PERGAMON

Phytochemistry 55 (2000) 683–710

PHYTOCHEMISTRY

www.elsevier.com/locate/phytochem

Review

Tetraoxygenated naturally occurring xanthones

Valdir Peres [a], Tanus Jorge Nagem [b,*], Fernando Faustino de Oliveira [b]

[a]Departamento de Química, Universidade Federal de Viçosa, Av. PH Rolfs, 36571-000, Viçosa, Minas Gerais, Brazil
[b]Departamento de Química da Universidade Federal de Ouro Preto, Universidade Campus do Cruzeiro, 35400-000, Ouro Preto, Minas Gerais, Brazil

Received 4 June 1999; received in revised form 19 June 2000

Abstract

This review, with 350 references, gives information on the chemical study of 234 naturally occurring tetraoxygenated xanthones in 12 families, 53 genus and 182 species of higher plants, and two which are described as fungal and lichen metabolites. The value of these groups of substances in connection with pharmacological activity and therapeutic use of some species is described. The structural formulas of 135 isolated compounds, and their distribution, are also given. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Xanthone; Tetraoxygenated xanthones; Pharmacological activity; Fungus; Lichen; Biosynthesis

Contents

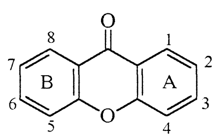
* Corresponding author. Tel.: +55-319-9611551; fax: 55-31-5591707.
E-mail address: tjnagem@bhnet.com.br (T.J. Nagem).

PII: S0031-9422(00)00303-4

1. Introduction

Xanthones are secondary metabolites commonly occurring in a few higher plant families, and in fungi and lichens. Their taxonomic importance in such families and their pharmacological properties has aroused great interest (Cardona et al., 1990).

The symmetrical nature of the xanthone nucleus coupled with its mixed biogenetic origin in higher plants necessitates that the carbons be numbered according to a biosynthetic convention. Carbons 1–4 are assigned to the acetate-derived ring **A**, and carbons 5–8 to the shikimate-derived ring **B** (Bennett and Lee, 1989). The numbering system is based on xanthene-9-one as the basic skeleton (Gottlieb, 1968), and in cases where only ring **B** is oxygenated the lowest numbers are used, except for biosynthetic discussions (Bennett and Lee, 1989).



Xanthone basic skeleton

2. Classification

The xanthones isolated so far may be classified into five major groups: simple oxygenated xanthones, xanthone glycosides, prenylated and related xanthones, xanthonolignoids, and miscellaneous xanthones (Mandal et al., 1992). The simple oxygenated xanthones can again be subdivided into six groups according to the degree of oxygenation, and we have previously reviewed trioxygenated xanthones (Peres and Nagem, 1997). In a continuation of our interest in these compounds, simple tetraoxygenated xanthones, as well as prenylated and related xanthones with the same degree of oxygenation, are listed in this review (Tables 2–6).

3. Methods of isolation and structural investigations

Xanthones are commonly separated by silica gel chromatography using different solvent mixtures (Harborne, 1973). Xanthones are also separated and identified by comparison with authentic samples by TLC (Chawla et al., 1975) and by HPLC (Hostettmann and Guillarmod, 1976a,b; Hostettmann and McNair, 1976). The structures of simple oxygenated xanthones have been established mainly from analysis of the UV, IR, MS and NMR spectroscopic data of these compounds (Roberts, 1961; Arends and Helboe, 1972; Arends et al., 1973; Sultanbawa, 1980).

Xanthones can be detected by their colour in UV light with and without ammonia, or by using a general phenolic spray (Harborne, 1973). The UV spectrum varies in a characteristic manner, depending on the oxygenation pattern, and with the availability of a considerable amount of data, assignments can be readily made. By the use of $AlCl_3$ shifts for chelated hydroxyls, as well as sodium acetate, sodium hydroxide and boric acid shifts, considerable information on the position of hydroxyl groups can be obtained (Mesquita et al., 1968; Sultanbawa, 1980).

The use of IR spectroscopy in xanthone chemistry is generally limited to the detection of the carbonyl stretching frequency (Roberts, 1961; Mourão et al., 1966). For example, the effect of chelation on the IR carbonyl frequency of hydroxy-xanthones may be a useful feature for analysis of spectra of substituted and extended xanthones (Scheinmann, 1962; Chawla et al., 1973). The use of IR for detecting other functional groups, such as unchelated hydroxyl and methyl groups, has been described elsewhere (Roberts, 1961; Santesson, 1968a,b, 1969).

By introducing lichen samples into a mass spectrometer via a direct inlet system, Santesson (1968a,b) obtained mass spectra of volatile lichen substances. The method proved to be well suited for tentative identification of lichen xanthones (Santesson, 1968a,b, 1969). Apart from discussion of the mass spectra of lichen xanthones, no systematic investigation of the electron-impact-induced fragmentation of xanthones appears to have been made, except by Arends et al. (1973) in their study of electron-impact-induced fragmentation of monohydroxy- and monomethoxyxanthones. Mass spectrometry has not been applied extensively to the study of naturally occurring xanthones, but the MS data available have been very valuable for preliminary examination (Barnes and Occolowitz, 1964).

The data obtained from ^{1}H NMR spectroscopic analysis are of great value in characterizing and identifying naturally occurring xanthones (Mathis and Goldstein, 1964). Indeed, these have been used to determine the structure of substituents and for locating aromatic protons, through comparison with reference data and analysis of spin–spin coupling. Closer scrutiny of the chemical shifts of aromatic protons allows prediction of the oxygenation pattern (Barraclough et al., 1970), and there are detailed NMR results for this class of compounds (Westerman et al., 1977).

^{1}H NMR and ^{13}C NMR spectroscopic analyses are the most useful tools in the structure elucidation of xanthones (Chaudhuri et al., 1978). The ^{13}C NMR spectra of a great number of naturally-occurring xanthones are reported, with all chemical shifts assigned (Castelão et al., 1977; Westerman et al., 1977; Frahm and Chaudhuri, 1979). Hambloch and Frahm (1980) introduced a computer program named SEOX 1, which rapidly identifies unknown xanthones with the help of additivity rules; this lends remarkable facility to structure elucidation.

4. Bioactivities of xanthones

The study of xanthones is interesting not only from a chemosystematic viewpoint, but also from a pharmacological point of view. Xanthones posses antidepressant action and antitubercular activity, while xanthone glycosides exhibit depressant action. The choleretic, diuretic, antimicrobial, antiviral and cardiotonic action of some xanthones has also been established (Hostettmann and Wagner, 1977; Suzuki et al., 1980, 1981; Kitanov and Blinova, 1987). The inhibition of type A and type B monoamine oxidases by a number of xanthones has also been observed (Suzuki et al., 1980, 1981). And in spite of their restricted occurrence in the plant kingdom, some xanthones are reported to possess antileukaemic, antitumour, antiulcer, antimicrobial, antihepatotoxic and CNS-depressant activities (Banerji et al., 1994). For example, bellidifolin (1,5,8-trihydroxy-3-methoxyxanthone) was found to be a selective inhibitor of MAO A, whereas psorospermin, a dihydrofuranoxanthone epoxide, exhibits significant activity against leukaemia and in colon and mammary tumour models (Beerhues and Berger, 1994). In general, xanthones and their derivatives have also been shown to be effective as allergy inhibitors and bronchodilators in the treatment of asthma (Balasubramanian and Rajagopalan, 1988).

A series of isoprenylated xanthones isolated from moraceous plants showed interesting biological activities such as hypotensive effect, anti-rhinoviral activity, inhibition of the formation of some prostanoids and anti-tumour promoting activity (Hano et al., 1990). In a study of structure–activity relationships, it was found that 1,3,5,6-, 1,3,6,7-, 2,3,6,7- and 3,4,6,7-tetraoxygenated xanthones possess antiplatelet effects, and that the mechanism of action of 1,3,6,7-tetraoxygenated xanthones is due to both inhibition of thromboxane formation and phosphoinositide breakdown (Lin et al., 1993). Some xanthone dicarboxylic acids have shown a potent inhibition of the binding of leukotriene B_4 to receptors on intact neutrophils. Norathyriol showed anti-inflammatory effects mediated partly through the supression of mast cell degranulation, and partly through (at least at higher doses) a non-selective blockade of the increase in vascular plasma exudation caused by various mediators (Lin et al., 1996). Bellidifolin, isolated from *Swertia japonica*, was found to be a potent hypoglycemic agent in STZ-induced diabetic rats by both oral and intraperitoneal administration (Basnet et al., 1995).

Recently, various bioactivities of xanthones including cytotoxic and antitumour activities, anti-inflammatory activity, antifungal activity, enhancement of choline acetyltransferase activity and inhibition of lipid peroxidase have been described (Iinuma et al., 1994). In 1994 Mehta et al., reported the total synthesis of novel xanthone antibiotics, cervinomycins A_1 and A_2, with promising activity against anaerobic bacteria, mycoplasma and some gram positive bacteria (Table 1).

5. Use of plant sources containing tetraoxygenated xanthones

Anthocleista vogelli (Planch), Loganiaceae, is a small tree which grows in the tropical rain forest areas of west Africa. The stem bark is used in local medicine for curing fever, stomach ache and as purgative (Okorie, 1976).

Among *Calophyllum* species, *C. inophyllum* is the most widespread and has superior timber qualities, particularly in Malaysia (Al-Jeboury and Locksley, 1971). The balsam from the bark of *C. inophyllum* ''Alexandrian Laurel'' is an oleoresin and used as a cicatrisant, whereas an infusion or decoction of the leaves has been traditionally used as an eye remedy in Asian medicine (Basnet et al., 1995). Xanthones from *C. inophyllum* produce CNS depression in rats and mice (Bennett and Lee, 1989). The tropical American tree *C. brasiliense* produces a strong and durable timber known as ''Santa Maria'' or ''jacareuba'' (King et al., 1953).

Canscora decussata Schult (Gentianaceae), an erect annual plant of height 0–6 m, finds use in indigenous medicine for a variety of purposes. The roots are used as a laxative, diuretic, for liver troubles, as a nerve tonic and in tuberculosis and fevers, while the aerial portions are used to treat cases of insanity, epilepsy and nervous debility (Ghosal and Chaudhuri, 1973; Okorie, 1976). The extract of *C. decussata* Schult is used in the treatment of certain mental disorders and tuberculosis (Ghosal and Chaudhuri, 1975).

The botanical source of the Taiwan folk remedy ''Hwang-jin-guey'' is the root and stem of *Cudrania cochinchinensis* (Lour.) Kudo and Masamune var. *gerontogea* (S. & Z.) Kudo and Masamune (Gottlieb et al., 1975). It was used in the treatment of neuralgia, rheumatics, hepatitis and contusions (Chang et al., 1994). Ethanolic extracts of the roots of this species also showed significant anti-inflammatory and liver protective effects, and the extract as well as isolated xanthone compounds exhibited anti-lipid peroxidative activities both in vivo and in vitro (Chang et al., 1995). *C. tricuspidata* (Carr.) Bur. (Japanese name ''Hariguwa'', Moraceae) is a deciduous tree whose cortex and root bark have been used as a Chinese crude drug (Hano et al., 1990a,b,c).

Plant extracts obtained from genera *Eustoma* are used to treat various ailments, including constipation, nervous debility, tuberculosis, fever and anorexia (Sullivan et al., 1977).

Table 1
Natural source of tetraoxygenated xanthone

Family Asteraceae

Genus *Senecio*—*S. mikanioides* [60]

Family Betulaceae

Genus *Alnus*—*A. glutinosa* [197]

Family Caryophyllaceae

Genus *Saponaria*—*S. vaccaria* [192,193]

Family Clusiaceae

Genus *Allanblackia*—*A. floribunda* [226,227]

Genus *Archytaea*—*A. multiflora* [206]

Genus *Bonnetia*—*B. dinizii* [270]

Genus *Calophyllum*—*C. austroindicum* [172]
C. apetalum [165]
C. bracteatum [312]
C. brasiliensis [72,124,198,280]
C. calaba [209,312]
C. canum [57]
C. cordato-oblongum [134]
C. cuneifolium [130]
C. fragrans [224]
C. inophyllum [10,119,171,173,184, 208]
C. neo-ebudicum [303]
C. ramiflorum [39]
C. sclerophyllum [182]
C. scriblitifolium [183]
C. thwaitesii [77]
C. tomentosum [28, 191]
C. trapezifolium [128]
C. walkeri [77]
C. zeylanicum [133]

Genus *Caraipa*—*C. densiflora* [59, 214,215]
C. grandifolia [104]
C. psidifolia [104]
C. valioi [104]

Genus *Cratoxylum*—*C. celebicum* [317,318]
C. cochinchinense [36, 310]
C. formosanum [166]
C. pruniflorum [199]

Genus *Garcinia*—*G. cowa* [202,211,280]
G. densivenia [339]
G. dioica [179]
G. dulcis [148, 164, 166, 167]
G. echinocarpa [27]
G. eugenifolia [184]
G. forbesii [147]
G. mangostana [20, 26, 92, 126, 152, 202, 275, 276, 298, 305, 306, 307, 308, 316, 328]
G. multiflora [70]
G. nervosa [12]
G. opaca [118]
G. ovalifolia [338]
G. pedunculata [289]
G. polyantha [12]
G. pyrifera [12]
G. staudtii [340]
G. subelliptica [103, 162, 163, 168, 169, 247, 248]
G. terpnophylla [27]
G. thwaitesii [135]

Genus *Haploclathra*—*H. leiantha* [256, 257, 259]
H. paniculata [258, 259]

Genus *Hypericum*—*H. androsaemum* [263,176]
H.aucheri [200]
H. canariensis [54]
H. ericoides [55, 117]
H. maculatum [14]
H. patulum [175, 176, 178, 179]
H. paturum [177]
H. reflexum [53]
H. roeperanum [290]
H. sampsonii [71]

Genus *Kayea*—*K. stylosa* [131]

Genus *Kielmeyera*—*K. candidissima* [98]
K. coriacea [59]
K. ferruginea [121]
K. rupestris [74, 91]
K. speciosa [120]

Genus *Lorostemon*—*L. coelhoi* [48]
L. negrensis [48]

Genus *Mammea*—*M. africana* [56]
M. acuminata [330]

Genus *Mesua*—*M. ferrea* [337]

Genus *Ochrocarpus*—*O. odoratus* [226]

Genus *Pentaphalangium*—*P. solomonse* [271]

Genus *Poeciloneuron*—*P. pauciflorum* [56]

Genus *Psorospermum*—*P. febrifugum* [2, 4, 138]

Genus *Rheedia*—*R. benthamiana* [80]
R. brasiliensis [82]
R. gardneriana [83, 84]

Genus *Symphonia*—*S. globulifera* [220, 221, 222, 223]

Genus *Tovomita*—*T. brasiliensis* [46]
T. macrophylla [245, 269]
T. mangle [237]
T. pyrifolium [47, 245]

Genus *Pentadesma*—*P. butyracea* [81]

Genus *Vismia*—*V. guaramirangae* [132]
V. guineensis [45]

Family Gentianaceae

Genus *Blackstonia*—*B. perfoliata* [334]

Genus *Canscora*—*C. decussata* [66,107–109]
C. cachanlahuen [335]

Genus *Centaurium*–*C. erythraea* [35, 190, 243, 261, 262, 327]
C. linarifolium [114, 116, 272–274]
C. littorale [35, 333]
C. pulchellum [246]

Genus *Chironia*—*C. krebsii* [342]

Genus *Erythraea*—*E. centaurium* [327]

Table 1 (*continued*)

Genus *Eustoma*—*E. grandiflorum* [319]

Genus *Frasera*—*F. albicaulis* [314]
F. albomarginata [90]
F. caroliniensis [313]
F. speciosa [90]

Genus *Gentiana*—*G. algida* [51, 326]
G. barbata [285]
G. bavarica [156, 158]
G. bellidifolia [52, 233, 234, 235]
G. brachyphylla [155, 156]
G. campestris [52, 188]
G. cerastioides [187]
G. ciliata [239]
G. detonsa [187]
G. favrati [156]
G. germanica [52, 186]
G. karelinii [50, 326]
G. kochiana [136, 292]
G. lactea [302]
G. nivalis [155, 156]
G. ramosa [52, 186]
G. rostanii [156]
G. schleicherii [156]
G. strictiflora [187]
G. tenella [52]
G. utriculosa [156]
G. verna [153,156]

Genus *Gentianopsis*—*G. paludosa* [349]

Genus *Halenia*—*H. asclepidea* [315]
H. campanulata [161]
H. corniculata [266, 286, 296]
H. elliptica [38, 87, 88, 322]

Genus *Hoppea*—*H. dichotoma* [110]
H. fastigiata [251–254]

Genus *Schultesia*—*S. lisianthoides* [328]

Genus *Swertia*—*S. bimaculata* [113]
S. calycina [295]
S. chirata [61, 79, 112, 231]
S. chirayita [22]
S. cuneata [196]
S. decussata [78, 292]
S. dilatata [329]
S. gracilescens [329]
S. hookeri [106]
S. erythrosticta [160]
S. iberica [85]
S. japonica [18, 19, 21, 33, 180, 189, 203]
S. lawii [19]
S. macrosperma [350]
S. mileensis [150, 219]
S. mussotii [31]
S. nervosa [329]
S. paniculata [13]
S. patens [149]
S. perennis [154, 292]
S. perfoliata [145]
S. petiolata [195, 207]
S. punicea [101]
S. purpurescens [8, 111]
S. racemosa [329]
S. speciosa [194, 238]
S. tetrapetala [7]

Genus *Veratrilla*—*V. baillonii* [348]

Family Gesneriaceae

Genus *Orphium*—*O. frutescens* [297]

Family Iridaceae

Genus *Iris*—*I. nigricans* [11]

Family Loganiaceae

Genus *Anthocleista*—*A. vogelli* [99]

Family Lytraceae

Genus *Lawsonia*—*L. inermis* [41, 42, 229]

Family Moraceae

Genus *Chlorophora*—*C. tinctoria* [122]

Genus *Cudrania*—*C. cochinchinensis* [62, 64]
C. javanensis [255]
C.tricuspidata [140, 141, 142, 264]

Genus *Maclura*—*M. aurantica* [17]
M. pomifera [75, 76, 86, 343–346]

Genus *Morus*—*M. insignis* [143, 144]
M. tinctoria [185]

Family Polygalaceae

Genus Bredemeyera—*B. brevifolia* [268]

Genus *Monnina*—*M. obtusifolia* [283]
M. sylvatica [31]

Genus *Polygala*—*P.arillata* [232]
P. nyikensis [236]
P. tenuifolia [100, 174, 181]
P. virgata [32]

Family Polypodiaceae

Genus *Athyrium*—*A. mesosorum* [265, 331, 332]

Fungus

Genus *Aspergillus*—*A. versicolor* [49, 151]

Lichen

Genus *Diploschistes*—*Diploschistes* sp [95]

Garcinia (Clusiaceae) is best known in Malaysia as a genus of fruit trees. The fruit of many species are edible and serves as a substitute for tamarinds in curries. Many species produce a yellow resin which is used in the making of varnishes and in treatment of wounds. Some species are used in traditional medicine and as a source of edible oils. Extracts and pure isolates of *Garcinia* species have been shown to exhibit significant antimicrobial and pharmacological activities (Goh et al., 1992).

Garcinia dulcis grows mainly in southeast Asia, and its leaves and seeds have been used in traditional medicine against lymphatitis, parotitis, struma and other disease conditions (Iinuma et al., 1996). The oil obtained from the seeds of *G. echinocarpa* is used for lighting lamps (Bandaranayake et al., 1975). *G. livingstonei* is a small to medium-sized tree producing edible fruits and growing at low altitude. It is found, particularly in South Africa, in riverine fringes and in open woodland. Extracts of the leaves and flowers are reported to exhibit antibiotic properties (Diserens et al., 1992). The fruit hull of *G. mangostana* L., the "Mangosteen" tree, is used in Thai folk medicine for healing skin infections and wounds, and for the relief of diarrhea (Mahabusarakam et al., 1987). It is fairly widespread in India, Sri Lanka and Burma, and is known for the sweet fruits called mangosteen. In the Ayurvedic system of medicine, the fruit hull of this plant finds wide application, mainly as an anti-inflammatory agent and in the treatment of diarrhoea (Balasubramanian and Rajagopalan, 1988).

Garcinia subelliptica is a small shrub 4–5 m in height or a large tree sometimes reaching 15–20 m, and has been extensively cultivated as a windbreak in the Yaeyama islands of Japan. Its bark has been utilized as a source of a yellow coloured dye (Fukuyama et al., 1991). The timber of *G. terpnophylla* is used for building purposes (Bandaranayake et al., 1975).

The roots and rhizomes of the yellow gentian (*Gentiana lutea*) have been much used for the production of a bitter tonic. Any medicinal value possessed by gentian preparations appears to be due to bitter, complex glycosides (Roberts, 1961). *Hoppea dichotoma* Willd. is used in the Ayurvedic system of medicine in the treatment of haemorrhoids, in cardiac disorders and in certain mental disorders (Ghosal et al., 1978).

A number of species of the genus *Hypericum* have been found to possess various biological properties. Among the activities is inhibition of monoamine oxidase (MAO; EC 1.4.3.4). MAO, which exists as two isoenzymes, MAO-A and MAO-B, plays a key role in the regulation of some physiological amines and is the target of inhibitors used as antidepressive drugs. The leaves and young twigs of *H. balearicum* contain lipophilic glandular products (Wollenweber et al., 1994). The xanthones of *H. brasiliense* inhibit MAO activity (Rocha et al., 1994); the stems, leaves and flowers of *H. ericoides* are used in Valentian folk medicine (Cardona and Seoane, 1982), and ethanol extracts of the aerial parts of *H. mysorense* show antifungal action (Nattaya et al., 1996). Extracts of *H. perforatum* are widely used in Europe as a drug for depression treatment. *H. roeperanum*, a shrub or small tree growing in central, eastern and south tropical Africa, is employed, alone or in association with various plants or animal parts, to cure female sterility (Rath et al., 1996). *H. sampsonii* Hance is known as a tumour inhibiting plant in Formosan folk medicine (Chen and Chen, 1985).

Lawsonia inermis L. ("Henna") is a plant used by ancient Egyptians for preserving mummies. It is presently used in India and Africa for dyeing hair and for staining hands and feet. It was also reported that the leaves are used for treating some skin diseases including Tinea of the legs (Mahmoud et al., 1980).

Mesua ferrea is commonly called ironwood in Malaya. The hard and durable trunkwood is used widely in agricultural tools and vehicles in southeast Asian countries (Chow and Quon, 1968). From the expressed oil of its seeds, two crystalline antibiotic principles have been isolated, mesuol and mesuone (Govindachari et al., 1967). In contrast to mangiferin, which is reported to be a CNS stimulant (Bhattacharya et al., 1972), xanthones from *M. ferrea* result in CNS depression in rats and mice (Bennett and Lee, 1989).

Monnina obtusifolia is used in the folk medicine of Ecuador as an antifungal, antitumoural, antipyorrhea and antiseptic and as a skin cleanser (Pinto et al., 1994).

The roots of *Polygala tenuifolia* are used as an expectorant, tonic and sedative agent under the names "Onji" in Japan and "Yuan zhi" in China (Ito et al., 1977; Ikeya et al., 1991). It is also effective in inhibiting congestive oedema in rats (Fujita et al., 1992).

Psorospermum febrifugum (Clusiaceae) is a woody plant of tropical Africa which has been used as a febrifuge, a leprosy treatment, a poison antidote, and a purgative. An ethanolic extract of *P. febrifugum* showed antileukaemic activity in vivo in the P388 lymphocytic leukaemia in mice and in vitro in the KB cell culture system (Kupchan et al., 1980). Six compounds isolated from the extract were found to exhibit significant in vitro cytotoxic activity against 9PS cells in culture, and another exhibited both in vitro cytotoxic and in vivo antitumour activity (Abou-Shoer et al., 1988, 1989a,b). One of these six xanthones exhibited significant cytotoxicity in the HT-29 human colon adenocarcinoma in vitro cell line (Abou-Shoer et al., 1993); the xanthone, sorospermin, isolated from *P. febrifugum*, exhibited cytotoxic and in vivo antitumour activity in the P388 mouse leukaemia, mammary (CD) and colon (C6) models (Habib et al., 1987).

Saponaria vaccaria is an annual herb growing as a weed in cultivated fields in northern Pakistan, and is widespread in the flora of Russia. It is reputed to possess sudorific, emetic and laxative properties, and is also used in the indigenous system of medicine for the treatment of jaundice, rheumatism, hepatic eruption and venereal ulcers. It also shows toxicity against worms, and paramecium and other unicellular organisms (Kazmi et al., 1989).

Plants of the genus *Swertia* (Gentianaceae) have been used in traditional medicine for many years. Because these herbs taste extremely bitter and possess the ability to reduce fever, detoxify and act as choleretic and liver tonics, they have been mainly used for the treatment of hepatic, choleric and inflammatory diseases, such as hepatitis, cholecystitis, pneumonia, osteomyelitis, dysentery, scabies, spasm, pain and neurasthenia. Both methanolic and dichloromethane extracts of *Swertia calycina* exhibit strong antifungal activity against *Cladosporium cucumerinum* and *Candida albicans* (Rodriguez et al., 1995).

Swertia chirata is widely distributed in India in the temperate Himalayas between 4000 and 10,000 ft, from Kashmir to Bhutan, and in Khasia Hills between 4000 and 5000 ft. It also grows abundantly in Nepal. The plant is well known for its use in the Indian system of medicine for a variety of purposes. The extract of the plant is used as a bitter tonic, stomachic, antimalarial and as a remedy for liver disorders, a febrifuge, an anthelmintic, a remedy for scanty urine, in epilepsy and for certain types of mental disorders (Ghosal et al., 1973). Recently, the hexane extract of the plant has been shown to possess promising hypoglycaemic activity (Chakravarty et al., 1994). *S. chirata* found a place among useful medicinal plants of east and southeast Asia as a bitter tonic, febrifuge, stomachic, laxative and blood purifier (Mukherjee and Mukherjee, 1987).

Swertia chirayita (Roxb. ex. Flem.) Karsh grows abundantly in the temperate regions of the Himalayas. It is used in India as a traditional remedy for chronic fever, anaemia, asthma and liver disorders, and as a bitter tonic. A recent report revealed hypoglycaemic activity in the hexane extract of this plant (Asthana et al., 1991).

The extract of *Swertia hookeri* is used by people for a variety of therapeutic purposes, e.g. in the treatment of microbial infections in man, in hypertension and as a mood enhancer (Ghosal et al., 1980). *S. japonica* Makino, a popular medicinal herb in Japan, usually grows in a cold climate. The whole plant has been widely used as a folk medicine for stomach complaints, and has a characteristic bitter taste. The Swertia herb has also been widely used in Ayurveda and Unani medicines as an anthelmintic, febrifuge and bitter tonic. The aqueous ethanolic extract of *S. japonica* and its fractions showed potent hypoglycaemic activity in STZ-induced diabetic rats (Basnet et al., 1994).

By using chemiluminescence assays (CL) Ashida et al. (1994) recently showed that a natural Japanese folk medicine, named "Senburi" (*Swertia japonica* Makino), contained components with antioxidant activity. Antioxidant activities of six isolated xanthone derivatives are comparable to α-tocopherol and BHT (Ashida et al., 1994). In India, *S. chirata* decoctions are a commonly used household remedy for constipation and weak liver function in children. An infusion of the plant has been used by Hindu physicians as a bitter tonic, stomachic, febrifuge and anthelmentic. Its use has also been reported in Unani medicine as a substitute for official gentiana preparations.

Swertia macrosperma is a medicinal plant used as a febrifuge, an antidote and a stomach tonic by the indigenous population in the southwestern part of China (Zhou et al., 1989). *S. mileensis* and *S. mussoti* are especialy efficaceous for treating acute viral hepatitis, some preparations have been produced industrially in China.

Swertia petiolata is bitter in taste and is used for its laxative and antimalarial properties in the folk medicine of the high altitude Himalayan region (Khetwal et al., 1990). *S. punicea* grows in moist, mountainous areas in the central district of mainland China, and has been used in the folk medicine as a bitter stomachic (Fukamiya et al., 1990). Extracts of *S. purpurescens* Wall are very commonly used as a tonic and febrifuge in the indigenous system of medicine in India (Ahmad et al., 1973).

Vismia guineensis is a small tree growing in west tropical Africa, whose roots and bark are used as a remedy for skin diseases (Gunasekera et al., 1977).

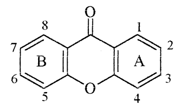
6. Tetraoxygenated xanthones

The first reported naturally occurring tetraoxygenated xanthone is mangostin, isolated in 1855 from *Garcinia mangostana*; in spite of numerous attempts, its structure was not fully elucidated until more than 100 years later (Roberts, 1961). The first naturally occurring tetraoxygenated xanthone whose structure is described in the literature is 1,5,8-trihydroxy-3-methoxyxanthone, isolated from *S. japonica* in 1942 (Asahina et al., 1942).

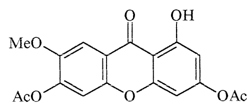
The review by Roberts (1961) refers to the natural occurrence of seven tetraoxygenated xanthones, namely decussatin, jacareubin, mangostin, swerchirin, swertianol, swertinin and asperxanthone. Afzal et al. (1979) described 51 tetraoxygenated xanthones isolated from higher plants, and also described fungal and lichen metabolites. The review by Sultanbawa (1980) included 37 tetraoxygenated xanthones from tropical plants, isolated from different mentioned species, with a dramatic increase in the number of known natural tetraoxygenated xanthones.

In a review of *Hypericum* genus, Kitanov and Blinova (1987) listed only five simple tetraoxygenated xanthones; two years later, in a review of xanthones from

Table 2
Simple tetraoxygenated maturally occurrinbg xanthones

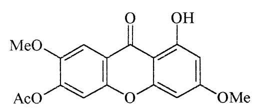


Laxanthone II (1)
Lawsonia inermis [42–229]



(1)

Laxanthone III (2)
Lawsonia inermis [41]



(2)

1-Hydroxy-2,3,5-trimethoxyxanthone (3)
Frasera albicaulis [314]
F. albomarginata [90]
F. caroliniensis [313]
F. speciosa [90]
Halenia asclepidea [315]
H. campanulata [161]
H. corniculata [266, 286]
H. elliptica [87]
S. millensis [219]
S. tetrapetala [7]
Veratrilla baillonii [348]

1-Hydroxy-2,3,7-trimethoxyxanthone (4)
F. caroliniensis [313]
Halenia elliptica [38, 87]
Veratrilla baillonii [348]

1-Hydroxy-3,4,5-trimethoxyxanthone (5)
Frasera albicaulis [314]

1-Hydroxy-3,4,7-trimethoxyxanthone (6)
Frasera albicaulis [314]
F. albomarginata [90]

1-Hydroxy-3,5,6-trimethoxyxanthone (7)
Canscora decussata [108]
Centaurium erythraea [190]
Hoppea dichotoma [110]

1-Hydroxy-3,5,8-trimethoxyxanthone (8)
Centaurium littorale [333]
Swertia chirata [112–161]
S. hookeri [106]
S. japonica [189]
S. lawii [105]
S. paniculata [13]
S. perfoliata [145]

1-Hydroxy-3,6,7-trimethoxyxanthone (9)
Polygala tenuifolia [174]

1-Hydroxy-3,6,8-trimethoxyxanthone (10) (Ellipticol)
Halenia elliptica [88]

1-Hydroxy-3,7,8-trimethoxyxanthone (11) (Decussatin)
Anthocleista vogelli [267]
Canscora decussata [66]
Centaurium cachanlahuen [335]
C. erythraea [190]
C. linarifolium [272]
C. pulchellum [246]
Chironia krebsii [342]
Eustoma grandiflorum [319]
Gentiana barbata [285]
G. bavarica [156-158]
G. brachyphylla [155, 156]
G. campestris [52]
G. ciliata [239]
G. detonsa [187]
G. favrati [156]
G. kochiana [136–292]
G. nivalis [155, 156]
G. ramosa [52]
G. rostanii [156]
G. schleicherii [156]
G. tenella [52]
G. utriculosa [156]
G. verna [156]
Gentianopsis paludosa [349]
Orphium frutescens [297]
Swertia bimaculata [113]
S. calycina [295]
S. chirata [112–161]
S. decussata [78]
S. dilatata [329]
S. gracilescens [329]
S. hookeri [106]
S. iberica [160]
S. lawii [105]
S. mileensis [150]
S. mussotii [321]
S. nervosa [329]
S. paniculata [13]
S. patens [149]
S. perennis [154]
S. perfoliata [145]
S. punicea [101]
S. purpurascens [111]
S. racemosa [329]
Schultesia lisianthoides [328]

2-Hydroxy-1,3,7-trimethoxyxanthone (12)
Frasera albicaulis [314]

2-Hydroxy-5,6,7-trimethoxyxanthone (13)
Hypericum ericoides [55-117]

3-Hydroxy-1,2,4-trimethoxyxanthone (14)
Psorospermum febrifugum [138]

3-Hydroxy-1,2,7-trimethoxyxanthone (15)
Polygala tenuifolia [100]

3-Hydroxy-1,5,6-trimethoxyxanthone (16)
Haploclathra leiantha [256]
Kielmeyera rupestris [74, 91]

3-Hydroxy-1,7,8-trimethoxyxanthone (17)
Swertia paniculata [13]

4-Hydroxy-2,3,6-trimethoxyxanthone (18)
Hypericum reflexum [53]

5-Hydroxy-1,2,3-methoxyxanthone (19)
Schultesia lisianthoides [328]

Table 2 (*continued*)

6-Hydroxy-1,3,5-trimethoxyxanthone (20)
Calophyllum austroindicum [172]

7-Hydroxy-1,2,3-trimethoxyxanthone (21) (Onjixanthone I)
Polygala tenuifolia [100, 174]

7-Hydroxy-1,3,8-trimethoxyxanthone (22)

(Anthaxanthone)
Haploclathra leiantha [257]

8-Hydroxy-1,3,5-trimethoxyxanthone (23)
Swertia bimaculata [113]
S. mussotii [321]

1,2-Dihydroxy-5,6-dimethoxyxanthone (24)
Garcinia subelliptica [247]

1,3-Dihydroxy-2,5-dimethoxyxanthone (25)
Bonnetia dinizii [270]
Calophyllum apetalum [165]
Centaurium linarifolium [114]
Monnina obtusifolia [283]

1,3-Dihydroxy-2,7-dimethoxyxanthone (26)
Veratrilla baillonii [348]

1,3-Dihydroxy-2,8-dimethoxyxanthone (27)
Kielmeyera candidissima [98]

1,3-Dihydroxy-4,5-dimethoxyxanthone (28)
Frasera caroliniensis [313]
F. speciosa [90]
Swertia bimaculata [113]

1,3-Dihydroxy-4,7-dimethoxyxanthone (29)
Frasera albicaulis [314]

1,3-Dihydroxy-5,6-dimethoxyxanthone (30) (Leiaxanthone)
Canscora decussata [107]
Centaurium linarifolium [116, 272]
Haploclathra leiantha [256]

1,3-Dihydroxy-5,8-dimethoxyxanthone (31)
Swertia petiolata [207]

1,3-Dihydroxy-6,7-dimethoxyxanthone (32)

(Laxanthone I)
Lawsonia inermis [42, 229]

1,3-Dihydroxy-7,8-dimethoxyxanthone (33) (Swertinin)
Gentiana kochiana [292]
Swertia decussata [78]
Carapia inophyllum [171]

1,4-Dihydroxy-3,5-dimethoxyxanthone (34)
Centaurium erythraea [261]

1,5-Dihydroxy-2,3-dimethoxyxanthone (35)
Calophyllum thwaitesii [77]
Calophyllum walkeri [77]
Halenia elliptica [322]
H. corniculata [296]
Monnina sylvatica [31]
Schultesia lisianthoides [328]

1,5-Dihydroxy-3,4-dimethoxyxanthone (36) (Tovopyrifolin-B)
Tovomita macrophylla [245]
T. pyrifolium [245, 47]

1,5-Dihydroxy-3,7-dimethoxyxanthone (37)
Hoppea fastigiata [254]

1,5-Dihydroxy-3,8-dimethoxyxanthone (38) (Chiratol)
Swertia chirayita [22]

1,5-Dihydroxy-6,7-dimethoxyxanthone (39)
Caraipa densiflora [215]
C. grandifolia [104]
C. psidifolia [104]
C. valioi [104]
Tovomita brasiliensis [46]

1,6-Dihydroxy-3,5-dimethoxyxanthone (40)
Canscora decussata [108]
Centaurium linarifolium [273, 274]
Chironia krebsii [342]
Hoppea dichotoma [110]

1,6-Dihydroxy-3,7-dimethoxyxanthone (41)
Iris nigricans [11]
Polygala tenuifolia [100–174]

1,6-Dihydroxy-5,7-dimethoxyxanthone (42)
Caraipa densiflora [214]
Hypericum canariensis [54]

1,6-Dihydroxy-7,8-dimethoxyxanthone (43)
Bonnetia dinizii [270]
Calophyllum trapezifolium [128]
Polygala nyikensis [236]

1,6-Dihydroxy-7,8-dimethylenedioxyxanthone (44)
Caraipa densiflora [215, 214]

1,7-Dihydroxy-2,3-dimethoxyxanthone (45)
Frasera speciosa [90]
Halenia corniculata [266–296]
H. elliptica [322]
Polygala tenuifolia [174, 100]

1,7-Dihydroxy-3,4-dimethoxyxanthone (46)
Polygala virgata [32]

1,7-Dihydroxy-3,5-dimethoxyxanthone (47)
Hoppea fastigiata [252]

1,7-Dihydroxy-3,6-dimethoxyxanthone (48)
Calophyllum inophyllum [208]

1,7-Dihydroxy-3,8-dimethoxyxanthone (49) (Gentiacaulein)
Gentiana barbata [285]
G. bavarica [156, 158]
G. brachyphyla [155, 156]
G. ciliata [239]
G. detonsa [187]
G. favrati [156]
G. karelinii [50]
G. kochiana [292]
G. nivalis [155, 156]
G. rostanii [156]
G. schleicheri [156]
G. utriculosa [156]
G. verna [156]
Gentianopsis pludosa [349]
Haploclathra leiantha [256]
H. paniculata [259]
Swertia dilatata [329]
S. gracilescens [329]
S. nervosa [329]
S. perenis [154]
S. punicea [101]

Table 2 (*continued*)

S. racemosa [329]
S. speciosa [238]

1,8-Dihydroxy-2,6-dimethoxyxanthone (50)[a]
Centaurium erythraea [327]
C. linarifolium [274]

1,8-Dihydroxy-3,5-dimethoxyxanthone (51)[a]

(Methylbellidifolin or Swerchirin)
Blackstonia perfoliata [334]
Centaurium cachanlahuen [335]
C. erythraea [35, 190]
C. littorale [35, 333]
C. pulchellum [246]
Frasera albicaulis [314]
F. albomarginata [90]
F. caroliniensis [313]
Gentiana algida [51]
Gentiana bellidifolia [233–252]
G. karelinii [326]
G. lactea [302]
Saponaria vaccaria [192]
Swertia bimaculata [113]
S. chirata [79, 112]
S. chirayita [22]
S. dilatata [329]
S. gracilescens [329]
S. japonica [180–189]
S. milensis [150]
S. mussotii [321]
S. nervosa [329]
S. paniculata [13]
S. patens [219]
S. petiolata [195]
S. racemosa [329]
S. speciosa [238]
S. tetrapetala [7]

1,8-Dihydroxy-3,6-dimethoxyxanthone (52)
Diploschistes sp [95]

1,8-Dihydroxy-3,7-dimethoxyxanthone (53)[a]
(Methylswertianin or Swertiaperennin)
Blackstonia perfoliata [334]
Canscora decussata [66]
C. cachanlahuen [335]
C. pulchellum [246]
Gentiana ciliata [239]
G. karelinii [50]
G. tenella [52]
Schultesia lisianthoides [328]
Swertia chirata [112]
S. chirayita [22]
S. dilatata [329]
S. erythrosticta [160]
S. gracilescens [329]
S. iberica [85]
S. japonica [180–189]
S. lawii [105]
S. milensis [150]
S. mussotii [321]
S. nervosa [329]
S. paniculata [13]
S.patens [149]
S.perenis [154, 292]
S. punicea [150]
S. racemosa [329]
S. speciosa [238]

1,8-dihydroxy-4,6-dimethoxyxanthone (54)[a]
Erythreae centaurium [327]
Swertia mileensis [150]

2,4-dihydroxy-3,6-dimethoxyxanthone (55)
Hypericum reflexum [53]

2,5-dihydroxy-1,6-dimethoxyxanthone (56)
Garcinia thwaitesii [135]

2,6-dihydroxy-1,5-dimethoxyxanthone (57)
Garcinia sublliptica [247]

2,7-Dihydroxy-1,8-dimethoxyxanthone (58)
Cratoxylum formosanum [166]

3,8-Dihydroxy-1,2-dimethoxyxanthone(59)
Cratoxylum formosanum [166]
Calophyllum apetalum [165]

3,7-Dihydroxy-1,8-dimethoxyxanthone (60)
Haploclathra paniculata [259]

3,6-Dihydroxy-1,5-dimethoxyxanthone (61)
Calophyllum austroindicum [172]

3,8-Dihydroxy-1,7-dimethoxyxanthone (62)

(Isogentiacaulein)
Gentiana kochiana [136, 292]
Haploclathra paniculata [259]

4,6-Dihydroxy-1,3-dimethoxyxanthone (63)
Alnus glutinosa [197]

5,6-Dihydroxy-1,3-dimethoxyxanthone (64) (Ferrxanthone)
Haploclathra leiantha [256]
H. piniculata [259]
Mesua ferrea [337]

1,2,3-Trihydroxy-5-methoxyxanthone (65)
Centaurium erythraea [162–243]

1,2,8-Trihydroxy-3-methoxyxanthone (66)[b]
Archytaea multiflora [206]

1,3,5-Trihydroxy-2-methoxyxanthone (67)

(Tovopyrifolin-C)
Bonnetia dinizii [270]

(Haploxanthone)
Calophyllum apetalum [165]
Calophyllum bracteatum [312]
C. inophyllum [171]
C. tomentosum [28]
C. trapezifolium [128]
Centaurium linarifolium [114]
Kayea stylosa [131]
Monnina obtusifolia [283]
Pentadesma butyracea [81]
Tovomita pyrifolium [245]

1,3,5-Trihydroxy-6-methoxyxanthone (68)
Canscora decussata [66–107]
Haplochlatra leiantha [256]
Hoppea dichotoma [110]

Table 2 (*continued*)

1,3,6-Trihydroxy-5-methoxyxanthone (69)
Canscora decussata [107, 108]
Hoppea dichotoma [110]

1,3,6-Trihydroxy-7-methoxyxanthone (70)
Poeciloneuron pauciflorum [330]

1,3,7-Trihydroxy-6-methoxyxanthone (71) (Isoathyriol)
Athyrium mesosorum [331,332]

1,3,7-Trihydroxy-8-methoxyxanthone (72)[b]
Hoppea fastigiata [253]
Haploclathra leiantha [259]
H. paniculata [259]

1,3,8-Trihydroxy-5-methoxyxanthone (73)

(Isobellidifolin or Swertianol)
Gentiana algida [326]
Gentiana bellidifolia [52-234]
G. campestris [52]
G. germanica [52]
G. karelinii [50]
G. ramosa [52]
G. tenella [52]
Swertia chirata [112]
S. erythrosticta [160]
S. hookeri [106]
S. japonica [19]
S. mussotii [321]
S paniculata [13]
S. purpurascens [111]
Schultesia lisianthoides [328]

1,3,8-Trihydroxy-7-methoxyxanthone (74)

(Isogentiakochianin)
Calophyllum inophyllum [171]
Canscora decussata [66]
G. Cerastioides [187]
G. Germanica [186]
Kielmeyera speciosa [120]
Swertia iberica [85]
Schultesia lisianthoides [328]

1,4,7-Trihydroxy-3-methoxyxanthone (75)
Garcinia eugenifolia [171]

1,4,7-Trihydroxy-8-methoxyxanthone (76)
Cratoxylum formosanum [166]

1,4,8-Trihydroxy-3-methoxyxanthone (77)[b]
Gentiana bellidifolia [235]

1,4,8-Trihydroxy-6-methoxyxanthone (78)
Swertia japonica [33]

1,5,6-Trihydroxy-3-methoxyxanthone (79)
Canscora decussata [109]
Hypericum androsaemum [263]
Swertia chirata [231]
Schultesia lisianthoides [328]

1,5,7-Trihydroxy-3-methoxyxanthone (80)[b]
Hoppea fastigiata [251]

1,5,8-Trihydroxy-3-methoxyxanthone (81) (Bellidifolin)
Gentiana algida [326]
G. bellidifolia [233]
G. campestris [188]

(Gentiakochianin or Swertianin)
Chironia krebsii [342]
G. lactea [302]
G. ramosa [186]
G. strictiflora [187]
Swertia chirata [112–161]
S. dilatata [329]
S. erythrosticta [160]
S. gracilescens [329]
S. hookeri [106]
S. japonica [180–188]
S. nervosa [329]
S. paniculata [13]
S. perennis [154]
S. perfoliata [145]
S. purpurescens [8–111]
S. racemosa [329]
S. speciosa [90]

1,6,7-Trihydroxy-3-methoxyxanthone (82)[b] **(Athyriol)**
Athyrium mesosorum [331, 332]

1,6,8-Trihydroxy-2-methoxyxanthone (83)
Iris nigricans [11]

1,7,8-Trihydroxy-3-methoxyxanthone (84)

1,7,8-Trihydroxy-6-methoxyxanthone (85)
Archytaea multiflora [206]

2,4,5-Trihydroxy-1-methoxyxanthone (86)
Gentiana bavarica [156–158]
G. brachyphylla [155, 156]
G. ciliata [239]
G. favrati [156]
G. karelinii [50]
G. kochiana [136–292]
G. nivalis [155, 156]
G. rostani [156]
G. verna [153, 156]
Orphium frutescens [297]
Swertia calycina [295]
S. decussata [292]
S. dilatata [78]
S. erythrosticta [160]
S. gracilescens [329]
S. iberica [85]
S. japonica [21–33]
S. lawii [105]
S. mussotii [321]
S. nervosa [329]
S. racemosa [329]
S. speciosa [238]

(BR-xanthone-B)
Garcinia mangostana [26]

3,5,6-Trihydroxy-1-methoxyxanthone (87)
Calophyllum sclerophyllum [182]

1,3,5,6-Tetrahydroxyxanthone (88)
Calophyllum brasiliense [198]
C. sclerophyllum [182]
Canscora decussata [66, 107]
Cratoxylum cochinchinense [310]
Hypericum androsaemum [263]
Hypericum patulum [178]

Table 2 (*continued*)

Mammea africana [56]
Morus tinctoria [185]
Ochrocarpus odoratus [227]
Psorospermum febrifugum [4]
Symphonia globulifera [220–222]

1,3,5,7-Tetrahydroxyxanthone (89)
Garcinia pedunculata [289]

1,3,5,8-Tetrahydroxyxanthone (90) (Demethylbellidifolin)
Gentiana bellidifolia [52–233]
G. lactea [302]
G. ramosa [52–186]
G. strictiflora [187]
Iris nigricans [11]
Swertia chirata [112]
S. dilatata [329]
S. erythrosticta [160]
S. gracilescens [329]
S. hookeri [106]
S. japonica [19, 21, 189]
S. lawii [105]
S. macrosperma [350]
S. nervosa [329]
S. purpurescens [111]
S. racemosa [329]

1,3,6,7-Tetrahydroxyxanthone (91) (Norathyriol)
Allanblackia floribunda [227]
Athyrium mesosorum [265, 332]
Canscora decussata [109]
Chlorophora tinctoria [122]
Cratoxylum pruniflorum [199]
Garcinia echinocarpa [27]
G. mangostana [152]
G. multiflora [70]
G. pedunculata [289]
G. terpnophylla [27]
Hypericum androsaemum [263]
H. aucheri [200]
Iris nigricans [11]
Maclura pomifera [343]
Mammea africana [56]
Morus tinctoria [185]
Ochrocarpus odoratus [227]
Pentaphalangium solomonse [271]
Symphonia globulifera [220, 222]

1,3,7,8-Tetrahydroxyxanthone (92) (Norswertianin)
Canscora decussata [66]
Chironia krebsii [342]
Gentiana bavarica [158]
Orphium frutescens [297]
Swertia chirata [112]
S. dilatata [329]
S. erythrosticta [160]
S. gracilescens [329]
S. hookeri [106]
S. iberica [85]
S. japonica [21, 189]
S. lawii [105]
S. nervosa [329]
S. perennis [154]
S. purpurascens [111]
S. racemosa [329]

1,7-Dimethoxy-2,3-methylenedioxyxanthone (93)
Polygala tenuifolia [100]

1,8-Dimethoxy-2,3-methylenedioxyxanthone (94)
Polygala nyikensis [236]

1,2,3,7-Tetramethoxyxanthone (95)
Frasera albicaulis [314]
Polygala tenuifolia [174–181]

1,2,6,8-Tetramethoxyxanthone (96)
Bredemeyera brevifolia [268]

1,3,4,5-Tetramethoxyxanthone (97)
Frasera albicaulis [314]

1,3,4,7-Tetramethoxyxanthone (98)
Frasera albicaulis [314]

1,3,5,8-Tetramethoxyxanthone (99)
Swertia hookeri [106]

1,3,6,7-Tetramethoxyxanthone (100)
Allanblackia floribunda [226]
Polygala tenuifolia [100]

2,3,4,5-Tetramethoxyxanthone (101)
Halenia campanulata [161]

[a] The compounds 51/53, 51/54, 66/84, 72/82, 77/80, have the same structure, but they are cited under different names in the references.
[b] The compounds 51/53, 51/54, 66/84, 72/82, 77/80, have the same structure, but they are cited under different names in the references.

Clusiaceae, Bennett and Lee (1989) listed 50 tetraoxygenated xanthones from Clusiaceae species. A review by Mandal et al. (1992) 113 simple tetraoxygenated, prenylated and related xanthones are listed. Between 1942 and mid 1995, approx. 115 tetraoxygenated naturally occurring xanthones were presented in reviews. In the present review, 228 of these compounds found in the literature are listed (Tables 2–6).

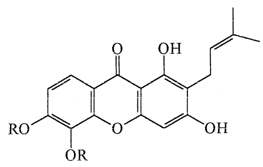
7. Synthesis and biosynthesis of xanthones

Some authors have reported the preparation of hydroxyxanthones (Atkinson and Heilbron, 1926; Grover et al., 1955; Shah and Shah, 1956; Quillinan and Scheinmann, 1972, 1973; Simoneau and Brassard, 1984), but the first xanthone synthesis was proposed by Kostanecki (1892) and the last by Ravi et al. (1994) describing a new route to xanthone synthesis, and Vitale et al. (1994) also describing a novel route for the preparation of xanthones and chromanones.

The preparation of nine 1,2,3,8-tetraoxygenated xanthones was proposed by Gil et al. (1990) and 1,3,5,6-, 3,4,5,6-, 3,4,6,7- and 2,3,6,7-tetrahydroxyxanthone were synthesized from benzophenone precursors (Sundholm, 1978). The total synthesis of lichen xanthones (Patel and Trivedi, 1983), synthesis of furanoxanthones (Pinto and Polonia, 1974; Patel and Trivedi, 1991), synthesis of new

Table 3
Mono C_5 tetraoxygenated naturally occurring xanthones

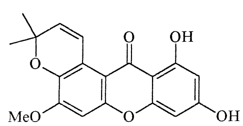
1,3,5,6-Tetrahydroxy-2-(3-methylbut-2-enyl)xanthone (102)
Calophyllum brasiliensis [72]
C. austroindicum [172]
C. canum [57]
C. neo-ebudicum [303]
C. sclerophyllum [182]
C. scriblitifolium [183]
C. fragrans [224]
C. inophyllum [10, 184]



(102 R = H) (103 R = CH₃)

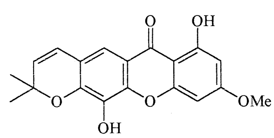
1-Hydroxy-3,5,6-trimethoxy-2-(3-methylbut-2-enyl)xanthone (103)
Calophyllum ramiflorum [39]

Paxanthone (104)
Hypericum paturum [177]



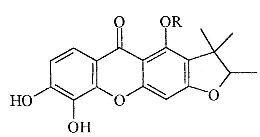
(104)

Forbexanthone (105)
Garcinia forbesii [147]



(105)

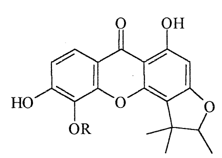
Toxyloxanthone C (106)
Calophyllum zeylanicum [133]
Kielmeyera ferruginea [121]
Maclura pomifera [86]



Geronthoxanthone J (107)
Cudrania cochinchinensis [64]

(106 R=H; 107 R=Me)

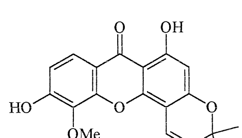
2-Deprenylrheediaxanthone B (108)
Hypericum roeperanum [290]



(108 R=H; 109 R=Me)

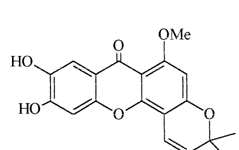
5-Methoxy-2-deprenylrheediaxanthone B (109)
Hypericum roeperanum [290]

5-*O*-Methyllisojacareubin (110)



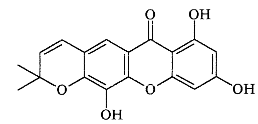
(110)

Lorostemin A (111)
Lorostemon coelhoi [48]
L. negrensis [48]



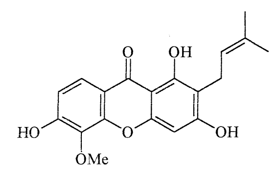
(111)

1,3,5-Trihydroxy-6′,6′-dimethylpyrano(2′,3′:6,7)xanthone (112)
Rheedia brasiliensis [82]



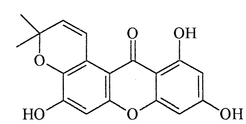
(112)

Morusignin D (113)
Morus insignis [144]
Hypericum patulum [179]



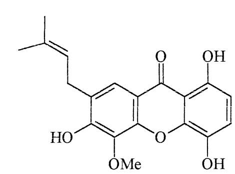
(113)

Toxyloxanthone-B (114)
Hypericum androsaemum [263]
H. paturum [177]
H. sampsonii [71]
Maclura pomifera [76–86]
Morus insignis [144]



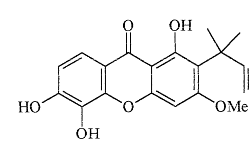
(114)

1,4,6-Trihydroxy-5-methoxy-7-(3-methylbut-2-enyl)xanthone (115)
Garcinia dulcis [148]



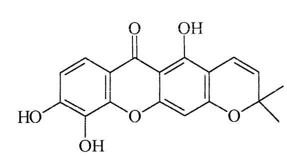
(115)

Cudraniaxanthone (116)
Cudrania cochinchinensis [62]
Cudrania javanensis [255]



(116)

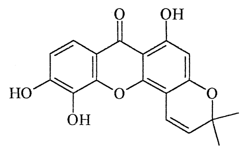
Jacareubin (117)
Calophyllum austroindicum [172]
C. bracteatum [312]
C. brasiliense [72, 280]
C. calaba [209, 312]
C. canum [57]
C. cordato-oblongum [134]
C. cuneifolium [130]
C. fragrans [224]
C. inophyllum [10–184, 208]
C. neo-ebudicum [303]
C. ramiflorum [39]
C. sclerophyllum [182]
C. scriblitifolium [183]
C. thwaitesii [77]
C. tomentosum [191]
C. trapezifolium [128]
C. walkerii [77]
C. zeylanicum [133]
Kielmeyera ferruginea [121]
Pentadesma butyracea [81]



(117)

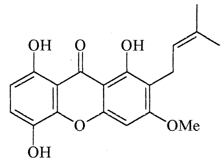
Table 3 (*continued*)

Isojacareubin (118)
Hypericum roeperanum [290]



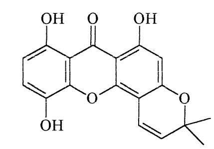
(118)

1,5,8-Trihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (119)
Garcinia mangostana [275, 276]



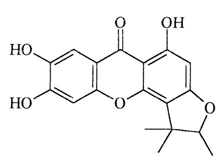
(119)

Morusignin C (120)
Morus insignis [144]



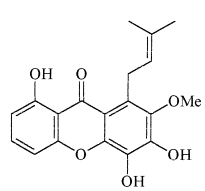
(120)

1,6,7-Trihydroxy-4,4,5-trimethyldihydrofurano-(2,3:3,4) xanthone (121)
Allanblackia floribunda [226]



(121)

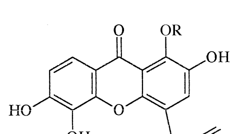
Celebixanthone (122)
Cratoxylum celebicum [317, 318]



(122)

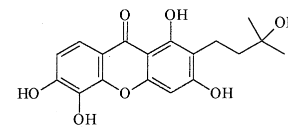
Symphoxanthone (123)
Garcinia subelliptica [248]
Symphonia globulifera [223]

1-Methylsymphoxanthone (124)
Garcinia subelliptica [248]



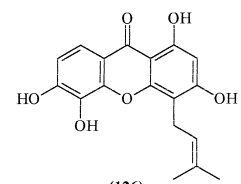
(123 R=H; 124 R=Me)

1,3,5,6-Tetrahydroxy-2-(3-hydroxy-3-methylbutyl)xanthone (125)
Calophyllum inophyllum [119]



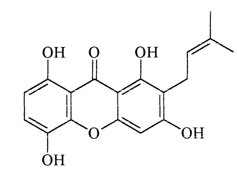
(125)

Ugaxanthone (126)
Symphonia globulifera [221]



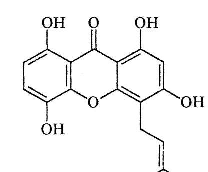
(126)

Morusignin B (127)
Morus insignis [144]



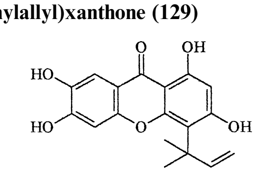
(127)

Morusignin A (128)
Morus insignis [144]



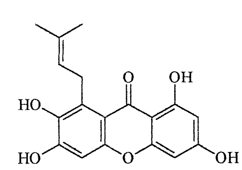
(128)

1,3,6,7-Tetrahydroxy-4-(1,1-dimethylallyl)xanthone (129)
Allanblackia floribunda [226]



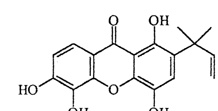
(129)

1,3,6,7-Tetrahydroxy-8-(3-methylbut-2-enyl)xanthone (130)
Hypericum androsaemum [176–263]



(130)

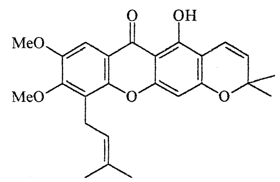
Subelliptenone F (131)
Garcinia subelliptica [168]
Garcinia dulcis [166]



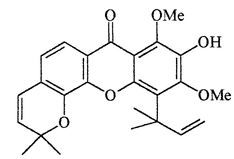
(131)

Table 4
Di-C_5 tetraoxygenated naturally occurring xanthones

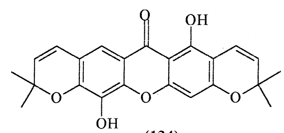
Tovopyrifolin D (132)
Tovomita pyrifolium [47]


(132)

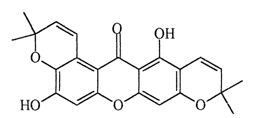
Kayeaxanthone (133)
Kayea stylosa [131]


(133)

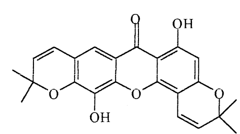
Pyranojacareubin (134)
Garcinia densivenia [339]
G. forbesii [147]
Rheedia brasiliensis [82]
R. gardneriana [83, 84]


(134)

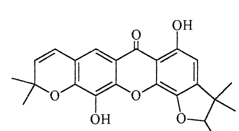
Padiaxanthone (135)
Hypericum patulum [175]


(135)

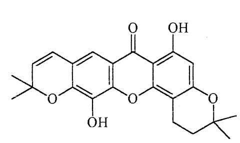
Rheediaxanthone A (136)
Garcinia staudtii [340]
Rheedia benthamiana [80]
R. brasiliensis [82]
R. gardneriana [83]


(136)

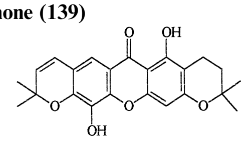
Gerontoxanthone A (137)
Cudrania cochinchinensis [64]
Rheedia brasiliensis [82]


(137)

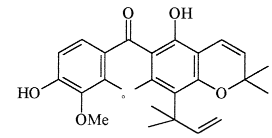
1,5-Dihydroxy-6,6-dimethylpyrano(2,3:6,7)-6″,6″-dimethyldihydropyrano(2″,3″:3,4)xanthone (138)
Rheedia brasiliensis [82]


(138)

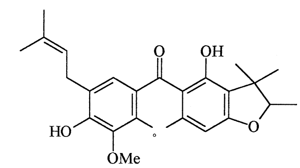
1,5-Dihydroxy-6,6-dimethylpyrano(2,3:6,7)-6″,6″-dimethyldihydropyrano(2″,3″:2,3)xanthone (139)
Rheedia brasiliensis [82]


(139)

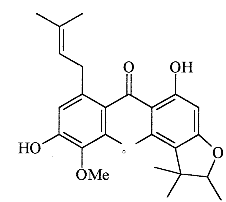
10-*O*-methylmacluraxanthone (140)
Kayea stylosa [131]


(140)

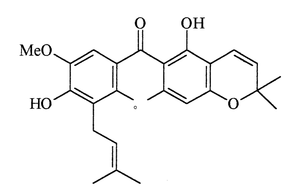
Gerontoxanthone E (141)
Cudrania cochinchinensis [62]


(141)

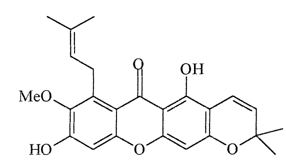
Caloxanthone B (142)
Carapia inophyllum [173]


(142)

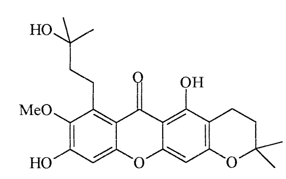
Tovopyrifolin A (143)
Tovomita pyrifolium [47, 245]


(143)

3-Isomangostin (144)
Garcinia mangostana [228, 305]


(144)

3-Isomangostin hydrate (145)
Garcinia mangostana [228]


(145)

β-Mangostin (146)
Cratoxylum cochinchinense [36]
Garcinia mangostana [20, 126, 228, 298]

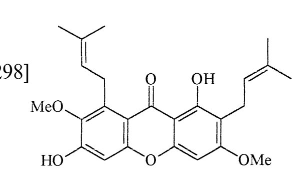
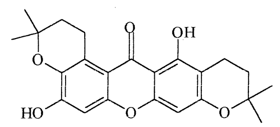
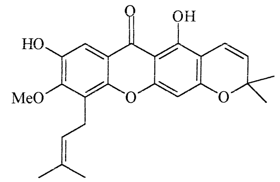

(146)

Table 4 (*continued*)

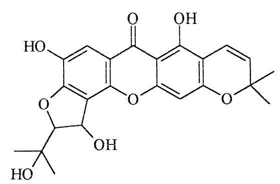
BR-xanthone A (147)
Garcinia mangostana [26]


(147)

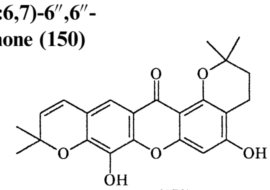
Manglexanthone (148)
Tovomita mangle [237]


(148)

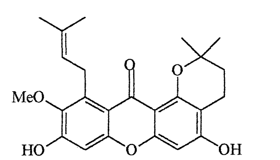
Caloxanthone D (149)
Calophyllum inophyllum [171]


(149)

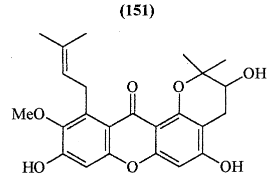
3,5-Dihydroxy-6,6-dimethylpyrano(2,3:6,7)-6″,6″-dimethyldihydropyrano(2″,3″:1,2)xanthone (150)
Rheedia brasiliensis [82]


(150)

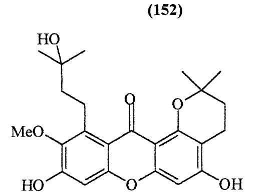
1-Isomangostin (151)
Garcinia mangostana [228]


(151)

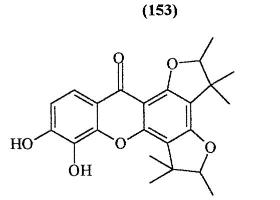
11-Hydroxy-1-isomangostin (152)
Cratoxylum cochinchinense [310]


(152)

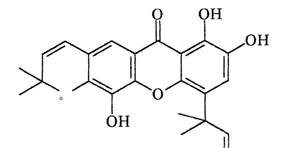
1-Isomangostin hydrate (153)
Garcinia mangostana [228]


(153)

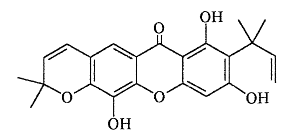
Rheediaxanthone C (154)
Rheedia brasiliensis [82]
R. gardneriana [83]
R. benthamiana [80]


(154)

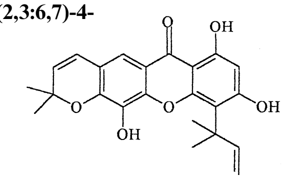
Subelliptenone H (155)
Garcinia subelliptica [169]


(155)

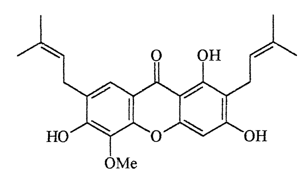
Gerontoxanthone B (156)
Cudrania cochinchinensis [64]


(156)

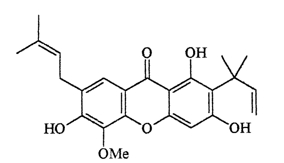
1,3,5-Trihydroxy-6,6-dimethylpyrano(2,3:6,7)-4-(1,1-dimethylallyl)xanthone (157)
Rheedia brasiliensis [82]
Garcinia opaca [118]


(157)

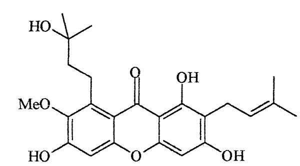
Cudraxanthone F (158)
Cudrania tricuspidata [142]


(158)

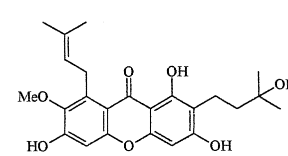
Cudraxanthone E (159)
Cudrania tricuspidata [142]


(159)

Garcinone D (160)
Cratoxylum cochinchinense [36]
Garcinia mangostana [307]


(160)

Cratoxylone (161)
Cratoxylum cochinchinense [36]


(161)

Cudraxanthone C (162)
Cudrania tricuspidata [141]

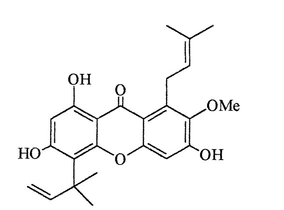
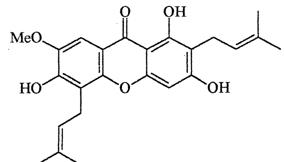

(162)

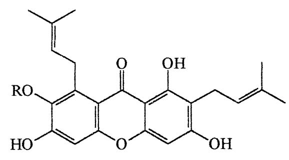
Table 4 (*continued*)

1,3,6-Trihydroxy-7-methoxy-2,5-*bis*(3-methyl-but-2-enyl)xanthone (163)
Garcinia cowa [280]



(163)

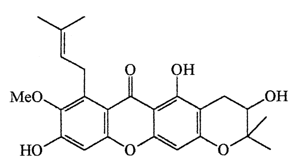
Mangostin (164)
Cratoxylum cochinchinense [36]
Garcinia echinocarpa [27]
G. mangostana
[20, 92, 126–228, 298, 316]
G. terpnophylla [27]



(164 R = Me; 165 R = H)

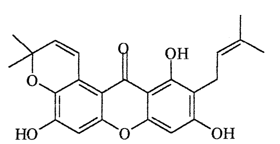
γ-Mangostin or Normangostin (165)
Garcinia mangostana
[20, 126, 228, 298]
Hypericum paturum [177]
Garcinia mangostana [260]

Mangostanol (166)
Garcinia mangostana [260]



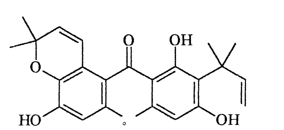
(166)

Garcinone B (167)
Garcinia mangostana [298, 306, 308]
Hypericum patulu [176]
Morus insignis [144]



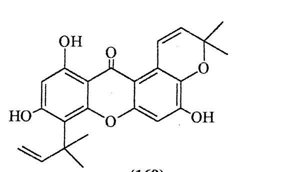
(167)

Cudraxanthone K (168)
Cudrania tricuspidata [141]



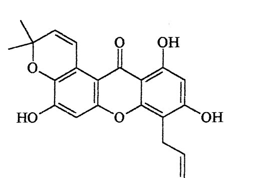
(168)

Cudraxanthone B (169)
Cudrania tricuspidata [264]



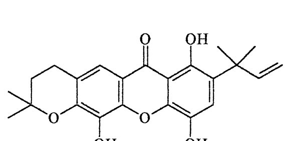
(169)

Paxanthone B (170)
Hypericum patulum [176]



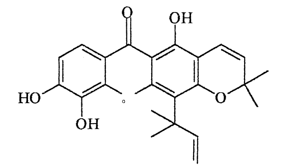
(170)

Subelliptenone I (171)
Garcinia subelliptica [169]



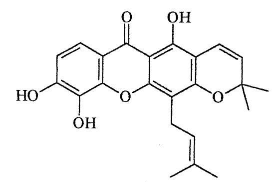
(171)

Macluraxanthone (172)
Calophyllum inophyllum [173]
Garcinia opaca [118]
G. ovalifolia [338]
Maclura aurantica [17]
M. pomifera [344, 345]
Rheedia benthamiana [80]
R. brasiliensis [82]
R. gardneriana [83]



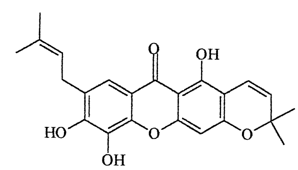
(172)

Xanthone V_1 (173)
Vismia guineensis [45]



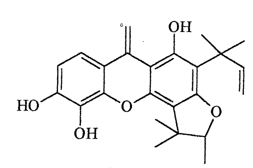
(173)

7-Prenyljacareubin (174)
Rheedia gardneriana [83]



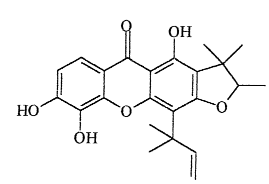
(174)

Rheediaxanthone B (175)
Garcinia polyantha [12]
Rheedia benthamiana [80]
R. brasiliensis [82]
R. gardneriana [83]



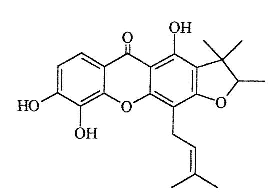
(175)

Isorheediaxanthone B (176)
Garcinia polyantha [12]
Rheedia brasiliensis [82]
R. gardneriana [83]



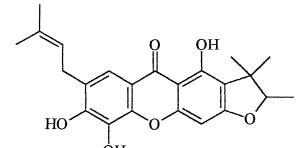
(176)

Gerontoxanthone C (177)
Cudrania cochinchinensis [64]



(177)

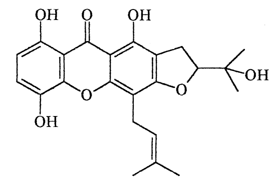
Gerontoxanthone G (178)
Cudrania cochinchinensis [62]



(178)

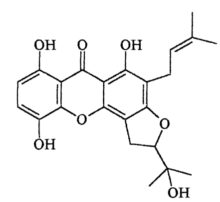
Table 4 (*continued*)

Morusignin E (179)
Morus insignis [143]



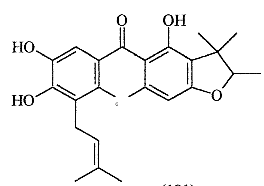
(179)

Morusignin F (180)
Morus insignis [143]



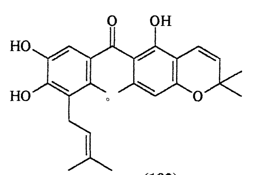
(180)

Cudraxanthone M (181)
Cudrania tricuspidata [140]



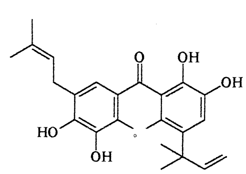
(181)

Caloxanthone A (182)
Carapia inophyllum [173]



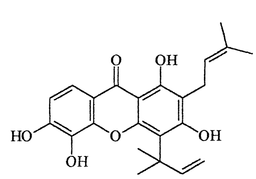
(182)

Subelliptenone B (183)
Garcinia subelliptica [163]



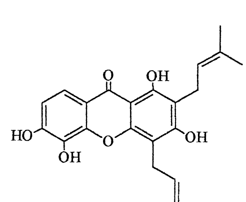
(183)

Gerontoxanthone I (184)
Cudrania cochinchinensis [62]



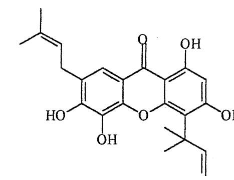
(184)

Xanthone V_{1a} (185)
Vismia guineensis [45]



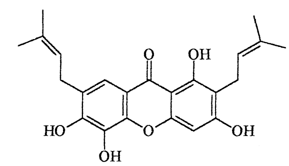
(185)

1,3,5,6-Tetrahydroxy-4-(1,1-dimethylallyl)-7-(3-methylbut-2-enyl)xanthone (186)
Rheedia brasiliensis [82]



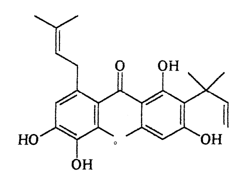
(186)

Toxyloxanthone-D (187)
Maclura pomifera [86]



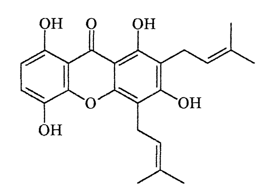
(187)

Alvaxanthone (188)
Maclura aurantica [17]
M. pomifera [344, 346]



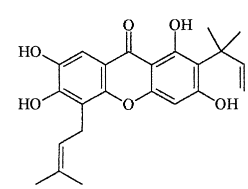
(188)

Gartanin (189)
Garcinia mangostana
[20, 126, 228, 260, 275, 298]
Morus insignis [144]



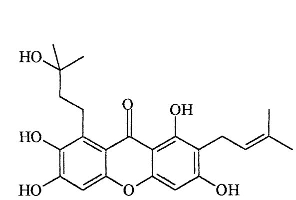
(189)

Cudraxanthone L (190)
Cudrania tricuspidata [140]



(190)

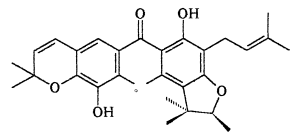
Garcinone C (191)
Garcinia mangostana [306]



(191)

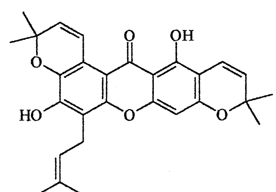
Table 5
Tri C_5 tetraoxygenated naturally occurring xanthones

1,5-Dihydroxy-6,6-dimethylpyrano(2,3:6,7)-4″,4″,5″-trimethylfurano(2″,3″:3,4)-2-(3-methylbut-2-enyl)xanthone (192)
Garcinia opaca [118]



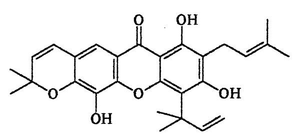
(192)

Tovophyllin B (193)
Tovomita macrophyla [269]
T. pyrifolium [47, 245]



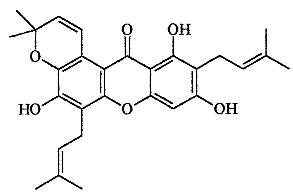
(193)

1,3,5-Trihydroxy-6,6-dimethylpyrano(2,3:6,7)-2-(3-methylbut-2-enyl)-4-(1,1-dimethylallyl)xanthone (194)
Garcinia opaca [118]



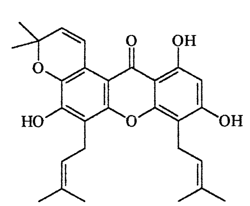
(194)

Tovophyllin A (195)
Cratoxylum cochinchinense [36]
Tovomita macrophyla [269]
T. pyrifolium [47, 245]



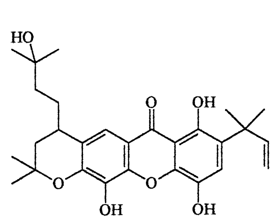
(195)

Pentadesmaxanthone (196)
Pentadesma butyracea [81]



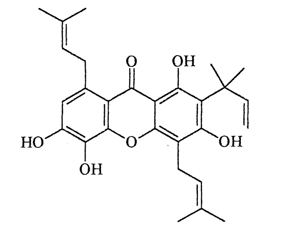
(196)

Subelliptenone E (197)
Garcinia subelliptica [168]



(197)

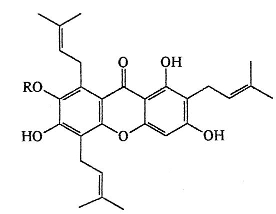
Nervosaxanthone (198)
Garcinia nervosa [12]



(198)

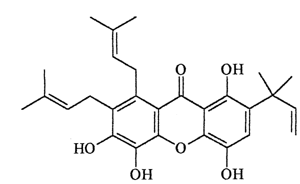
Garcinone E (199)
Garcinia mangostana
[20, 92, 202, 260, 298]

7-*O*-methiylgarcinone (200)
Garcinia cowa [202]



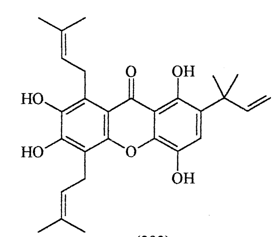
(199 R = H; 200 R = Me)

Subelliptenone A (201)
Garcinia subelliptica [163, 248]



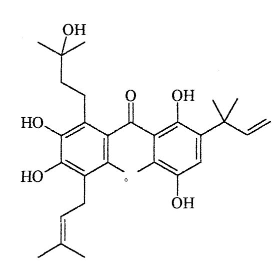
(201)

Dulciol B (202)
Garcinia dulcis [166]



(202)

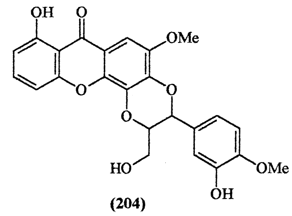
Dulciol C (203)
Garcinia dulcis [166]



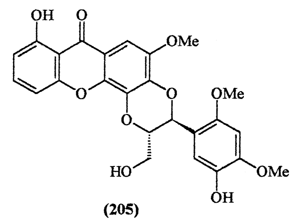
(203)

Table 6
More complex tetraoxygenated naturally occurring xanthones

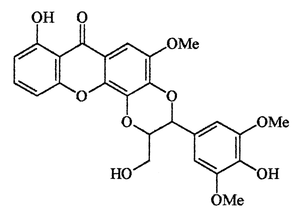
Cadensin A (204)
Caraipa densiflora [59]
C. grandifolia [104]
C. valioi [104]
Kielmeyera coriacea [59]
Vismia guaramirangae [132]


(204)

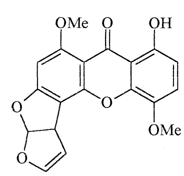
Cadensin-B (205)
Caraipa densiflora [59]
Kielmeyera coriacea [59]
Vismia guaramirangae [132]


(205)

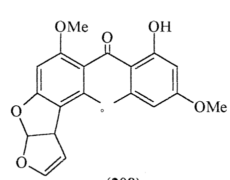
Cadensin C (206)
Vismia guaramirangae [132]


(206)

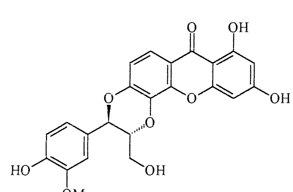
5-Methoxysterigmatocystin (207)
Aspergillus versicolor [151]


(207)

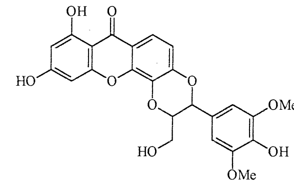
6-Methoxysterigmatocystin (208)
Aspergillus versicolor [49]


(208)

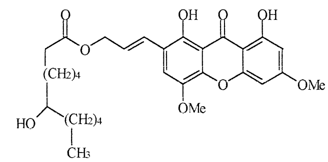
5′-Demethoxycadensin G (209)
Cratoxylum cochinchinense [310]


(209)

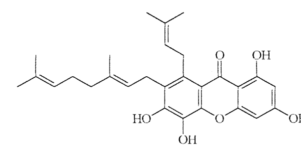
Cadensin G (210)
Psorospermum febrifugum [2]


(210)

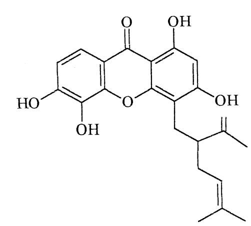
Sapxanthone (211)
Saponaria vaccaria [193]


(211)

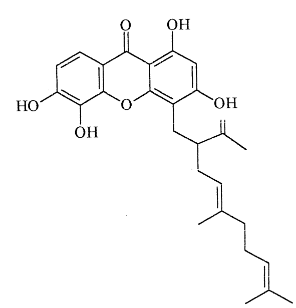
Garciniaxanthone E (212)
Garcinia subelliptica [248]


(212)

Calycinoxanthone D (213)
Hypericum roeperanum [290]


(213)

Roeperanone (214)
Hypericum roeperanum [290]


(214)

5-*O*-Demethylpaxanthonin (215)
Hypericum roeperanum [290]
H. patulum [175]

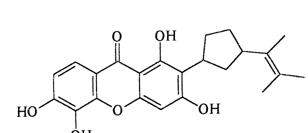
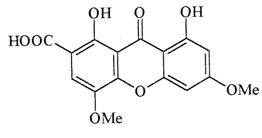

(215)

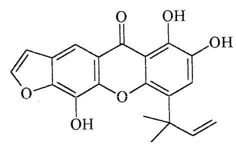
Table 6 (*continued*)

Vaccaxanthone (216)
Saponaria vaccaria [192]



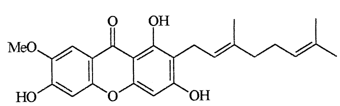
(216)

1,2,5-Trihydroxy-4-(1,1-dimethylallyl)-furano(2,3:6,7)xanthone (217)
Garcinia subelliptica [162]



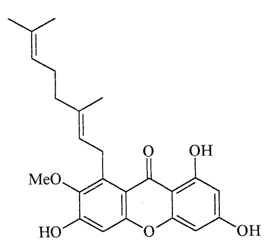
(217)

Cowaxanthone (218)
Garcinia cowa [280]



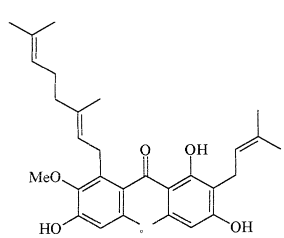
(218)

Rubraxanthone (219)
Garcinia cowa [211]
G. nervosa [12]
G. pyrifera [12]



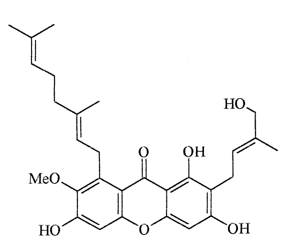
(219)

Cowanin (220)
Garcinia cowa [280]



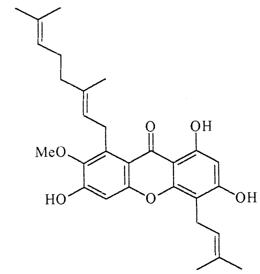
(220)

Cowanol (221)
Garcinia cowa [280]



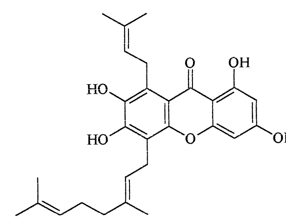
(221)

Isocowanin (222)
Garcinia pyrifera [12]



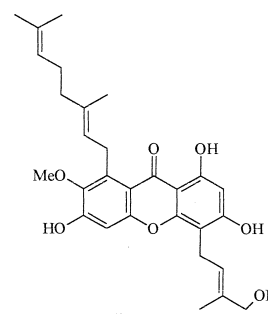
(222)

Dulciol A (223)
Garcinia dulcis [166]



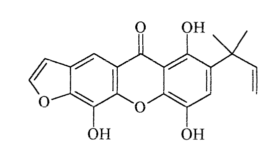
(223)

Isocowanol (224)
Garcinia pyrifera [12]



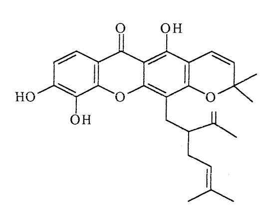
(224)

Subelliptenone C (225)
Garcinia subelliptica [162]
G. dulcis [166]



(225)

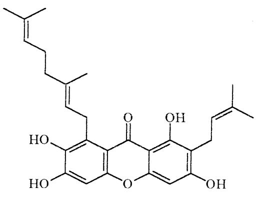
Maculatoxanthone (226)
Hypericum maculatum [14]



(226)

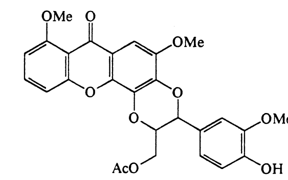
Table 6 (*continued*)

Norcowanin (227)
Garcinia cowa [280]



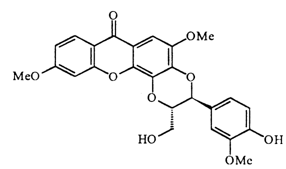
(227)

Isocadensin D — monoacetate (231)
Psorospermum febrifugum [2]



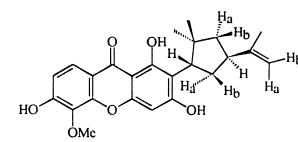
(231)

6-Methoxykielcorin (228)
Hypericum reflexum [53]



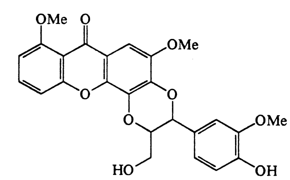
(228)

Paxanthonin (232)
Hypericum patulum [176, 179]



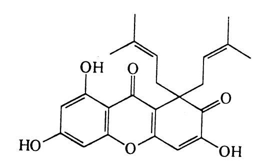
(232)

Isocadensin D (229)
Psorospermum febrifugum [2]



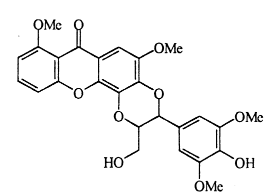
(229)

1,2-Dihydro-3,6,8-trihydroxy-1,1-*bis*(3-methylbut-2-enyl)xanthen-2,9-dione (233)
Hypericum patulum [178]



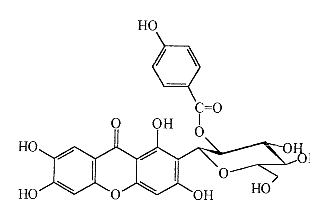
(233)

Cadensin F (230)
Psorospermum febrifugum [2]



(230)

Muraxanthone (234)
Seneico mikanioides [60]



(234)

xanthones (Patolia and Trivedi, 1983), a new one-step method (Atkinson and Lewis, 1969) and a general study for synthesis of dioxygenated xanthones are in a recent report by Lin et al. (1992).

The biosynthetic pathways to xanthones have been discussed in recent years. Initially, these attempted to interrelate the observed oxygen pattern of natural xanthones and correlate them with recognized oxygenation patterns. In general it seems that ring **A** and the attached CO group are provided by the shikimic acid pathway, whereas ring **B** arises via the acetate–malonate polyketide route (Locksley and Murray, 1970; Afzal and Al-Hassan, 1980; Sultanbawa, 1980). Therefore Locksley et al. (1967) reported the significance of maclurin in xanthone biosynthesis and the biogenetic-type synthesis of xanthones from their benzophenone precursors (Locksley and Murray, 1970). Gottlieb (Gottlieb and Magalhães, 1966; Gottlieb, 1968; Gottlieb et al., 1968) offered biogenetic proposals regarding xanthones, and Bhanu et al. (1972) related the biogenetic implications in the conversion of 4-phenylcoumarins into xanthones. More recently; biosynthetic studies on tajixanthone and shamixanthone (Ahmed et al., 1992) were reported.

Some xanthones in lower plants have been proven to be totally acetate-derived, from seven acetate units (McMaster et al., 1960; Birch et al., 1976). However, the oxygenation patterns of all xanthones in higher plants suggest that these are formed by a mixed shikimate–acetate pathway. This involves the condensation of shikimate and acetate-derived moieties to form benzophenones or benzophenone-like intermediates, which then react intramolecularly to form xanthones. Mechanisms for this intramolecular reaction have been postulated involving either direct phenol oxidative coupling (Lewis, 1963), quinone addition (Ellis et al., 1967), dehydration between hydroxyl groups on the acetate and shikimate-derived rings (Markham, 1965), or spirodienone formation and subsequent rearrangement to form the xanthone (Gottlieb, 1968; Carpenter et al., 1969).

Regarding lichen and fungi biosynthesis, it is important to say that many secondary metabolites found in lichen-forming fungi play a dominant role in the systematics of these organisms due to extensive morphological parallels and their clear ecological significance. Despite their common occurrence in a number of important genera, lichen xanthones have not featured prominently in the repertoire of lichen taxonomists. Nevertheless, with the availability of more sensitive methods of detection and synthetic materials for comparison, these compounds have been effectively employed in recent systematic studies of lichens (Leuckert et al., 1990; Elix and Crook, 1992; Elix et al., 1992).

Elix and Crook (1992) reported the unambiguous total synthesis of 17 chlorine-containing derivatives of norlichexanthone, achieved using the condensation of an appropriately substituted methyl or ethyl orsellinate and phloroglucinol or 2-chlorophloroglucinol in the key step. Previously, Elix et al. (1992) reported the synthesis of several trioxygenated lichen xanthones (Elix et al., 1984).

8. Conclusion

The majority of xanthones that have been isolated so far are of the tetraoxygenated-type. The main natural source of these xanthones are plants from the Gentianaceae (14 genus, 72 species), Clusiaceae (23 genus, 84 species), Moraceae (4 genus, 8 species) and Polygalaceae (3 genus, 7 species) families. Other families of higher plants that produce tetraoxygenated xanthones are Betulaceae, Caryophyllaceae, Gesneriaceae, Iridaceae, Loganiaceae, Lytraceae and Polypodiaceae. Only three tetraoxygenated xanthones have been identified as fungal and lichen metabolites: two in *Aspergillus versicolor* and one in *Diploschistes* sp. Therefore, tetraoxygenated xanthones have no application in chemosystematics studies of these organisms.

Acknowledgements

Part of the PhD thesis of Valdir Peres, submitted at Universidade Federal de Minas, Gerais, Belo Horizonte, 31270-901, Minas Gerais, Brasil.

References

[1] Abou-Shoer, M., Boettner, F.E., Chang, C.J., Cassady, J.M., 1988. Phytochemistry 27, 2795.
[2] Abou-Shoer, M., Habib, A.A., Chang, C.J., Cassady, J.M., 1989. Phytochemistry 28, 2483.
[3] Abou-Shoer, M., Suwanborirux, K., Chang, C.J., Cassady, J.M., 1989. Tetrahedron Letters 30, 3385.
[4] Abou-Shoer, M., Suwanborirux, K., Habib, A.A.M., Chang, C.J., Cassady, J.M., 1993. Phytochemistry 34, 1413.
[5] Afzal, M., Al-Hassan, J.M., 1980. Heterocycles 14, 1173.
[6] Afzal, M., Al-Hassan, J.M., Al-Masad, F.N., 1979. Heterocycles 12, 269.
[7] Agata, I., Sekizaki, H., Sakushima, A., Nishibe, S., Hisada, S., Kimura, K., 1981. Yakugaku Zasshi 101, 1067.
[8] Ahmad, S., Ikram, M., Khan, I., Galbraith, M.N., 1973. Phytochemistry 12, 2542.
[9] Ahmed, S.A., Bardshiri, E., McIntyre, C.R., Simpson, T.J., 1992. Australian Journal of Chemistry 45, 249.
[10] Al-Jeboury, F.S., Locksley, H.D., 1971. Phytochemistry 10, 603.
[11] Al-Khalil, S., Tosa, H., Iinuma, M., 1995. Phytochemistry 38, 729.
[12] Ampofo, S.A., Waterman, P.G., 1986. Phytochemistry 25, 2351.
[13] Anand, S.M., Basumatary, P.C., Ghosal, S., Handa, S.S., 1982. Planta Medica 45, 61.
[14] Arends, P., 1969. Tetrahedron Letters 55, 4893.
[15] Arends, P., Helboe, P., 1972. Acta Chemica Scandinavica 26, 4180.
[16] Arends, P., Helboe, P., Moller, J., 1973. Organic Mass Spectrometry 7, 667.
[17] Artamonova, N.A., Nikonov, G.K., Kiseleva, V.V., 1989. Chemical Natural Compounds 3, 373.
[18] Asahina, Y., Asano, J., Uyeno, Y., 1942. Bulletin of the Chemical Society Japan 17, 104.
[19] Asahina, Y., Asano, J., Uyeno, Y., 1942. Journal of the Pharmaceutical Society Japan 62, 22.
[20] Asai, F., Tosa, H., Tanaka, T., Iinuma, M., 1995. Phytochemistry 39, 943.
[21] Ashida, S., Noguchi, S.F., Suzuki, T., 1994. Journal of the America Oil Chemical Society 71, 1095.
[22] Asthana, R.K., Sharma, N.K., Kulshreshtha, D.K., Chatterjee, S.K., 1991. Phytochemistry 30, 1037.
[23] Atkinson, H., Heilbron, I.M., 1926. Journal of the Chemical Society, 2688.
[24] Atkinson, J.E., Lewis, J.R., 1969. Journal of the Chemical Society, 281.
[25] Balachandran, S., Vishwakarma, R.A., Popli, S.P., Kapil, R.S., 1988. Indian Journal of Chemistry 27B, 385.
[26] Balasubramanian, K., Rajagopalan, K., 1988. Phytochemistry 27, 1552.
[27] Bandaranayake, W.M., Selliah, S.S., Sultanbawa, M.U.S., Ollis, W.D., 1975. Phytochemistry 14, 1878.
[28] Banerji, A., Deshpande, A.D., Prabhu, B.R., Pradhan, P., 1994. Journal of Natural Products 57, 396.
[29] Barnes, C.S., Occolowitz, J.L., 1964. Australian Journal of Chemistry 17, 975.
[30] Barraclough, D., Locksley, H.D., Scheinmann, F., Magalhães, M.T., Gottlieb, O.R., 1970. Journal of the Chemical Society B, 603.
[31] Bashir, A., Hamburger, M., Gupta, M.P., Solis, P., Hostettmann, K., 1992. Phytochemistry 31, 3203.
[32] Bashir, A., Hamburger, M., Msonthi, J.D., Hostettmann, K., 1992. Phytochemistry 31, 309.
[33] Basnet, P., Kadota, S., Namba, T., 1994. Planta Medica 60, 507.
[34] Basnet, P., Kadota, S., Shimizu, M., Takata, Y., Kobayashi, M., Namba, T., 1995. Planta Medica 61, 402.
[35] Beerhues, L., Berger, U., 1994. Phytochemistry 35, 1227.
[36] Bennett, G.J., Harrison, L.J., Sai, G.L., Sim, K.Y., 1993. Phytochemistry 32, 1245.
[37] Bennett, G.J., Lee, H.H., 1989. Phytochemistry 28, 967.
[38] Bennett, G.J., Lee, H.H., 1991. Phytochemistry 30, 1347.
[39] Bhanu, S., Scheinmann, F., Jefferson, A., 1975. Phytochemistry 14, 298.

[40] Bhanu, S., Saroja, T., Seshadri, T.R., Mukerjee, S.K., 1972. Indian Journal of Chemistry 10, 577.
[41] Bhardwaj, D.K., Jain, R.K., Jain, B.C., Mehta, C.K., 1978. Phytochemistry 17, 1440.
[42] Bhardwaj, D.K., Seshadri, T.R., Singh, R., 1977. Phytochemistry 16, 1616.
[43] Bhattacharya, S.K., Ghosal, S., Chaudhuri, R.K., Sanyal, A.K., 1972. Journal of Pharmaceutical Science 61, 1838.
[44] Birch, A.J., Baldas, J., Hlubucek, J.R., Simpson, T.J., Westerman, P.W., 1976. Journal of the Chemical Society Perkin Transactions I, 898.
[45] Botta, B., Delle-Monache, G., Delle-Monache, F., Bettolo, G.B.M., Menichini, F., 1986. Phytochemistry 25, 1217.
[46] Braz Filho, R., Miranda, C.A.S., Gottlieb, O.R., Magalhães, M.T., 1982. Acta Amazonica 12, 801.
[47] Braz Filho, R., Costa, S.B.S., Rocha, A.I., 1983. Arquivo da Universidade Federal Rural do Rio de Janeiro 6, 31.
[48] Braz Filho, R., Lemos, M.J.C., Gottlieb, O.R., 1973. Phytochemistry 12, 947.
[49] Bullock, E., Kirkaldy, D., Roberts, J.C., Underwood, J.G., 1963. Journal of the Chemical Society, 829.
[50] Butayarov, A.V., Batirov, E.K., Tadzhibaev, M.M., Malikov, V.M., 1993. Journal Natural Compounds 3, 469.
[51] Butayarov, A.V., Batirov, E.K., Tadzhibaev, M.M., Ibragimov, E.E., Malikov, V.M., 1993. Khimiya Prirodnykh Soedinenii 6, 901.
[52] Carbonnier, J., Massias, M., Molho, D., 1977. Bulletin of the Museum of National History Natural Paris 13, 23.
[53] Cardona, M.L., Fernandez, M.I., Pedro, J.R., Serrano, A., 1990. Phytochemistry 29, 3003.
[54] Cardona, M.L., Fernandez, M.I., Pedro, J.R., Seoane, E., Vidal, R., 1986. Journal of Natural Products 49, 95.
[55] Cardona, M.L., Seoane, E., 1982. Journal of Natural Products 45, 134.
[56] Carpenter, I., Locksley, H.D., Scheinmann, F., 1969. Journal of the Chemical Society C, 2421.
[57] Carpenter, I., Locksley, H.D., Scheinmann, F., 1969. Journal of the Chemical Society C, 486.
[58] Carpenter, I., Locksley, H.D., Scheinmann, F., 1969. Phytochemistry 8, 2013.
[59] Castelão, J.F. Jr., Gottlieb, O.R., Lima, R.A., Mesquita, A.A.L., Gottlieb, H.E., Wenkert, E., 1977. Phytochemistry 16, 735.
[60] Catalano, S., Luschi, S., Flamini, G., Luigi, P., Neri, E.M., Morelli, I., 1996. Phytochemistry 42 (6), 1605.
[61] Chakravarty, A.K., Mukhopadhyay, S., Moitra, S.K., Das, B., 1994. Indian Journal of Chemistry 33B, 405.
[62] Chang, C.H., Lin, C.C., Kawata, Y., Hattori, M., Namba, T., 1989. Phytochemistry 28, 823.
[63] Chang, C.H., Lin, C.C., Hattori, M., Namba, T., 1989. Phytochemistry 28, 595.
[64] Chang, C.H., Lin, C.C., Hattori, M., Namba, T., 1994. Journal of Ethnopharmacology 44, 79.
[65] Chang, C.H., Lin, C.C., Kadota, S., Hattori, M., Namba, T., 1995. Phytochemistry 40, 945.
[66] Chaudhuri, R.K., Ghosal, S., 1971. Phytochemistry 10, 2425.
[67] Chaudhuri, R.K., Zymalkowski, F., Frahm, A.W., 1978. Tetrahedron 34, 1837.
[68] Chawla, H.M., Chibber, S.S., Khera, U., 1975. Journal of Chromatography 111, 246.
[69] Chawla, H.M., Chibber, S.S., Seshadri, T.R., 1973. Proccedings Indian Academic Science, 141
[70] Chen, F.C., Lin, Y.M., Hung, J.C., 1975. Phytochemistry 14, 300.
[71] Chen, M.T., Chen, C.M., 1985. Heterocycles 23, 2543.
[72] Chilpa, R.R., Estrada, M.J., Muñiz, E.E., 1997. Journal of Chemical Ecology 23, 1901.
[73] Chow, Y.L., Quon, H.H., 1968. Phytochemistry 7, 1871.
[74] Correa, D.B., Silva, L.G.F., Gottlieb, O.R., Gonçalves, S.J., 1970. Phytochemistry 9, 447.
[75] Cotterill, P.J., Scheinmann F., 1975. Journal of the Chemical Society Chemical Communications, 664.
[76] Cotterill, P.J., Scheinmann, F., 1980. Journal of the Chemical Society Perkin Transactions I, 2353.
[77] Dahanayake, M., Kitagawa, I., Somanathan, R., Sultanbawa, M.U.S., 1974. Journal of the Chemical Society, Perkin Transactions I, 2510.
[78] Dalal, M.S.R., Sethna, S., Shah, R.C., 1953. Journal of the Indian Chemical Society 30, 457.
[79] Dalal, S.R., Shah, R.C., 1956. Chemistry and Industry 7, 664.
[80] Delle-Monache, F., Botta, B., Nicoletti, M., Coelho, J.S.B., Lyra, F.D.A., 1981. Journal of the Chemical Society Perkin Transactions I, 484.
[81] Delle-Monache, F., Mac-Quhae, M.M., Delle-Monache, G., Bettolo, G.B.M., Lima, R.A., 1983. Phytochemistry 22, 227.
[82] Delle-Monache, G., Botta, B., Mello, J.F., Coelho, J.S.B., Menichini, F., 1984. Journal of Natural Products 47, 620.
[83] Delle-Monache, G., Delle-Monache, F., Bettolo, G.B.M., Lima, R.A., 1983. Journal of Natural Products 46, 655.
[84] Delle-Monache, G., Delle-Monache, F., Waterman, P.G., Crichton, E.G., Lima, R.A., 1984. Phytochemistry 23, 1757.
[85] Denisova, O.A., Glyzin, V.I., Patudin, A.V., Fesenko, D.A., 1980. Chemical and Natural Compounds 2, 145.
[86] Deshpande, V.H., Rao, A.V.R., Varadan, M., Venkataraman, K., 1973. Indian Journal of Chemistry 11, 518.
[87] Dhasmana, H., Garg, H.S., 1989. Phytochemistry 28, 2819.
[88] Dhasmana, H., Garg, H.S., 1990. Phytochemistry 29, 961.
[89] Diserens, I.S., Rogers, C., Sordat, B., Hostettmann, K., 1992. Phytochemistry 31, 313.
[90] Dreyer, D.L., Bourell, J.H., 1981. Phytochemistry 20, 493.
[91] Duarte, A.P., Correa, D.B., Silva, L.G.F., Janot, S., Gottlieb, O.R., 1968. Anais da Academia Brasileira de Ciências 40, 307.
[92] Dutta, P.K., Sem, A.K., Sarkar, K.K., Banerji, N., 1987. Indian Journal of Chemistry 26B, 281.
[93] Elix, J.A., Crook, C.E., Jiang, H., Zhi-Ning, Z., 1992. Australian Journal of Chemistry 45, 845.
[94] Elix, J.A., Crook, C.E., 1992. The Bryologist 95, 52.
[95] Elix, J.A., Gaul, K.L., Lumbsch, H.T., 1987. Australian Journal of Chemistry 40, 1031.
[96] Elix, J.A., Whitton, A.A., Sargent, M.V., 1984. Chemical Organic Naturstoffe 45, 103.
[97] Ellis, R.C., Whalley, W.B., Ball, K., 1967. Chemical Communications, 803
[98] Ferreira, G.A.L., Gottlieb, O.R., Mesquita, A.A.L., 1972. Phytochemistry 11, 1512.
[99] Frahm, A.W., Chaudhuri, R.K., 1979. Tetrahedron 35, 2035.
[100] Fujita, T., Liu, D.Y., Ueda, S., Takeda, Y., 1992. Phytochemistry 31, 3997.
[101] Fukamiya, N., Okano, M., Kondo, K., Tagahara, K., 1990. Journal of Natural Products 53, 1543.
[102] Fukuyama, Y., Kamiyama, A., Mima, Y., Kodama, M., 1991. Phytochemistry 30, 3433.
[103] Fukuyama, Y., Mitsunami, H., Yoshizawa, T., Taki, J., Nakagawa, K., 1996. Heisei July, 7.
[104] Gabriel, S.J., Gottlieb, O.R., Lima, R.A., Mesquita, A.A.L., 1977. Acta Amazonica 7, 289.
[105] Ghosal, S., Sharma, P.V., Chaudhuri, R.K., 1975. Phytochemistry 14, 1393.
[106] Ghosal, S., Biswas, K., Jaiswal, D., 1980. Phytochemistry 19, 123.
[107] Ghosal, S., Chaudhuri, R.K., 1975. Journal of Pharmaceutical Science 64, 888.
[108] Ghosal, S., Chaudhuri, R.K., Nath, A., 1973. Journal of Pharmaceutical Science 62, 137.

[109] Ghosal, S., Chaudhuri, R.K., 1973. Phytochemistry 12, 2035.
[110] Ghosal, S., Jaiswal, D.K., Biswas, K., 1978. Phytochemistry 17, 2119.
[111] Ghosal, S., Sharma, P.V., Chaudhuri, R.K., Bhattacharya, S.K., 1975. Journal of Pharmaceutical Science 64, 80.
[112] Ghosal, S., Sharma, P.V., Chaudhuri, R.K., Bhattacharya, S.K., 1973. Journal of Pharmaceutical Science 62, 926.
[113] Ghosal, S., Sharma, P.V., Chaudhuri, R.K., 1975. Phytochemistry 14, 2671.
[114] Gil, S., Palanca, P., Sanz, V., Tortajada, A., 1991. Journal of Natural Products 54, 127.
[115] Gil, S., Palanca, P., Sanz, V., Tortajada, A., 1990. Journal of Natural Products 53, 1198.
[116] Gil, S., Parra, M., Sanz, V., Tortajada, A., 1988. Journal of Natural Products 51, 339.
[117] Gil, S., Sanz, V., Tortajada, V., 1987. Journal of Natural Products 50, 301.
[118] Goh, S.H., Jantan, I., Gray, A.I., Waterman, P.G., 1992. Phytochemistry 31, 1383.
[119] Goh, O.S.H., Jantan, O.I., 1991. Phytochemistry 30, 366.
[120] Gottlieb, O.R., Mesquita, A.A.L., Oliveira, G.G., Melo, M.T., 1970. Phytochemistry 9, 2537.
[121] Gottlieb, O.R., Mesquita, A.A.L., Silva, E.M., Melo, M.T., 1969. Phytochemistry 8, 665.
[122] Gottlieb, O.R., Lima, R.A., Mendes, P.H., Magalhães, M.T., 1975. Phytochemistry 14, 1674.
[123] Gottlieb, O.R., Magalhães, M.T., 1966. Anais da Academia Brasileira de Ciências 38, 439.
[124] Gottlieb, O.R., Magalhães, M.T., Pereira, M.O.S., Mesquita, A.A.L., Correa, D.B., Oliveira, G.G., 1968. Tetrahedron 24, 1601.
[125] Gottlieb, O.R., 1968. Phytochemistry 7, 411.
[126] Govindachari, T.R., Kalyanaraman, P.S., Muthukumaraswamy, N., Pai, B.R., 1971. Tetrahedron 27, 3919.
[127] Govindachari, T.R., Pai, B.R., Subramaniam, P.S., Rao, U.R., Muthukumaraswamy, N., 1967. Tetrahedron 23, 243.
[128] Govindachari, T.R., Subramaniam, P.S., Pai, B.R., Kalyanaraman, P.S., Rao, U.R., 1971. Indian Journal of Chemistry 9, 772.
[129] Grover, P.K., Shah, G.D., Shah, R.C., 1955. Journal of the Chemical Society, 3982.
[130] Gunasekera, S.P., Jayatilake, G.S., Selliah, S.S., Sultanbawa, M.U.S., 1977. Journal of the Chemical Society, Perkin Transactions I, 1505.
[131] Gunasekera, S.P., Selliah, S.S., Sultanbawa, M.U.S., 1975. Journal of the Chemical Society, Perkin Transactions I, 1539.
[132] Gunasekera, S.P., Sivapalan, K., Sultanbawa, M.U.S., Ollis, W.D., 1977. Journal of the Chemical Society, Perkin Transactions I, 11.
[133] Gunasekera, S.P., Sotheeswaran, S., Sultanbawa, M.U.S., 1981. Journal of the Chemical Society, Perkin Transactions I, 1831.
[134] Gunasekera, S.P., Sultanbawa, M.U.S., 1975. Journal of the Chemical Society, Perkin Transactions I, 2215.
[135] Gunatilaka, A.A.L., Sriyani, H.T.B., Sotheeswaran, S., Waight, E.S., 1983. Phytochemistry 22, 233.
[136] Guyot, M., Massicot, J., Rivaille, P., Normant, H.C.R., 1968. Academic Science Paris 267, 423.
[137] Habib, A.M., Ho, D.K., Masuda, S., McCloud, T., Reddy, K.S., Abou-Shoer, M., McKenzie, A., Byrn, S.R., Chang, C.J., Cassady, J.M., 1987. The Journal of Organic Chemistry 52, 412.
[138] Habib, A.M., Reddy, K.S., McCloud, T.G., Chang, C.J., Cassady, J.M., 1987. Journal of Natural Products 50, 141.
[139] Hambloch, H., Frahm, A.W., 1980. Tetrahedron 36, 3273.
[140] Hano, Y., Matsumoto, Y., Shinohara, K., Sun, J.Y., Nomura, T., 1991. Planta Medica 57, 172.
[141] Hano, Y., Matsumoto, Y., Sun, J.Y., Nomura, T., 1990. Planta Medica 56, 478.
[142] Hano, Y., Matsumoto, Y., Sun, J.Y., Nomura, T., 1990. Planta Medica 56, 399.
[143] Hano, Y., Okamoto, T., Nomura, T., 1991. Heterocycles 32, 1357.
[144] Hano, Y., Okamoto, T., Nomura, T., Momose, Y., 1990e. Heterocycles 31, 1345.
[145] Haqqani, M.H., 1981. Fitoterapia 52, 5.
[146] Harborne, J.B., 1973. Phytochemical Methods. Chapman & Hall, London, pp. 278.
[147] Harrison, L.J., Leong, L.S., Sai, G.L., Sim, K.Y., Tan, H.T.W., 1993. Phytochemistry 33, 727.
[148] Harrison, L.J., Leong, L.S., Leong, Y.W., Lee, S.G., Sai, K.Y., Sim, K.Y. et al., 1994. Natural Product Letters 5, 11.
[149] He, R., Feng, S., Nie, R., 1984. Yunnan Zhiwu Yanjin 6, 341.
[150] He, R., Shuji, F., Nie, R., 1982. Yunnan Zhiwu Yanjin 4, 68.
[151] Holker, J.S.E., Kagal, S.A., 1968. Chemical Communications, 1574.
[152] Holloway, D.M., Scheinmann, F., 1975. Phytochemistry 14, 2517.
[153] Hostettmann, K., Guillarmod, A.J., 1974. Helvetica Chimica Acta 57, 1155.
[154] Hostettmann, K., Guillarmod, A.J., 1976. Helvetica Chimica Acta 59, 1584.
[155] Hostettmann, K., Guillarmod, A.J., 1976. Journal of Chromatography 124, 381.
[156] Hostettmann, K., Guillarmod, A.J., 1977. Phytochemistry 16, 481.
[157] Hostettmann, K., McNair, H.M., 1976. Journal of Chromatography 116, 201.
[158] Hostettmann, K., Tabacchi, R., Guillarmod, A.J., 1974. Helvetica Chimica Acta 57, 294.
[159] Hostettmann, K., Wagner, H., 1977. Phytochemistry 16, 821.
[160] Hu, B., Hongfa, S., Shufen, F., Jingye, D., 1992. Zhiwu Xuebao 34, 886.
[161] Iglesias, M.C.R., Marston, A., Hostettmann, K., 1992. Phytochemistry 31, 1387.
[162] Iinuma, M., Tosa, H., Tanaka, T., Asai, F., Shimano, R., 1995. Heterocycles 40, 279.
[163] Iinuma, M., Tosa, H., Tanaka, T., Shimano, R., Asai, F., Yonemori, S., 1994. Phytochemistry 35, 1355.
[164] Iinuma, M., Ito, T., Tosa, H., Tanaka, T., 1996. Journal of Natural Products 59, 472.
[165] Iinuma, M., Ito, T., Tosa, H., Tanaka, T., Miyake, R., Chelladura, V., 1997. Phytochemistry 46, 1423.
[166] Iinuma, M., Tosa, H., Ito, T., Tanaka, T., Madulid, D.A., 1996. Phytochemistry 42, 1195.
[167] Iinuma, M., Tosa, H., Ito, T., Tanaka, T., Riswan, S., 1996. Chemical and Pharmaceutical Bulletin 4 (9), 1744.
[168] Iinuma, M., Tosa, H., Tanaka, T., Asai, F., Shimano, R., 1995. Phytochemistry 38, 247.
[169] Iinuma, M., Tosa, H., Tanaka, T., Asai, F., Shimano, R., 1995. Phytochemistry 39, 945.
[170] Iinuma, M., Tosa, H., Tanaka, T., Riswan, S., 1996. Chemical and Pharmaceutical Bulletin 44 (1), 232.
[171] Iinuma, M., Tosa, H., Tanaka, T., Yonemori, S., 1995. Phytochemistry 38, 725.
[172] Iinuma, M., Tosa, H., Toriyama, N., Tanaka, T., Ito, T., Chelladurai, V., 1996. Phytochemistry 43, 681.
[173] Iinuma, M., Tosa, H., Tanaka, T., Yonemori, S., 1994. Phytochemistry 35, 527.
[174] Ikeya, Y., Sugama, K., Okada, M., Mitsuhashi, H., 1991. Phytochemistry 30, 2061.
[175] Ishiguro, K., Fukumoto, H., Suitani, A., Nakajima, M., Isoi, K., 1996. Phytochemistry 42, 435.
[176] Ishiguro, K., Nakajima, M., Fukumoto, H., Isoi, K., 1995. Phytochemistry 38, 867.

[177] Ishiguro, K., Fukumoto, H., Nakajima, M., Isoi, K., 1993. Phytochemistry 33, 839.
[178] Ishiguro, K., Nagareya, N., Suitani, A., Fukumoto, H., 1997. Phytochemistry 44, 1065.
[179] Ishiguro, K., Nakajima, M., Fukumoto, H., Isoi, K., 1995. Phytochemistry 39, 903.
[180] Ishimaru, K., Sudo, H., Satake, M., Matsunaga, Y., Hasegawa, Y., Takemoto, S. et al., 1990. Phytochemistry 29, 1563.
[181] Ito, H., Taniguchi, H., Kita, T., Matsuki, Y., Tachikawa, E., Fujita, T., 1977. Phytochemistry 16, 1614.
[182] Jackson, B., Locksley, H.D., Scheinmann, F., 1966. Journal of the Chemical Society C, 178.
[183] Jackson, B., Locksley, H.D., Scheinmann, F., 1967. Journal of the Chemical Society C, 2500.
[184] Jackson, B., Locksley, H.D., Scheinmann, F., 1969. Phytochemistry 8, 927.
[185] Jefferson, A., Scheinmann, F., 1965. Nature 207, 1193.
[186] Kaldas, M.H., Guillarmod, A.J., 1978. Phytochemistry 17, 2083.
[187] Kaldas, M.H., Hostettmann, K., Sticher, O., 1981. Phytochemistry 20, 443.
[188] Kaldas, M., Hostettmann, K., Guillarmod, A.J., 1974. Helvetica Chimica Acta 57, 2557.
[189] Kanamori, H., Sakamoto, I., Mizuta, M., Hashimoto, K., Tanaka, O., 1984. Chemical and Pharmaceutical Bulletin 32, 2290.
[190] Kaouadji, M., Vaillant, I., Mariotte, A.M., 1986. Journal of Natural Products 49, 359.
[191] Karunanayake, S., Sotheeswaran, S., Sultanbawa, M.U.S., Balasubramaniam, S., 1981. Phytochemistry 20, 1303.
[192] Kazmi, S.N.U.H., Ahmed, Z., Malik, A., 1989. Heterocycles 29, 1923.
[193] Kazmi, S.N.U.H., Ahmed, Z., Malik, A., 1989. Phytochemistry 28, 3572.
[194] Khetwal, K.S., Bisht, R.S., 1988. Phytochemistry 27, 1910.
[195] Khetwal, K.S., Joshi, B., Bisht, R.S., 1990. Phytochemistry 29, 1265.
[196] Khetwal, K.S., Pande, S., 1997. Indian Journal of Chemistry 36B, 833.
[197] Khvorost, O.P., Serbin, A.G., Komissarenko, N.F., Bublik, N.P., 1987. Chemical Natural Compounds 4, 506.
[198] King, F.E., King, T.J., Manning, L.C., 1953. Journal of the Chemical Society, 3932.
[199] Kitanov, G.M., Assenov, I., Van, A.T., 1988. Pharmazie 43, 879.
[200] Kitanov, G.M., Blinova, K.F., 1980. Khimiya Prirodnykh Soedinenii 2, 256.
[201] Kitanov, G.M., Blinova, K.F., 1987. Chemical Natural Compounds 2, 151.
[202] Kittisak, L., Thatree, P., Chulabhorn, M., Somsak, R., 1997. Phytochemistry 45 (6), 1299.
[203] Komatsu, M., Tomimori, T., Mikuriya, N., 1969. Chemical and Pharmaceutical Bulletin 17, 155.
[204] Kostanecki, V., 1892. Ber. D. Chemistry 25, 1640.
[205] Kostanecki, V., Rutishauser, R., 1892. Ber. D. Chemistry 25, 1648.
[206] Kubitzki, K., Mesquita, A.A.L., Gottlieb, O.R., 1978. Biochemical Systematics Ecology 6, 185.
[207] Kulanthaivel, P., Pelletier, S.W., Khetwal, O.K.S., Verna, D.L., 1988. Journal of Natural Products 51, 379.
[208] Kumar, V., Ramachandran, S., Sultanbawa, M.U.S., 1976. Phytochemistry 15, 2016.
[209] Kumar, V., Sotheeswaran, S., Surendrakumar, S., Balasubramaniam, S., 1982. Phytochemistry 21, 807.
[210] Kupchan, S.M., Streelman, D.R., Sneden, A.T., 1980. Journal of Natural Products 43, 296.
[211] Lee, H.H., Chan, H.K., 1977. Phytochemistry 16, 2038.
[212] Leuckert, C., Ahmadjian, V., Culberson, C.F., Johnson, A., 1990. Mycologia 82, 370.
[213] Lewis, J.R., 1963. Proceedings of the Chemistry Society 363, 373.
[214] Lima, R.A., Gottlieb, O.R., Mesquita, A.A.L., 1970. Anais da Academia Brasileira de Ciências 42, 133.
[215] Lima, R.A., Gottlieb, O.R., Mesquita, A.A.L., 1972. Phytochemistry 11, 2307.
[216] Lin, C.N., Chung, Mi, Liou, S.J., Lee, T.H., Wang, J.P., 1996. Journal of Pharmaceutical Pharmacology 48, 532.
[217] Lin, C.N., Liou, S.S., Ko, F.N., Teng, C.M., 1993. Journal of Pharmaceutical Science 82, 11.
[218] Lin, C.N., Liou, S.S., Ko, F.N., Teng, C.M., 1992. Journal of Pharmaceutical Science 81, 1109.
[219] Liu, J., Huang, M., 1982. Zhongcaoyao 13, 433.
[220] Locksley, H.D., Moore, I., Scheinmann, F., 1966. Journal of the Chemical Society C, 430.
[221] Locksley, H.D., Moore, I., Scheinmann, F., 1966. Journal of the Chemical Society C, 2265.
[222] Locksley, H.D., Moore, I., Scheinmann, F., 1967. Tetrahedron 23, 2229.
[223] Locksley, H.D., Moore, I., Scheinmann, F., 1966. Journal of the Chemical Society C, 2186.
[224] Locksley, H.D., Murray, I.G., 1969. Journal of the Chemical Society C, 1567.
[225] Locksley, H.D., Murray, I.G., 1970. Journal of the Chemical Society C, 392.
[226] Locksley, H.D., Murray, I.G., 1971. Journal of the Chemical Society C, 1332.
[227] Locksley, H.D., Murray, I.G., 1971. Phytochemistry 10, 3179.
[228] Mahabusarakam, W., Wiriyachitra, P., Taylor, W., 1987. Journal of Natural Products 50, 474.
[229] Mahmoud, Z.F., Salam, N.A.A., Khafagy, S.M., 1980. Fitoterapia 51, 153.
[230] Mandal, S., Das, P.C., Joshi, P.C., 1992. Journal of the Indian Chemical Society 69, 611.
[231] Mandal, S., Chatterjee, A., 1987. Tetrahedron Letters 28, 1309.
[232] Mao, S., Liao, S., Wu, J., Liang, H., Chen, H., Zhang, C., 1996. Yaoxue Xuebao 31 (2), 118.
[233] Markham, K.R., 1964. Tetrahedron 20, 991.
[234] Markham, K.R., 1965. Tetrahedron 21, 1449.
[235] Markham, K.R., 1965. Tetrahedron 21, 3687.
[236] Marston, A., Hamburger, M., Diserens, I.S., Msonthi, J.D., Hostettmann, K., 1993. Phytochemistry 33, 809.
[237] Marta, M., Delle-Monache, F., Bettolo, G.B.M., Lyra, D.A., Mello, J.F., Lima, O.G., 1976. Gazzeta Chimica Italiana 106, 651.
[238] Massias, M., Carbonnier, J., Molho, D., 1977. Bulletin of the Museum of National History Natural Paris 13, 55.
[239] Massias, M., Carbonnier, J., Molho, D., 1976. Bulletin of the Museum of National History Natural Paris 10, 45.
[240] Mathis, C.T., Goldstein, J.H., 1964. Spectrochimica Acta 20, 871.
[241] McMaster, W.J., Scott, A.I., Trippett, S., 1960. Journal of the Chemical Society, 4628.
[242] Mehta, G., Shah, S.R., Venkateswarlu, Y., 1994. Tetrahedron 50, 11729.
[243] Meravy, L., 1987. Biology of Plants 29, 81.
[244] Mesquita, A.A.L., Correa, D.B., Gottlieb, O.R., Magalhães, M.T., 1968. Anais Chimica Acta 42, 311.
[245] Mesquita, A.A.L., Oliveira, W.G., Neiva, R.M.T., Gottlieb, O.R., 1975. Phytochemistry 14, 803.
[246] Miana, G.A., Al-Hazimi, H.M.G., 1984. Phytochemistry 23, 1637.
[247] Minami, H., Kinoshita, M., Fukuyama, Y., Kodama, M., Yoshizawa, T., Sugiura, M., Nakagawa, K., Tago, H., 1994. Phytochemistry 36, 501.

[248] Minami, H., Takahashi, E., Kodama, M., Fukuyama, Y., 1996. Phytochemistry 41, 629.
[249] Mourão, J.C., Gottlieb, O.R., Magalhães, M.T., 1966. Anais da Academia Brasileira Ciências 38, 435.
[250] Mukherjee, B., Mukherjee, S.K., 1987. International Journal of Crude Drug Research 25, 97.
[251] Mukherjee, K.S., Chakraborty, C.K., Chatterjee, T.P., Bhattacharjee, D., Laha, S., 1991. Phytochemistry 30, 1036.
[252] Mukherjee, K.S., Chakraborty, C.K., Laha, S., Bhattacharya, D., Chatterjee, T.P., 1990. Journal Indian Chemical Society 67, 1003.
[253] Mukherjee, K.S., Laha, S., Manna, T.K., Roy, S.C., 1995. Journal of the Indian Chemical Society 72, 63.
[254] Mukherjee, K.S., Manna, T.K., Laha, S., Chakravorty, C.K., 1994. International Journal Pharmacology 32, 201.
[255] Murti, V.V.S., Seshadri, T.R., Sivakumaran, S., 1972. Phytochemistry 11, 2089.
[256] Nagem, T.J., Silveira, J.C., 1986. Phytochemistry 25, 503.
[257] Nagem, T.J., Silveira, J.C., 1988. Phytochemistry 27, 646.
[258] Nagem, T.J., Silveira, J.C., 1986. Phytochemistry 25, 2681.
[259] Nagem, T.J., Silveira, J.C., 1989. Phytochemistry 28, 2211.
[260] Nattaya, C., Kazuya, T., Yasushi, O., Shigeo, N., Tomohisa, O., 1996. Phytochemistry 43 (5), 1099.
[261] Neshta, N.M., Glyzin, V.I., Patudin, A.V., 1984. Chemical Natural Compounds 1, 108.
[262] Neshta, N.M., Glyzin, V.I., Savina, A.A., Patudin, A.V., 1983. Chemical Natural Compounds 6, 750.
[263] Nielsen, H., Arends, P., 1979. Journal of Natural Products 42, 301.
[264] Nomura, T., Hano, Y., Fujimoto, T., 1983. Heterocycles 20, 213.
[265] Noro, T., Ueno, A., Mizutani, M., Hashimoto, T., Miyase, T., Kuroyanage, M., Fukushima, S., 1984. Chemical and Pharmaceutical Bulletin 32, 4455.
[266] Odontyuya, G., Purev, O., Sambuu, D.G., Nasreen, A., Atta-Ur, R., 1995. Natural Products Letters 5, 269.
[267] Okorie, D.A., 1976. Phytochemistry 15, 1799.
[268] Oliveira, M.C.F., Silveira, E.R., 1995. In: 18th Reunião Anual da Sociedade Brasileira de Química, PN 029.
[269] Oliveira, W.G., Gottlieb, O.R., Mesquita, A.A.L., 1972. Phytochemistry 11, 3323.
[270] Oliveira, W.G., Mesquita, A.A.L., Kubitzki, K., Gottlieb, O.R., 1990. Phytochemistry 29, 1893.
[271] Owen, P.J., Scheinmann, F., 1974. Journal of the Chemical Society, Perkin Transactions I, 1018.
[272] Parra, M., Picher, M.T., Seoane, E., Tortajada, A., 1985. Journal of Natural Products 48, 998.
[273] Parra, M., Picher, M.T., Seoane, E., Tortajada, A., 1984. Journal of Natural Products 47, 123.
[274] Parra, M., Seoane, E., Tortajada, A., 1984. Journal of Natural Products 47, 868.
[275] Parveen, M., Khan, N.U.D., 1988. Phytochemistry 27, 3694.
[276] Parveen, M., Khan, N.U.D., 1987. Chemistry and Industry 12, 418.
[277] Patel, G.N., Trivedi, K.N., 1983. Indian Journal of Chemistry 22B, 755.
[278] Patel, G.N., Trivedi, K.N., 1991. Indian Journal of Chemistry 30B, 437.
[279] Patolia, R.J., Trivedi, K.N., 1983. Indian Journal of Chemistry 22B, 444.
[280] Pattalung, P., Thongtheeraparp, W., Wiriyachitra, P., Taylor, W.C., 1994. Planta Medica 60, 365.
[281] Pereira, M.O.S., Gottlieb, O.R., Magalhães, M.T., 1966. Anais da Academia Brasileira de Ciências 38, 425.
[282] Peres, V., Nagem, T.J., 1997. Phytochemistry 44, 191.
[283] Pinto, D.C.G., Fuzzati, N., Pazmino, X.C., Hostettmann, K., 1994. Phytochemistry 7, 875.
[284] Pinto, M.M., Polonia, J., 1974. Helvetica Chimica Acta 57, 286.
[285] Pureb, O., Vansan, Y.Z., Oyuun, K., 1991. Chemical Natural Compounds 2, 245.
[286] Purev, O., Odontyuya, G., Oyun, H., Maksimovna, T.L., Nasreen, A., Atta-Ur, R., 1995. Natural Products Letters 5, 261.
[287] Quillinan, A.J., Scheinmann, F., 1972. Journal of the Chemical Society, Perkin Transactions I, 1382.
[288] Quillinan, A.J., Scheinmann, F., 1973. Journal of the Chemical Society, Perkin Transactions I, 1329.
[289] Rao, A.V.R., Sarma, M.R., Venkataraman, K., Yemul, S.S., 1974. Phytochemistry 13, 1241.
[290] Rath, G., Potterat, O., Mavi, S., Hostettmann, K., 1996. Phytochemistry 43, 513.
[291] Ravi, P., Vathani, P., Reddy, G.C., 1994. Indian Journal of Heterocycles Chemistry 3, 209.
[292] Rivaille, P., Massicot, J., Guyot, M., Plouvier, V., Massias, M., 1969. Phytochemistry 8, 1533.
[293] Roberts, J.C., 1961. Chemical Reviews 61, 591.
[294] Rocha, L., Marston, A., Kaplan, M.A.C., Evans, H.S., Thull, U., Testa, B., Hostettman, K., 1994. Phytochemistry 36, 1381.
[295] Rodriguez, S., Wolfender, J.L., Hakizamungu, E., Hostettmann, K., 1995. Planta Medica 61, 362.
[296] Rodriguez, S., Wolfender, J.L., Odontuya, G., Purev, O., Hostettmann, K., 1995. Phytochemistry 40, 1265.
[297] Roitman, J.N., Wollenweber, E., Giner, F.J.A., 1992. Journal Plant Physiology 139, 632.
[298] Sakai, S.I., Katsura, M., Takayama, H., Aimi, N., Chokethaworn, N., Suttajit, M.E., 1993. Chemical and Pharmaceutical Bulletin 41, 958.
[299] Santesson, J., 1968a. Arkiv Kemi 30, 363.
[300] Santesson, J., 1968b. Acta Chemica Scandinavica 22, 2393.
[301] Santesson, J., 1969. Arkiv Kemi 30, 479.
[302] Schaufelberger, D., Hostettmann, K., 1988. Planta Medica 54, 219.
[303] Scheinmann, F., Sripong, N.A., 1971. Phytochemistry 10, 1331.
[304] Scheinmann, F., 1962. Tetrahedron 18, 853.
[305] Sem, A.K., Sarkar, K.K., Majumder, P.C., Banerji, N., Usvuori, R., Hase, T.A., 1980. Phytochemistry 19, 2223.
[306] Sen, A.K., Sarkar, K.K., Majumder, P.C., Banerji, N., 1980. Indian Journal of Chemistry 19B, 1008.
[307] Sen, A.K., Sarkar, K.K., Majumder, P.C., Banerji, N., 1986. Indian Journal of Chemistry 25B, 1157.
[308] Sen, A.K., Sarkar, K.K., Majumder, P.C., Banerji, N., Uusvuori, R., Hase, T.A., 1982. Phytochemistry 21, 1747.
[309] Shah, G.D., Shah, R.C., 1956. Journal of Science Industry Research 15B, 630.
[310] Sia, G.L., Bennett, G.J., Harrison, L.J., Sim, K.Y., 1995. Phytochemistry 38, 1521.
[311] Simoneau, B., Brassard, P.A., 1984. Journal of the Chemical Society, Perkin Transactions I, 1507.
[312] Somanathan, R., Sultanbawa, M.U.S., 1992. Journal of the Chemical Society, Perkin Transactions I, 1935.
[313] Stout, G.H., Balkenhol, W.J., 1969. Tetrahedron 25, 1947.
[314] Stout, G.H., Christensen, E.N., Balkenhol, W.J., Stevens, K.L., 1969. Tetrahedron 25, 1961.
[315] Stout, G.H., Fries, J.L., 1970. Phytochemistry 9, 235.
[316] Stout, G.H., Krahn, M.M., Yates, P., Bhat, H.B., 1968. Chemical Communications, 211
[317] Stout, G.H., Stout, V.F., Welsh, M.J., Jensen, L.H., 1962. Tetrahedron Letters 13, 541.
[318] Stout, G.H., Stout, V.F., Welsh, M.J., 1963. Tetrahedron 19, 667.
[319] Sullivan, G., Stiles, F.D., Rosler, K.H.A., 1977. Journal of Pharmaceutical Science 66, 828.
[320] Sultanbawa, M.U.S., 1980. Tetrahedron 36, 1465.
[321] Sun, H., Jingye, D., 1981. Zhiwu Xuebao 23, 464.
[322] Sun, H., Hu, B., Fan, S., Ding, J., 1983. Zhiwu Xuebao 25, 460.

[323] Sundholm, E.G., 1978. Tetrahedron 34, 577.
[324] Suzuki, O., Katsumata, Y., Oya, M., Chari, V.M., Klapfenberger, R., Wagner, H., Hostettman, K., 1980. Planta Medica 39, 19.
[325] Suzuki, O., Katsumata, Y., Oya, M., Chari, V.M., Vermes, B., Wagner, H., Hostettman, K., 1981. Planta Medica 42, 17.
[326] Tadzhibaev, M.M., Butayarov, A.V., Batirov, E.K., Malikov, V.M., 1992. Chemical Natural Compounds 2, 244.
[327] Takagi, S., Yamari, M., 1982. Yakugaku Zasshi 102, 546.
[328] Terreaux, C., Maillard, M., Gupt, M.P., Hostettmann, K., 1995. Phytochemistry 40, 1791.
[329] Tomimori, T., Yoshizaki, M., Namba, T., 1974. Yakugaku Zasshi 94, 647.
[330] Tosa, H., Linuma, M., Murakami, K., Ito, T., Tanaka, T., Chelladura, V. et al., 1997. Phytochemistry 45, 133.
[331] Ueno, A., 1962. Yakugaku Zasshi 82, 1486.
[332] Ueno, A., 1962. Yakugaku Zasshi 82, 1482.
[333] Van Der Sluis, W.G., Labadie, R.P., 1985. Phytochemistry 24, 2601.
[334] Van Der Sluis, W.G., 1985. Plant System Evolution 149, 253.
[335] Versluys, C., Cortés, M., López, J.T., Sierra, J.R., Razmilié, I., 1982. Experientia 38, 771.
[336] Vitale, A.A., Romanelli, G.P., Autino, J.C., Pomilio, A.B., 1994. Journal of Chemical Research S, 82.
[337] Walia, S., Mukerjee, S.K., 1984. Phytochemistry 23, 1816.
[338] Waterman, P.G., Crichton, E.G., 1980. Planta Medica 40, 351.
[339] Waterman, P.G., Crichton, E.G., 1980. Phytochemistry 19, 2723.
[340] Waterman, P.G., Hussain, R.A., 1982. Phytochemistry 21, 2099.
[341] Westerman, P.W., Gunasekera, S.P., Sultanbawa, M.U.S., Kazlauskas, R., 1977. Organic Magnetic Resonance 9, 631.
[342] Wolfender, J.L., Hamburger, M., Msonthi, J.D., Hostettmann, K., 1991. Phytochemistry 30, 3625.
[343] Wolfrom, M.L., Bhat, H.B., 1965. Phytochemistry 4, 765.
[344] Wolfrom, M.L., Dickey, E.E., McWain, P., Thompson, A., Looker, J.H., Windrath, O.M. et al., 1964. The Journal of Organic Chemistry 29, 689.
[345] Wolfrom, M.L., Komitsky, F. Jr., Fraenkel, G., Looker, J.H., Dickey, E.E., McWain, P. et al., 1963. Tetrahedron Letters 12, 749.
[346] Wolfrom, M.L., Komitsky, F. Jr., Mundell, P.M., 1965. Journal of Organic Chemistry 30, 1088.
[347] Wollenweber, E., Dorr, M., Roitman, J.N., Giner, F.J.A., 1994. Zhurnal of Naturforsch 49c, 393.
[348] Yan-Bin, Y., Zhou, J., 1980. Yun-nan, Chih Wu Yen Chiu 2, 468.
[349] Zang, B.C., Cheng, J.T., Hu, P.L., Ho, S.H., 1980. Chun Ts'ao Yao 11, 149.
[350] Zhou, H.M., Liu, Y.L., Blasko, G., Cordell, G.A., 1989. Phytochemistry 28, 3569.