

NATURALLY OCCURRING PENTAOXYGENATED, HEXAOXYGENATED AND DIMERIC XANTHONES: A LITERATURE SURVEY*#

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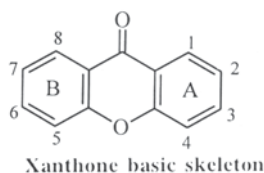
This review gives information on the chemical study of 71 penta-oxygenated, 11 hexa-oxygenated and 9 dimeric and more complex xanthenes naturally occurring in 7 families, 29 genus and 62 species of higher plants, and 11 described as fern and fungal metabolites. The value of these groups of substances in the connection with the pharmacological activity and the therapeutic use of some species is shown. The structural formulas of 23 isolated compounds and their distribution in the species studied are given.

Keywords: xanthone; penta-oxygenated xanthenes; hexa-oxygenated xanthenes; dimeric xanthenes; pharmacological activity; fungus; biosynthesis.

1. INTRODUCTION

Xanthenes are secondary metabolites commonly occurring in a few higher plant families, fungi and lichen. Their high taxonomic value in such families and their pharmacological properties have roused great interest³¹.

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 B²⁴. The numbering system is based on xanthone-9-one as the basic skeleton⁶² and in cases where only ring B is oxygenated the lowest numbers are used, except in the biosynthetic discussion²⁴.



2. CLASSIFICATION

The Xanthenes isolated so far may be classified into five major groups: simple oxygenated xanthenes, xanthenes glycosides, prenylated and related xanthenes, xanthonolignoids and miscellaneous¹⁰³. Simple penta-oxygenated, Simple hexa-oxygenated and dimeric xanthenes, as well as prenylated and related xanthenes with the same degree of oxygenation are listed in this review (Tables 1-3).

3. METHODS OF ISOLATION AND STRUCTURAL INVESTIGATION

Xanthenes are commonly separated by chromatography on silica gel, using different solvent mixtures⁷². Xanthenes are also

separated and identified by comparison with authentic samples by Thin-Layer Chromatography³⁸ and High-Pressure Liquid Chromatography^{74,75}. The structure of the simple oxygenated xanthenes have been established mainly from the UV, IR, MS and NMR data of these compounds^{13,14,132,148}.

Xanthenes can be detected by their colours in UV light with and without ammonia or by using a general phenolic spray⁷². 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. Besides use of AlCl₃ shifts for chelated hydroxyl, sodium acetate, sodium hydroxide and boric acid shifts, considerable information of the position of hydroxyl groups in other locations can be obtained^{112,148}.

The use of infrared spectroscopy in xanthone chemistry is limited in detecting the carbonyl stretching frequency^{114,132}. In special, effect of chelation on the infrared carbonyl frequency of hydroxy-xanthenes may be useful in spectra of some substituted and extended xanthenes^{39,137}. The use of IR for detecting other functional groups, such as unchelated hydroxyl and methyl groups does not require comment^{132,135,136}.

By introducing lichen samples in a mass spectrometer via a direct inlet system Santesson¹³⁴ obtained mass spectra of the volatile lichen substances. The method showed well suited for tentative identification of lichen xanthenes^{134,136}. Apart from discussion of the mass spectra of lichen xanthenes, no systematic investigation of the electron-impact-induced fragmentation of xanthenes appears to have been made, except by Arends *et al* in the study of electron-impact-induced fragmentation of monohydroxy- and monomethoxyxanthenes¹⁴. Mass spectrometry has not been applied extensively to the study of naturally occurring xanthenes, but the MS data have been very valuable for a preliminary examination²⁰.

The data obtained in proton magnetic resonance spectra should be of great value in characterizing and identifying, naturally occurring xanthenes¹⁰⁸. ¹H NMR spectroscopy has been used for determining the structure of substituents and for locating aromatic protons by comparison with reference data and

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by analysis of spin-spin coupling. A closer scrutiny of chemical shifts of the aromatic protons allows prediction of the oxygenation pattern²¹. There are detailed NMR results for this class of compounds¹⁵⁹.

¹H NMR and ¹³C NMR are the most useful tools in structure elucidation of xanthenes³⁷. The ¹³C NMR spectra of a great number of naturally occurring xanthenes are reported and all chemical shifts assigned^{33,50,159}. Hambloch and Frahm⁷⁰ introduced a computer program nominated SEOX 1, which rapidly identifies unknown xanthenes with the help of additivity rules that represents a remarkable facilitation in structure elucidation.

4. BIOACTIVITIES OF XANTHONES

The study of xanthenes is interesting not only for the chemosystematic investigation but also from the pharmacological point of view. Xanthenes possess an antidepressant action and an antitubercular activity, while xanthone glycosides have a depressant action. A choleric, diuretic, antimicrobial, antiviral and cardiotoxic action of some xanthenes has also been established^{76,88,151,152}. The inhibition of Type A and Type B monoamine oxidases by a number of xanthenes have also been observed^{151,152}.

Recently, the various bioactivities of xanthenes cytotoxic and antitumour activity, anti-inflammatory activity, anti-fungal activity, enhancement of choline acetyltransferase activity and inhibition of lipid peroxidase have been revealed⁷⁸. In 1994 Mehta *et al*¹¹⁰ reported the total synthesis of novel xanthone antibiotics Cervinomycins A₁ and A₂, with promising activity against anaerobic bacteria, mycoplasma and some gram positive bacteria and their structural novelty.

Over recent years, xanthenes have emerged as a class of compounds possessing a broad spectrum of biological and pharmacological activities^{43,44}. The pharmacological interest in xanthenes is based on their inhibitory effect on monoamine oxidase (MAO) as well as their cytotoxic and antitumour activity²³. In general, xanthenes and their derivatives were shown to be effective as an allergy inhibitor and bronchodilator in treatment of asthma¹⁸.

A series of isoprenylated xanthenes isolated from moraceous plants showed interesting biological activities such as hypotensive effect, anti-rhinoviral activity, inhibition of the formation of some prostanoids and anti-tumor promoting activity⁷¹.

The actinoplanones, polycyclic xanthenes isolated from culture broth of *Actinoplanes* sp showed strong antimicrobial activities against bacteria and the rice fungus as well as exhibited strong cytotoxicity against the cells and inhibitory action on DNA synthesis⁹⁰. Fermentations of *Penicillium glabrum* produce a complex mixture of dimeric xanthenes with potent CD4-binding activity in an ELISA based on the binding of the monoclonal antibody anti-Leu 3a to soluble recombinant CD4¹⁶¹.

Xanthenes, in spite of their restricted occurrence in the plant kingdom, are reported to possess antileukemic, antitumor, antiulcer, antimicrobial, antihepatotoxic, and CNS-depressant activities¹⁹.

5. NATURAL SOURCE OF PENTAOXYGENATED, HEXAOXYGENATED AND DIMERIC XANTHONES

The penta-oxygenated, hexa-oxygenated and dimeric xanthenes are described in this review as occurring in 7 families, 29 genera and 62 species of higher plants, one fern and two fungi species:

Genus Uvaria
Family Annonaceae
 - *U. Kirkii*¹⁵⁴

Genus Alnus
Family Betulaceae
 - *A. glutinosa*⁸⁷

Genus Croton
Family Euphorbiaceae
 - *C. californicus*¹⁵⁴

Genus Blackstonia
Family Gentianaceae
 - *B. perfoliata*¹⁵⁵

Genus Canscora
Genus Centaurium
 - *C. decussata*^{36,54-57}
 - *C. cachenlahuen*¹⁵⁷
 - *C. erythraea*^{23,86,111,115}
 - *C. linarifolium*^{119,120,121}
 - *C. littorale*^{23,156}

Genus Chironia
Genus Erythraea
Genus Eustoma
Genus Frasera
 - *C. krebsii*¹⁶⁰
 - *E. centaurium*¹⁵³
 - *E. grandiflorum*¹⁴⁷
 - *F. albicaulis*¹⁴⁴
 - *F. albomarginata*⁴⁶
 - *F. caroliniensis*^{143,144}
 - *F. speciosa*⁴⁶
 - *F. tetrapetala*⁷

Genus Gentiana
 - *G. bellidifolia*^{30,105}
 - *G. campestris*^{30,84}
 - *G. corymbifera*^{107,133}
 - *G. germanica*^{30,85}
 - *G. ramosa*^{30,85}

Genus Halenia
 - *H. asclepidea*¹⁴⁶
 - *H. campanulata*⁷⁷
 - *H. corniculata*^{116,127}
 - *H. elliptica*^{42,149}

Genus Hoppea
 - *H. dichotoma*⁵⁸

Genus Ixanthus
Genus Swertia
 - *I. viscosus*¹¹⁸
 - *S. bimaculata*⁵⁹
 - *S. milensis*⁹⁹
 - *S. tetrapetala*⁸
 - *S. purpurascens*^{9,60}
 - *S. lawii*⁵⁹
 - *S. paniculata*¹¹
 - *S. cordata*¹³⁰
 - *S. punicea*⁵²
 - *S. mussotii*⁷³
 - *S. iberica*⁴¹
 - *S. chirata*¹⁰²
 - *S. macrosperma*¹⁶³

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Family Guttiferae

- *C. bracteatum*¹⁴²
 - *C. inophyllum*⁷⁹

Genus Cratoxylum
 - *C. cochinchinense*¹³⁹

Genus Garcinia
 - *G. livingstonei*⁴³

Genus Kielmeyera
 - *K. rubriflora*⁶⁴

Genus Mesua
 - *M. ferrea*⁶⁷

Genus Ploiarium
 - *P. alternifolium*²⁵

Genus Psorospermum
 - *P. febrifugum*^{2,69}

Genus Vismia
 - *V. guineensis*²⁹

Family Moraceae

- *C. cochinchinensis*³⁴

Family Polygalaceae

- *B. brevifolia*¹¹⁷

- *B. floribunda*¹⁴⁰

- *M. obtusifolia*¹²⁵

- *P. macradenia*^{45,145}

- *P. nyikensis*¹⁰⁶

- *P. paenea*¹¹³

- *P. tenuifolia*^{51,80,82}

- *P. triphylla*⁵³

- *P. spectabilis*¹²

- *P. virgata*²²

Genus *Cystopteris*
- *C. Fragilis*⁸¹

Fern

Fungi

*Penicillium glabrum*¹⁶¹
Actinoplanes sp^{89,90}

6. USES OF PLANTS SOURCE OF PENTAOXYGENATED, HEXAOXYGENATED AND DIMERIC XANTHONES

Among *Calophyllum* species (Guttiferae), *C. inophyllum* is the most widespread and has superior timber qualities in Malaysia⁶¹. The balsam from the bark of *C. inophyllum* "Alexandrian Laurel" is called 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 medicine⁷⁸. Xanthonenes from *C. inophyllum* produces CNS depression in rats and mice²⁴.

Canscora decussata Schult (Gentianaceae), an erect annual plant of height 0.6m, founds use in the Ayurvedic system of medicine in India for a variety of purposes. The roots are used as laxative, diuretic, for liver troubles, nerve tonic, in tuberculosis and fevers, while the aerial portions are used in insanity, epilepsy and nervous debility^{27,36}. The extract of *C. decussata* Schult is used in the treatment of tuberculosis and of certain mental disorders in the Indian system of medicine⁵⁵.

Centaurium linarifolium (Gentianaceae) is used in Spain folk medicine as a digestive, antipyretic, and a drug helpful in increasing blood circulation¹¹⁹. The botanical source of the Taiwan folk remedy "Hwang-jin-guey" is the root and stem of *Cudrania cochinchinensis* (Lour.) Kudo & Masamune var. *gerontogea* (S. & Z.) Kudo & Masamune³⁴. It was used in the treatment of neuralgia, rheumatics, hepatitis and contused wounds³⁵. Plant extracts obtained from genus *Eustoma* are used to treat various ailments including constipation, nervous debility, tuberculosis, fever, and anorexia¹⁴⁷.

Mesua ferrea (Guttiferae) is commonly called ironwood in Malaya. The hard and durable trunk-wood is used widely in agricultural tools and vehicles in the south-east Asian countries⁴⁰. From the expressed oil of its seeds had been isolated two crystalline antibiotic principles, mesul and mesuone⁶⁵. In contrast to mangiferin, which is reported to be CNS stimulant²⁷, xanthonenes from *M. ferrea* produces CNS depression in rats and mice²⁴.

Monnina obtusifolia (Polygalaceae) is used in the folk medicine of Ecuador as an antifungal, antitumoural, antipyorrhea, antiseptic and as a skin cleanser¹²⁵.

Polygala spectabilis DC (Polygalaceae), trivial name caa-membeca, is a common shrub of the estuary of the Amazon and the coastal region of Pará State, where it is used in popular medicine as expectorant, and in the treatment of hemorrhoids and amoebal infection¹². The roots of *P. tenuifolia* are used as an expectorant, tonic and sedative agent under the names "Onji" in Japan and "Yuan zhi" in China^{80,82}. It is also effective in inhibiting congestive oedema in rats⁵¹.

Psorospermum febrifugum (Guttiferae) 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* was fractionated with antileukemic activity *in vivo* in the P388 lymphocytic leukemia in mice and *in vitro* in the KB cell culture system used as a guide⁹³. From the extract was isolated six compounds 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 activity¹⁻³. One of these six xanthonenes exhibited significant cytotoxicity in the HT-29 human colon adenocarcinoma *in vitro* cell line⁴. In special, the xanthone Psorospermin, isolated from *P. febrifugum* exhibited cytotoxic and *in vivo*

antitumour activity in the P388 mouse leukemia, mammary (CD), and colon (C6) models⁶⁸.

Plants of the genus *Swertia* (Gentianaceae) have been used in traditional medicines for many years. Because these herbs taste extremely bitter and possess the ability to reduce fever, detoxify and act as choleric and liver tonics, they have been mainly used for the treatment of hepatic and choleric and inflammatory diseases, such as hepatitis, cholecystitis, pneumonia, osteomyelitis, dysentery, scabies, spasm, pain and neurasthenia¹⁶³.

Swertia cordata is a perennial herb widely distributed in the northern areas of Pakistan. The plant finds extensive usage in folk medicine as an alterative, febrifuge, and anthelmintic as well as a bitter tonic¹³⁰. *S. macrosperma* is a medicinal plant used as febrifuge, poison antidote and stomach tonic by the indigenous population in the south-western part of China¹⁶³. *S. mileensis* and *S. mussoti* are especially efficacious for acute viral hepatitis and some preparations have been produced industrially in China. Extracts of *S. purpurescens* Wall are very commonly used as a tonic and febrifuge in the indigenous system of medicine in India⁹.

Vismia guineensis (Guttiferae) is a small tree growing in West Tropical Africa whose roots and bark are used as a tropical remedy for skin diseases²⁹.

7. SYNTHESIS AND BIOSYNTHESIS OF XANTHONES

Some authors have reported the preparation of hydroxyxanthonenes^{15,66,128,129,138,141} but the first xanthone synthesis was proposed by Kostanecki^{91,92} and the last by Ravi *et al*¹³¹, with a new route to xanthone synthesis and Vitale *et al*¹⁵⁸ with a novel route for the preparation of xanthonenes and chromanones.

Polyoxygenated xanthonenes of potential therapeutic and taxonomic value have been synthesized by a number of methods⁵. From 1,3-Dibenzoyloxy-5,6,7,8-tetramethoxyxanthone Aurell *et al*¹⁷ synthesized 1,3-Dihydroxy-5,6,7,8-tetramethoxyxanthone and 1-Hydroxy-3,5,6,7,8-pentamethoxy-xanthone. The 1,8-Dihydroxy-2,3,4,6-tetramethoxyxanthone has been synthesized by trifluoroacetic anhydride (TFAA) condensation. The 1,6-Dihydroxy-3,5,7,8-tetramethoxyxanthone has been synthesized by Friedel-Crafts acylation¹⁷.

The 1,3,4-Trimethoxy-6,7-methylenedioxyxanthone (isopolygalaxanthone-A) has been synthesized From 1,3-Dihydroxy-6,7-methylendioxyxanthone by hydroxylation with alkaline persulphate followed by methylation. The 1-Hydroxy-3,4,7-trimethoxyxanthone on two-stage oxidation affords 1,2-Dihydroxy-3,4,7-trimethoxyxanthone⁸³.

The total synthesis of lichen xanthonenes¹⁵⁰, synthesis of furanoxanthonenes^{122,123}, synthesis of new xanthonenes¹²⁶, a new one-step method¹²⁴ and a general study for synthesis of polyoxygenated xanthonenes are reported recently by Lin *et al*⁹⁸.

The biosynthetic pathways to xanthonenes have been discussed in recent years. Initially these attempted to interrelate the observed oxygen pattern of natural xanthonenes and correlate them with recognized oxygenation patterns. In general it is seen that ring A and attached CO group are provided by the shikimic acid pathway whereas ring B arises via the acetate-malonate polyketide route^{5,16,148}. Therefore Locksley *et al*¹⁰⁰ reported the significance of Maclurin in xanthone biosynthesis and the biogenetic-type synthesis of xanthonenes from their benzophenone precursors¹⁰¹. Gottlieb^{62,63} showed biogenetic proposals regarding xanthonenes and Bhanu *et al*²⁶ related the biogenetic implications in the conversion of 4-phenilcoumarins into xanthonenes. More recently was reported the biosynthetic studies on Tajixanthone and Shamixanthone¹⁰.

Some xanthonenes in lower plants have been proved to be totally acetate derived, from seven acetate units^{28,109}. However, the oxygenation patterns of all xanthonenes 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 xanthenes. Mechanisms for this intramolecular reaction have been postulated involving either direct phenol oxidative coupling⁹⁶, quinone addition⁴⁹, dehydration between hydroxyl groups on the acetate and shikimate-derived rings¹⁰⁴ or spirodienone formation and subsequent rearrangement to form the xanthone^{32,62}.

About lichen and fungi biosynthesis it is important to say that the many secondary metabolites found in the lichen-forming fungi play a dominant role in the systematics of these organisms because of the extensive parallels with morphology and their clear ecological significance. Despite their common occurrence in a number of important genera, lichen xanthenes have not featured prominently in the repertoire of lichen taxonomists for several reasons. 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^{47,48,95}.

Elix and Crook⁴⁸ reported the unambiguous total synthesis of seventeen chlorine-containing derivatives of norlichexanthone, achieved by using the condensation of an appropriately substituted methyl or ethyl orsellinate and phloroglucinol or 2-chlorophloroglucinol in the key step.

8. PENTAOXYGENATED, HEXAOXYGENATED, DIMERIC AND MORE COMPLEX XANTHONES

The first naturally occurring penta-oxygenated xanthone is Corymbiferin (1,3,8-Trihydroxy-4,5-dimethoxyxanthone), isolated in 1950 from *Gentiana corymbifera*¹³³. The first naturally occurring hexaoxygenated xanthone is 1,2,3,4,6,7-hexamethoxyxanthone, isolated in 1969 from *Polygala macradenia*⁴⁵. The first dimeric naturally occurring xanthone is Chiratanin, isolated from *Swertia chirata* in 1987¹⁰². Till to date, a large number of these naturally occurring xanthenes have been isolated from higher plants, ferns and fungi¹⁰³.

The review by Roberts¹³² only refers to the natural occurrence of the penta-oxygenated xanthone Corymbiferin. The next review, by Afzal *et al*⁶ included 24 penta-oxygenated xanthenes and only one hexaoxygenated xanthone isolated from higher plants.

The review by Sultanbawa¹⁴⁸ included more 4 penta-oxygenated xanthenes from tropical plants, isolated from different mentioned species. Seven years later, in a review of xanthenes from Guttiferae, Bennett and Lee²⁴ listed only one new penta-oxygenated xanthone from Guttiferae species. Finally, in a review by Mandal *et al*¹⁰³ 23 penta-oxygenated, 7 hexaoxygenated and 3 dimeric xanthenes are listed. How demonstrated, by 1989 the number of characterized natural xanthenes of this species had considerably increased. During the period 1950 end 1995 was presented in reviews approximately 49 naturally occurring xanthenes of these species. In present review 102 of these compounds found in the literature are next listed (Tables 1-3).

Table 1. Penta-oxygenated naturally occurring xanthenes.

1-Hydroxy-2,3,4,5-tetramethoxyxanthone (01)

*Frasera albomarginata*⁴⁶
*F. caroliniensis*¹⁴³
*F. speciosa*⁴⁶
*F. tetrapetala*⁷
*Halenia asclepidea*¹⁴⁶
*H. campanulata*⁷⁷
*H. corniculata*¹²⁷
*H. elliptica*⁴²
*Swertia bimaculata*⁵⁹
*S. milensis*⁹⁹
*Veratrilla bailonii*¹⁶²

Continuação Table 1

1-Hydroxy-2,3,4,7-tetramethoxyxanthone (02)

*Frasera albicaulis*¹⁴⁴
*F. albomarginata*⁴⁶
*F. caroliniensis*¹⁴³
*F. speciosa*⁴⁶
*Halenia asclepidea*¹⁴⁶
*H. elliptica*⁴²
*Swertia bimaculata*⁵⁹
*S. tetrapetala*⁸

1-Hydroxy-2,3,5,7-tetramethoxyxanthone (03)

*Halenia corniculata*¹²⁷

1-Hydroxy-3,4,5,8-tetramethoxyxanthone (04)

*Swertia purpurascens*⁶⁰

1-Hydroxy-3,4,7,8-tetramethoxyxanthone (05)

*Swertia lawii*⁵⁹
*S. paniculata*¹¹
*S. purpurascens*⁶⁰

1-Hydroxy-3,5,6,7-tetramethoxyxanthone (06)

*Canscora decussata*⁵⁶
Centaurium erythrae^{86,111}
*Eustoma grandiflorum*¹⁴⁷

1-Hydroxy-3,5,7,8-tetramethoxyxanthone (07)

*Swertia cordata*¹³⁰
*S. punicea*⁵²
*S. purpurescens*⁹

1-Hydroxy-3,6,7,8-tetramethoxyxanthone (08)

*Canscora decussata*³⁶

2-Hydroxy-1,3-dimethoxy-7,8-methylenedioxyxanthone (09)

*Polygala spectabilis*¹²

2-Hydroxy-1,3,4,7-tetramethoxyxanthone (10)

*Frasera albicaulis*¹⁴⁴
*Swertia bimaculata*⁵⁹

6-Hydroxy-1,2,3,7-tetramethoxyxanthone (11)

Polygala tenuifolia^{80,82}

7-Hydroxy-1,2,3,4-tetramethoxyxanthone (12)

*Polygala macradenia*⁴⁵

7-Hydroxy-1,8-dimethoxy-2,3-methylenedioxyxanthone (13)

*Bredemeyera brevifolia*¹¹⁷

1,2-Dihydroxy-3,4,5-trihydroxyxanthone (14)

*Halenia elliptica*¹⁴⁹

1,3-Dihydroxy-2,4,7-trimethoxyxanthone (15)

*Frasera tetrapetala*⁷

1,3-Dihydroxy-4,5,8-trimethoxyxanthone (16)

*Swertia bimaculata*⁵⁹

1,3-Dihydroxy-4,7,8-trimethoxyxanthone (17)

(Methyllanceolin)

*Tripterosperrum lamceolatum*⁹⁷

1,3-Dihydroxy-5,6,7-trimethoxyxanthone (18)

*Cystopteris fragilis*⁸¹

1,4-Dihydroxy-2,3,7-trimethoxyxanthone (19)

*Swertia bimaculata*⁵⁹
*Veratrilla bailonii*¹⁶²

1,4-Dihydroxy-2,5,6-trimethoxyxanthone (20)

*Alnus glutinosa*⁸⁷

1,5-Dihydroxy-2,3,7-trimethoxyxanthone (21)

*Halenia elliptica*¹⁴⁹

1,6-Dihydroxy-3,5,7-trimethoxyxanthone (22)

*Polygala tenuifolia*⁸⁰

1,7-Dihydroxy-2,3,4-trimethoxyxanthone (23)

*Frasera speciosa*⁴⁶
*Halenia campanulata*⁷⁷

Continuação **Table 1**

*Polygala virgata*²²

1,7-Dihydroxy-3,4,8-trimethoxyxanthone (24)
*Bredemeyera brevifolia*¹¹⁷
*B. floribunda*¹⁴⁰
*Swertia mussotii*⁷³

1,7-Dihydroxy-3,5,6-trimethoxyxanthone (25)
Canscora decussata^{55,56}
*Polygala nyikensis*¹⁰⁶

1,7-Dihydroxy-3,5,8-trimethoxyxanthone (26)
*Swertia cordata*¹³⁰

1,8-Dihydroxy-2,3,6-trimethoxyxanthone (27)
*Ixanthus viscosus*¹¹⁸

1,8-Dihydroxy-2,3,7-trimethoxyxanthone (28)
*Calophyllum bracteatum*¹⁴²

1,8-Dihydroxy-2,3,8-trimethoxyxanthone (29)
*Calophyllum bracteatum*¹⁴²

1,8-Dihydroxy-2,4,6-trimethoxyxanthone (30)
*Swertia punicea*⁵²

1,8-Dihydroxy-3,4,5-trimethoxyxanthone (31)
(3-Methylcorymbiferin)
*Gentiana corymbifera*¹⁰⁷

1,8-Dihydroxy-3,4,6-trimethoxyxanthone (32)
*Centaurium linarifolium*¹²¹
*Erythraea centaurium*¹⁵³

1,8-Dihydroxy-3,6,7-trimethoxyxanthone (33)
*Canscora decussata*³⁶

3,6-Dihydroxy-1,7,8-trimethoxyxanthone (34)
*Mesua ferrea*⁶⁷

3,8-Dihydroxy-1,2,4-trimethoxyxanthone (35)
*Psorospermum febrifugum*⁶⁹

6,8-Dihydroxy-1,2,3-trimethoxyxanthone (36)
*Polygala tenuifolia*⁵¹

6,8-Dihydroxy-1,2,4-trimethoxyxanthone (37)
*Polygala tenuifolia*⁵¹

1,2,3-Trihydroxy-7,8-dimethoxyxanthone (38)
(Swertiaiberin)
*Swertia iberica*⁴¹

1,3,5-Trihydroxy-6,7-dimethoxyxanthone (39)
*Canscora decussata*⁵⁴

1,3,6-Trihydroxy-2,5-dimethoxyxanthone (40)
*Monnina obtusifolia*¹²⁵

1,3,6-Trihydroxy-2,7-dimethoxyxanthone (41)
(Onjixanthone II)
*Bredemeyera floribunda*¹⁴⁰
*Polygala tenuifolia*⁸⁰

1,3,6-Trihydroxy-7,8-dimethoxyxanthone (42)
*Mesua ferrea*⁶⁷

1,3,7-Trihydroxy-4,8-dimethoxyxanthone (43)
*Bredemeyera floribunda*¹⁴⁰

1,3,7-Trihydroxy-5,6-dimethoxyxanthone (44)
Canscora decussata^{55,56}

1,3,8-Trihydroxy-2,6-dimethoxyxanthone (45)
*Ixanthus viscosus*¹¹⁸

1,3,8-Trihydroxy-4,5-dimethoxyxanthone (46)
(Curymbiferin = 4,5-Di-O-methylcorymbin)
*Gentiana bellidifolia*³⁰
*G. campestris*³⁰
*G. corymbifera*¹³³
G. germanica^{30,85}
G. ramosa^{30,85}

Continuação **Table 1**

1,3,8-Trihydroxy-4,7-dimethoxyxanthone (47)
(4,7-Dimethoxybellidifolin = 4,7-Di-O-methylbellidifolin)
Gentiana bellidifolia^{30,105}

1,3,8-Trihydroxy-6,7-dimethoxyxanthone (48)
*Canscora decussata*³⁶

1,4,8-Trihydroxy-3,7-dimethoxyxanthone (49)
(Lanceolin)
*Tipterospermum lanceolatum*⁹⁷

1,5,6-Trihydroxy-3,7-dimethoxyxanthone (50)
*Canscora decussata*⁵⁴

1,5,7-Trihydroxy-3,6-dimethoxyxanthone (51)
*Canscora decussata*⁵⁴

1,5,8-Trihydroxy-3,4-dimethoxyxanthone (52)
*Gentiana campestris*⁸⁴

1,6,7-Trihydroxy-2,3-dimethoxyxanthone (53)
*Bredemeyera brevifolia*¹¹⁷

1,6,7-Trihydroxy-3,5-dimethoxyxanthone (54)
Canscora decussata^{55,56}
*Hoppea dichotoma*⁵⁸

2,3,8-Trihydroxy-1,7-dimethoxyxanthone (55)
*Kielmeyera rubriflora*⁶⁴

1,3,5,6-Tetrahydroxyxanthone-7-methoxyxanthone (56)
(Caloxanthone E)
*Calophyllum inophyllum*⁷⁹

1,3,5,6,7-Pentahydroxyxanthone (57)
*Canscora decussata*⁵⁵

1,3,6,7,8-Pentahydroxyxanthone (58)
*Canscora decussata*³⁶

1-Methoxy-2,3,6,7-dimethylenedioxyxanthone (59)
*Polygala macradenia*⁴⁵
*P. triphylla*⁵³

1-Methoxy-2,3,7,8-dimethylenedioxyxanthone (60)
*Bredemeyera brevifolia*¹¹⁷

1,2,3-Trimethoxy-6,7-methylenedioxyxanthone (61)
(Polygalaxanthone A)
Polygala macradenia^{45,145}
*P. paenea*¹¹³

1,2,3-Trimethoxy-7,8-methylenedioxyxanthone (62)
*Polygala spectabilis*¹²

1,7,8-Trimethoxy-2,3-methylenedioxyxanthone (63)
*Bredemeyera brevifolia*¹¹⁷

1,2,3,4,5-Pentamethoxyxanthone (64)
*Frasera albicaulis*¹⁴⁴

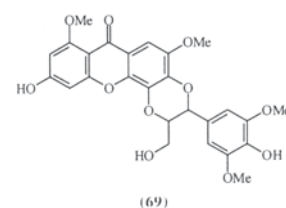
1,2,3,4,7-Pentamethoxyxanthone (65)
(Pulygalaxanthone B)
*Polygala paenea*¹¹³

1,2,3,5,8-Pentamethoxyxanthone (66)
*Frasera carolinensis*¹⁴⁴

1,2,3,6,7-Pentamethylurxyxanthone (67)
Polygala tenuifolia^{80,82}

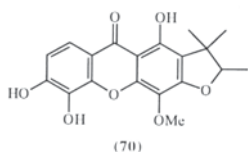
1,2,3,7,8-Pentamethoxyxanthone (68)
*Polygala spectabilis*¹²

6-Hydroxyisocadensin F (69)
Psorospermum febrifugum 2

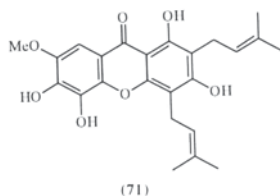


Continuação **Table 1**

Gerontoxanthone D (70)
*Cudrania cochinchinensis*³⁴



Xanthone V_{2a} (71)
*Vismia guineensis*²⁹



Xanthone V₂(72)
*Vismia guineensis*²⁹

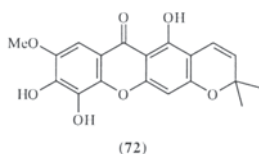


Table 2. Hexaoxygenated naturally occurring xanthenes.

1-Hydroxy-3,5,6,7,8-pentamethoxyxanthone (73)
(Eustomin)

Centaurium erythraea^{23,86}
*C. linarifolium*¹²⁰
C. littorale^{23,156}
*Chironia krebsii*¹⁶⁰
*Eustoma grandiflorum*¹⁴⁷

1,3-Dihydroxy-2,5,6,7-tetramethoxyxanthone (74)
*Bredemeyera brevifolia*¹¹⁷

1,6-Dihydroxy-2,3,4,8-tetramethoxyxanthone (75)
*Halenia corniculata*¹¹⁶

1,6-Dihydroxy-3,5,7,8-tetramethoxyxanthone (76)
Centaurium linarifolium^{119,121,160}

1,7-Dihydroxy-2,3,4,5-tetramethoxyxanthone (77)
*Halenia elliptica*¹⁴⁹
*H. corniculata*¹¹⁶

1,8-Dihydroxy-2,3,4,6-tetramethoxyxanthone (78)
*Centaurium cachanlahuen*¹⁵⁷
C. Linarifolium^{119,121}
*C. erythraea*¹¹¹
*Erithraea centaurium*¹⁵³

1,8-Dihydroxy-3,5,6,7-tetramethoxyxanthone (79)
(8-Desmethyleustomin)
*Blackstonia perfoliata*¹⁵⁵
Centaurium erythraea^{23,86,115}
C. littorale^{23,156}
*Chironia krebsii*¹⁶⁰

1,3,8-Trihydroxy-2,4,6-trimethoxyxanthone (80)
*Centaurium linarifolium*¹²¹

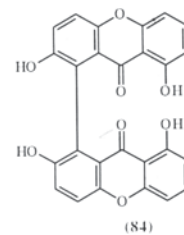
1,6,8-Trihydroxy-3,5,7-trimethoxyxanthone (81)
*Chironia krebsii*¹⁶⁰

1,2,3,4,6,7-Hexamethoxyxanthone (82)
*Cansora decussata*⁵⁷
*Croton californicus*¹⁵⁴
*Polygata macradenia*⁴⁵
*Uvaria kirkii*¹⁵⁴

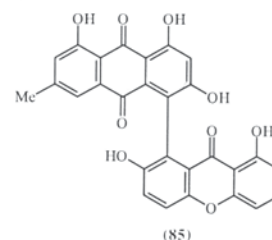
1,3,5,6,7,8-Hexamethoxyxanthone (83)
*Cansora decussata*⁵⁷

Table 3. Dimeric and more complex naturally occurring xanthenes

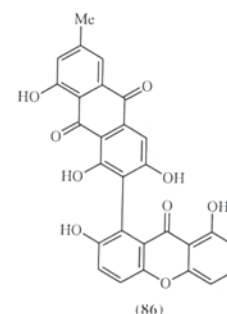
Ploiarixanthone (84)
*Ploiarium alternifolium*²⁵



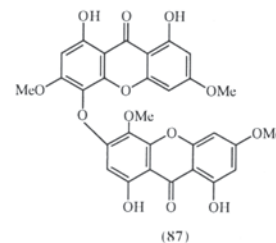
Euxanmodin A (85)
*Ploiarium alternifolium*²⁵



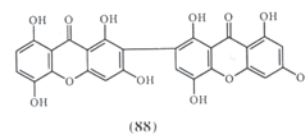
Euxanmodin B (86)
*Ploiarium alternifolium*²⁵



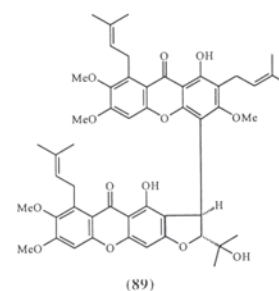
Chiratanin (87)
*Swertia chirata*¹⁰²



Swertiabixanthone I (88)
*Swertia macroserma*¹⁶³

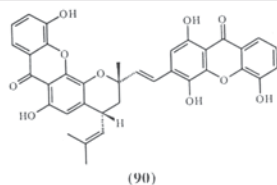


Cratoxyxanthone (89)
*Cratoxylum cochinchinense*¹³⁵

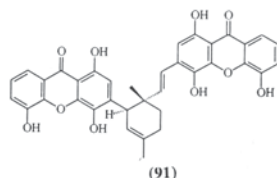


Continuação **Table 3**

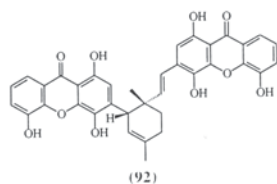
Garcilivin B (90)
*Garcinia livingstonei*⁴³



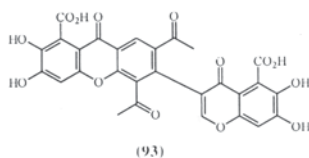
Garcilivin A (91)
*Garcinia livingstonei*⁴³



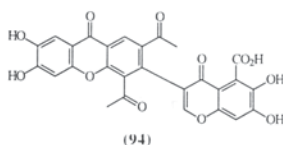
Garcilivin C (92)
*Garcinia livingstonei*⁴³



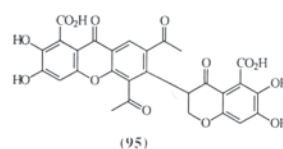
Xanthone 411F or Vinaxanthone (93)
*Penicillium glabrum*¹⁶¹



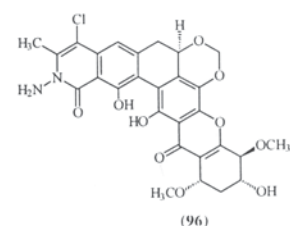
Xanthone 411P (94)
*Penicillium glabrum*¹⁶¹



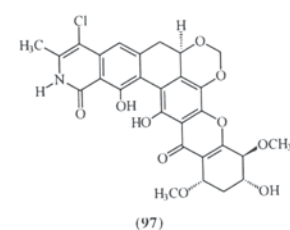
Xanthone 411J (95)
*Penicillium glabrum*¹⁶¹



Actinoplanone A (96)
Actinoplanes sp⁸⁹

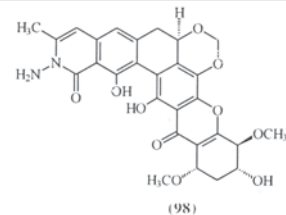


Actinoplanone B (97)
Actinoplanes sp⁸⁹

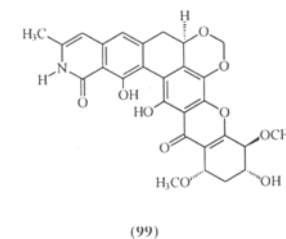


Continuação **Table 3**

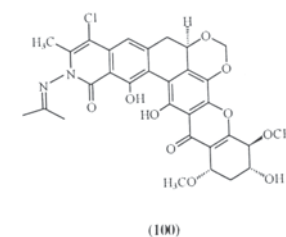
Actinoplanone C (98)
Actinoplanes sp⁹⁰



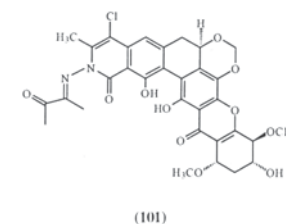
Actinoplanone D (99)
Actinoplanes sp⁹⁰



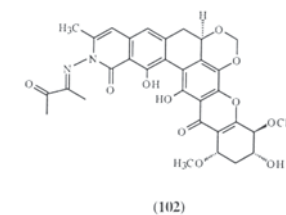
Actinoplanone E (100)
Actinoplanes sp⁹⁰



Actinoplanone F (101)
Actinoplanes sp⁹⁰



Actinoplanone G (102)
Actinoplanes sp⁹⁰



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