rubiaceae. Another example concerns the insecticidal monoterpenoid pyrethrins (e.g. 3) from chinese *Chrysanthemum* species, while the cinnamic acid derived rotenones (e.g. 4) are abundant constituents of Amazonian *Lonchocarpus* species. Finally the very poisonous diterpene alkaloids of atisan and aconan types (e.g. 5) come from herbaceous chinese Ranunculaceae of the genera *Aconitum* and *Delphinium*, while the famous brazilian curares (e.g. 6) are phenylalanine derived bis-benzylisoquinoline alkaloids of the woody genus *Chondondendron*, family Menispermaceae.

Although the concept by which one can distinguish between herbaceous and lignous chemistries is rather a theoretical one, its practical importance becomes evident through an historical perspective. The most important concentrated efforts towards the production of potentially interesting compounds from brazilian plants (Gottlieb & Mors, 1978, 1980) centered mainly but not exclusively around the woody families Lauraceae, Myristicaceae, Leguminosae, Apocynaceae and Bignoniaceae. From species of Lauraceae come chiefly cinnamic acid derived 2-pyrones (e.g. 7) and neolignans (e.g. 8). The former class of compounds is known to possess analgesic, antiedemic, antimicotic, antiphlogistic, local anesthetic, smooth muscle relaxant and spasmolytic activities, besides potentiating barbiturate narcosis and protecting against chemo- and electroshock.



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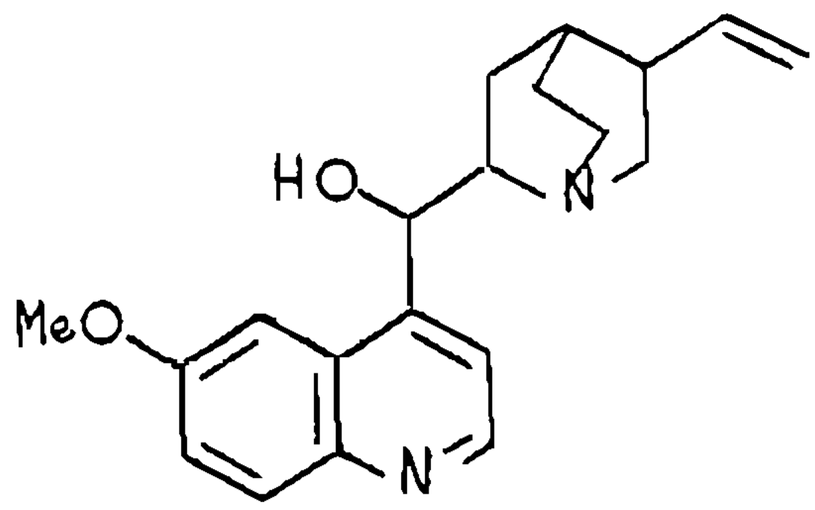

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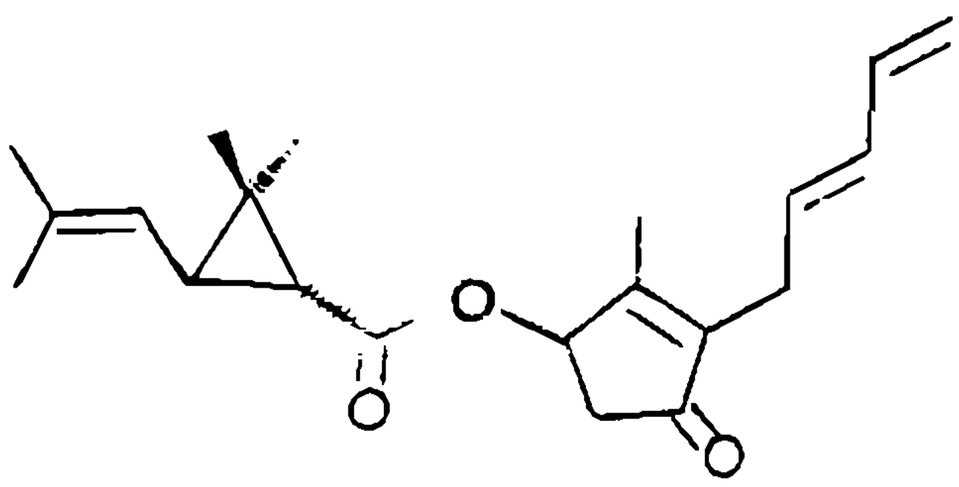

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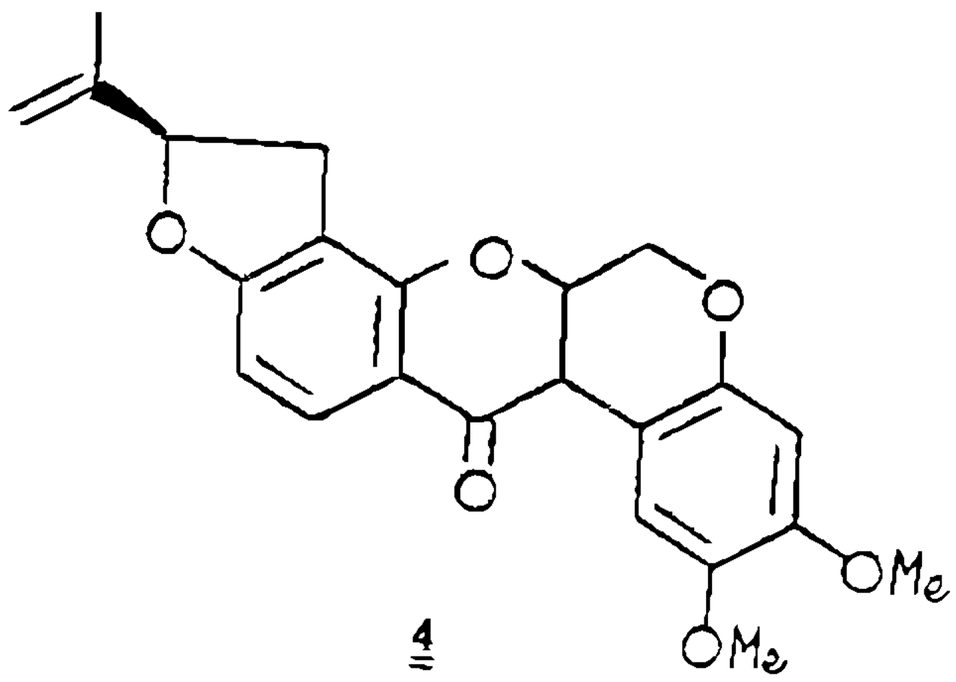

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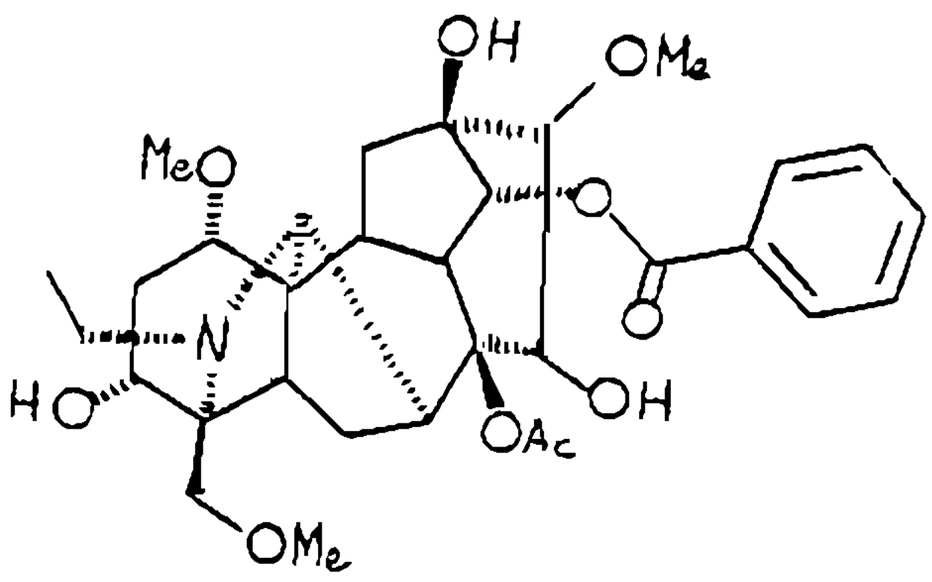

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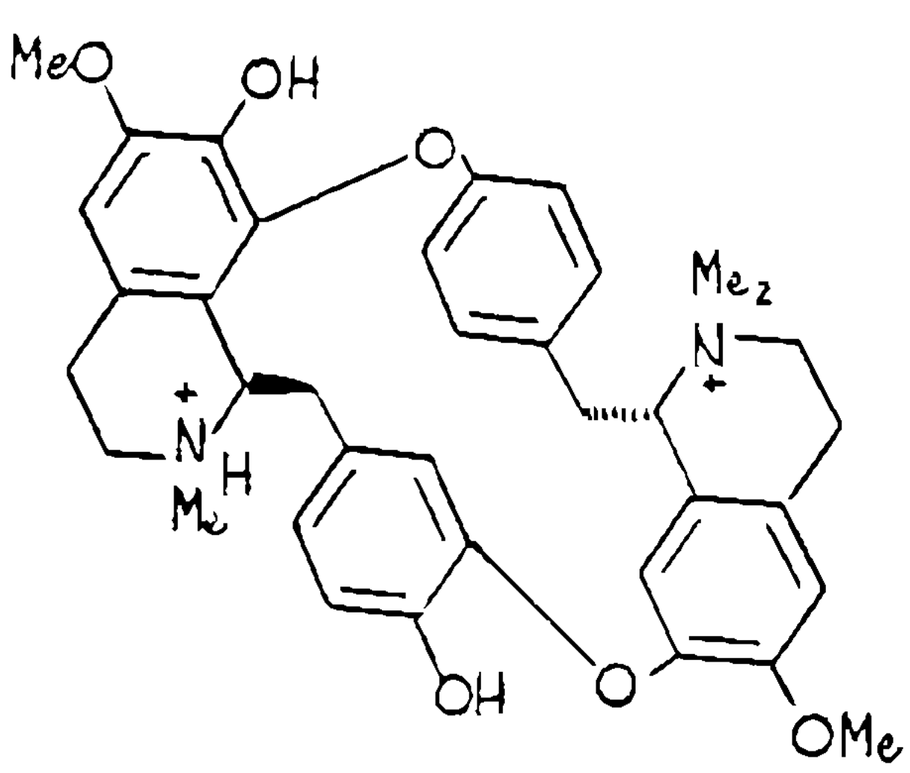

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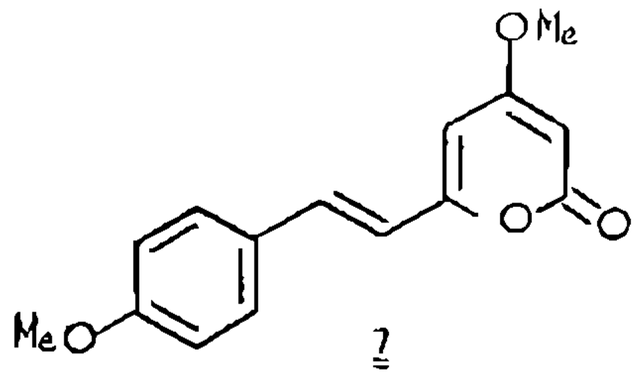
Several hundred neolignans of many types have recently been discovered in Brazil (Gottlieb & Yoshida, 1989). Although diverse activities have been demonstrated for such compounds abroad, very few samples of our derivatives have yet been submitted to tests, such as for instance antagonism of PAF. The family Myristicaceae contains not only a great variety of neolignans but also a series of very special flavonoids. One group of these flavonoids possesses a trimethylene chain linking two aromatic rings (e.g. 9) (Gottlieb, 1977) and another group is formed by very special flavonolignoids (e.g. 10) (Conserva et al., 1990). Practically nothing is known concerning the pharmacological activity of these compounds. This is a pity since other flavonolignoids, as the silymarins, are known chemotherapeutic agents. The family Leguminosae is well known for many useful products, among which one can include even the compound brazilin (11) from brazilwood (*Caesalpinia echinata*), a commodity to which the country may owe its name, as well as rotenoids (e.g. 4) the ichthyotoxic and insecticidal principles from *Lonchocarpus* species. As in rotenone, the flavonoid



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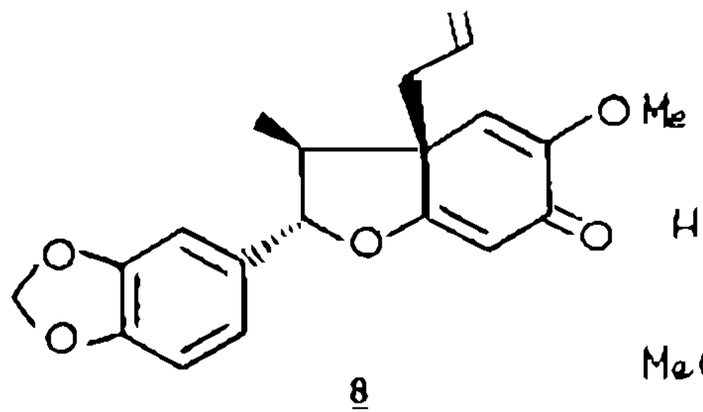

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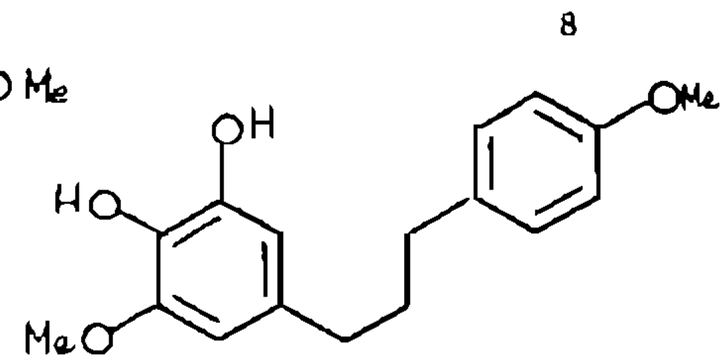

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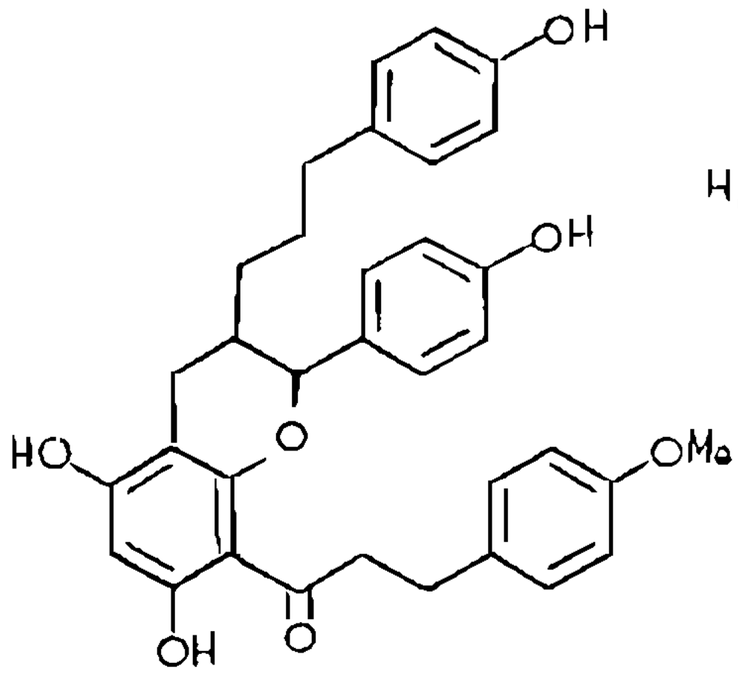

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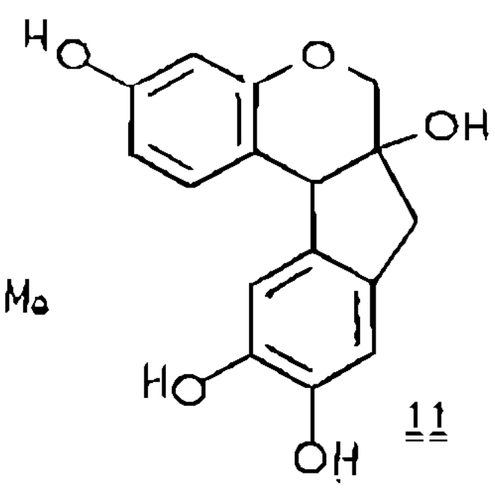

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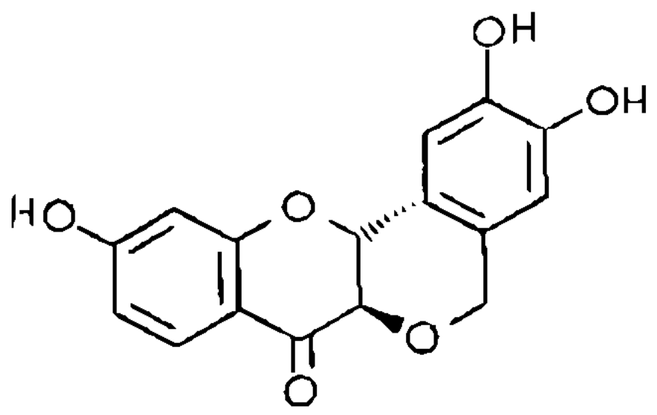

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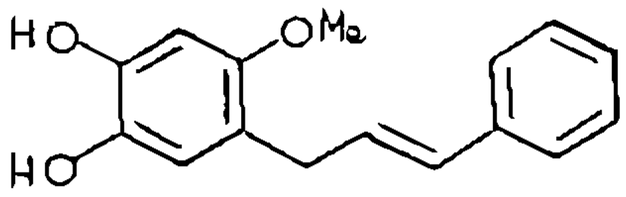

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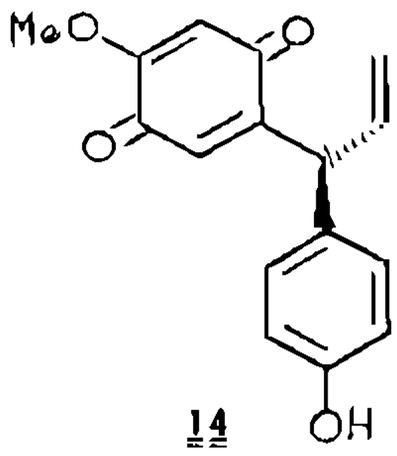

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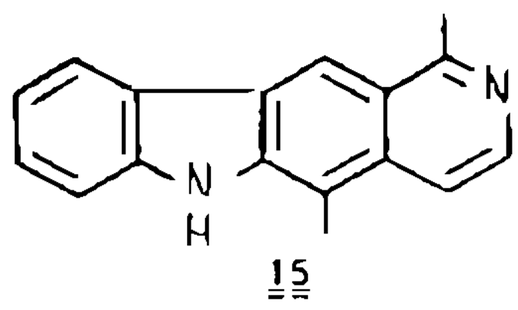

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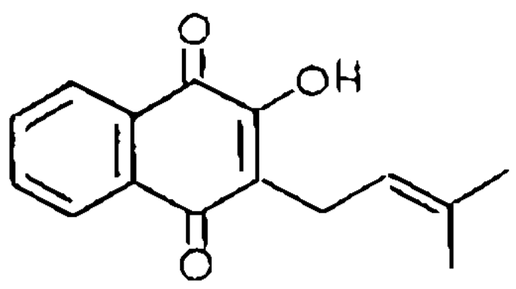

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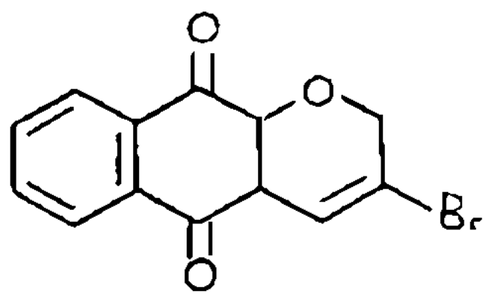

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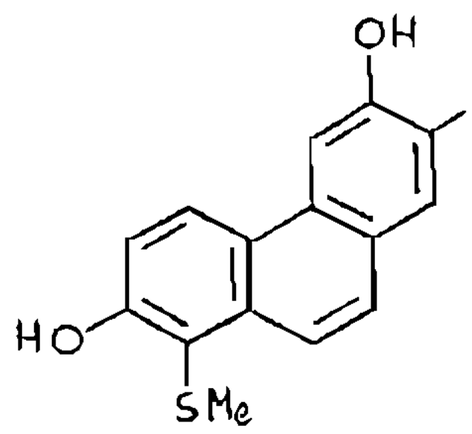

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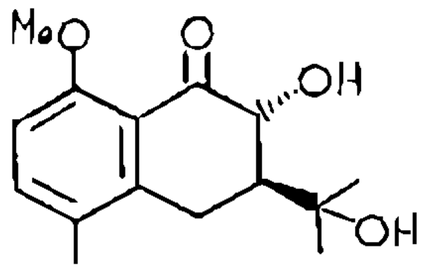

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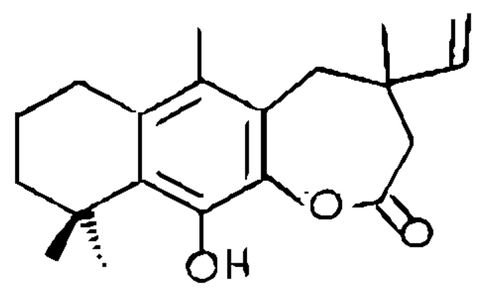

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skeleta of peltogynoids (e.g. 12), obtained from *Peltogyne* and *Goniorrhachis*, contain an additional carbon atom. However, in contrast to rotenoids peltogynoids are much less known pharmacologically. Still from Leguminosae derive compounds as cinnamylphenols (e.g. 13) and dalbergiones (e.g. 14) from *Dalbergia* species. Chiefly the history of cinnamylphenols is of interest. These compounds were recognized as phytoalexins and are active in sterilizing female insects which transmit malaria. Synthetic analogs of cinnamylphenols were patented in USA against pests of agriculture (Jurd & Manners, 1980). Finally, although twenty years have passed since the isolation of more than one hundred complex indole alkaloids (e.g. 15) from Apocynaceae, the great majority of the samples continue waiting for biological tests.

Very different is the situation concerning lapachol (16) and derivatives from Bigoniaceae and semisynthetic analogs (e.g. 17) which were intensively studied as chemotherapic agents against cancer.

In spite of all this evidence it must not be forgotten that Brazil is a very big country and of course only partly covered by forest. Thus additional work centered around families from which mainly terpenoids were isolated. Examples are the Euphorbiaceae, the Icacinaceae and the Velloziaceae. From the Euphorbiaceae come phenanthrenoid diterpenes (e.g. 18), from the Icacinaceae come sesquiterpenoid emmotins (e.g. 19) and from the Velloziaceae come interesting compounds belonging to di- (e.g. 20) and triterpenoid classes. Few of these substances have been submitted to conclusive pharmacological tests.

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