Chapter 10

Xanthones identified in the medicinal plants of Africa

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Introduction

The term xanthone comes from the Greek "xanthós" which means yellow was coined in 1855 by Schmid demonstrating the yellow color of the compound isolated from the pericarp of mangosteen (*Garcinia mangostana* L.), a tropical fruit belonging to the Clusiaceae (or Guttiferae) family [1]. They are oxygenated heterocyclic molecules, with a dibenzo-γ-pirone **1** scaffold, known as 9H-xanthen-9-one, with the molecular formula of $C_{13}H_8O_2$ (Fig. 10.1). The structure of **3** was identified by X-ray crystallographic analysis [2]. They have a structural relationship with other γ-pyrone derivatives, flavonoids, and chromones **2** [3]. The numbering and class of rings A and B derive from the biosynthetic pathways in higher plants leading to the acetate-derived A-ring (carbons 1−4) and the shikimic acid pathway-derived B-ring (carbons 5−8); the other carbon atoms are numbered according to IUPAC 2004 recommendations for structure elucidation purposes. Xanthone derivatives consist of slight differences that can be found depending on the nature of the substituents and their localization on the scaffold. Different possible configurations of the two benzene rings and various substituents can be found, leading to higher complexity.

Xanthones constitute a group of secondary metabolites commonly encountered in nature and synthesized by several living organisms. Plants remain the prevalent source of xanthones, accounting for nearly 80% of natural xanthones. Fungi represent 15% [4] while lichens represent the remaining 5% [5]. Algae and bacteria are also able to synthesize xanthones [5]. Xanthones have been found even in fossil fuels, demonstrating their chemical stability [6,7]. Plants can therefore be considered as the main prevalent source of xanthones.

In 1821, gentisin (1,7-dihydroxy3-methoxyxanthone) was found to be the first natural xanthone described, isolated from *Gentiana lutea* L. [8] and the first prenylxanthone derivative, tajixanthone, was isolated from the mycelium of *Aspergillus stellatus* in 1970 [9]. The most studied plant species producing xanthones belong to the Clusiaceae, Hypericaceae, Gentianaceae, and Caryophyllaceae families [10,11]. In 2016, the *Dictionary of Natural Products* revealed that natural xanthones are ca. 2000, including their reduced derivatives di-, tetra-, and hexahydroxanthones.

Xanthones have gradually risen to great importance because of their medicinal properties, oxygenation nature, and diversity of functional groups. Their chemotaxonomic

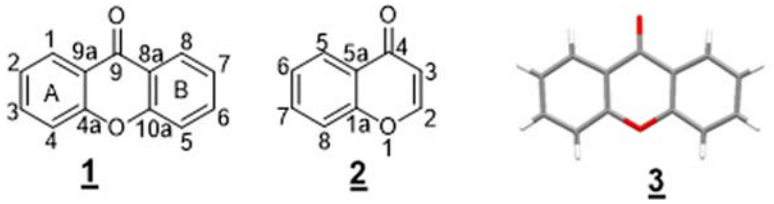

FIGURE 10.1 The basic skeleton of xanthone.

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importance in some families and their pharmacological properties have raised great interest [12]. Xanthones are well-known to have "privileged structures" because this simple tricyclic compound exhibits wide biological activities such as anticancer, antimicrobial, antifungal, antimalarial, anti-HIV, anticonvulsant, anticholinesterase, antioxidant, anti-inflammatory, antimalarial, antibacterial, antiviral, antioxidative, antiproliferative, antihypertensive, antithrombotic, in vitro and in vivo antitumor, cytotoxic, coagulant, monoamine oxidase (MAO) inhibition, gastroprotective effects, antiatherosclerosis activity, inhibition of hypotension, cardioprotection, inhibition of cholinesterase, cyclooxygenase activity, immunosuppression, and binding to transthyretin (TTR) [3,5,13–44].

These interesting structural scaffolds and pharmacological importance have encouraged scientists to isolate these compounds from natural products and synthesize them as novel drug candidates. In this review, we present an updated literature survey of naturally occurring xanthones published in the last decade (from 20,013 up to date) and tabulate these xanthones along with their structures (including stereochemistry if available), and the way to separate them. The spectral methods are to elucidate their structure. We have tried to summarize the different classes of xanthones, their biosynthesis, and trafficking mechanisms in plant organisms reported in the literature over the last decades. Their biological activities are also discussed. The selected articles for this work have been screened from the Web of Science, Scopus, PubMed, and Google Scholar to highlight the current advancement and future direction toward the completion of the study of xanthones.

Classification

In the last decades, there has been widespread interest in studying the classification of xanthones, motivated primarily by the great potential of these compounds for their medically useful biological properties. Because of the great diversity of substituents and the discovery and synthesis of new xanthones, their classification by groups has evolved. Except for simple xanthones that have only methyl groups attached to the core structure, all other xanthones can be divided into six main groups based on their substituents: oxygenated xanthones, glycosylated xanthones, prenylated xanthones, xanthonolignoids, bisxanthones, and various xanthones [45,46]. These molecules are biosynthesized and accumulated in various plant organs (leaves, stems, roots, flowers, and fruits) and tissues, and in other organisms [47,48]. In the present review, we will follow this way to classify the compounds in higher plants (Table 10.1).

Simple oxygenated xanthones

Simple oxygenated xanthones are subdivided according to the degree of oxygenation into non-, mono-, di-, tri-, tetra-, penta-, and hexaoxygenated substances [50]. In these xanthones, the substituents are simple hydroxy, methoxy, or methyl groups. This group is abundant in many natural products and is the starting point for many more complex xanthones. Mono, di, tri, tetra, penta, and hexa-oxygenated xanthones have been found in different plant families such as Gentianaceae, Clusiaceae, Hypericaceae, and Moraceae. The examples of xanthone derivatives in each subgroup of oxygenated-xanthone are shown in Fig. 10.1.

TABLE 10.1 Classification of xanthone derivatives with some examples for each group [49].

Group of xanthones	Example
Simple oxygenated xanthones	Mono-oxygenated xanthone (**4**) (R_2=OH, R_1=R_3 = R_4=R_5 = R_6=R_7 = H) Di-oxygenated xanthone (**5**) (R_2=OMe, R_3=OH, R_1=R_4 = R_5=R_6 = R_7=H) Tri-oxygenated xanthone (**6**) (gentisin) (R_1=R_6 = OH, R_3= OMe, R_2=R_4 = R_5= R_7 = H) Tetra-oxygenated xanthone (**7**) (R_1=OH, R_3=R_6 = R_7=OMe, R_2=R_4 = R_5=H) Penta-oxygenated xanthone (**8**) (R_1=OH, R_2=R_3 = R_4=R_5 = OMe, R_6=R_7 = H) Hexa-oxygenated xanthone (**9**) (R_1=OH, R_2=R_3 = R_4=R_5 = R_6=OMe, R_7=H)
Glycosylated xanthones	Norswertianolin (**10**) Mangiferin (**11**)
Prenylated xanthones	α-Mangostin **(12)** Caloxanthone **(13)** Calozeylxanthone **(14)**
Bisxanthones	Swertipunicoside (**15**) Phomoxanthone A (**16**)
Xanthonolignoids	Cadensin D (**17**)
Miscellaneous xanthones	Xanthofulvin (**18**) Vinaxanthone (**19**)

Glycosylated xanthones

Xanthone glycosides are synthesized in higher plants and are mainly found in the families Gentianaceae and Polygalaceae. Several naturally occurring glycosylated xanthones have been reported as *C*- or *O*-glycosides. Many xanthones of this group have the glycosidic residue linked to C-6 carbon and may consist of xylose, glucose, or epiose. The presence of two glycosidic residues can also be observed, the second generally being linked to the C-2 of the main structure. In *O*-glycosides, the glycosidic bond is formed between the anomeric carbon atom of the sugar ring and the oxygen atom of the hydroxyl group present in the xanthone skeleton. In *C*-glycosides, xanthone is connected with glycosyl moiety through the C—C bond [51]. Norswertianolin (**10**) and mangiferin (**11**) are examples of *O*-glycoside and *C*-glycoside xanthones [49], respectively (Fig. 10.2).

Prenylated and related xanthones

The prenylated xanthone group is characterized by the presence of prenyl or geranyl substituents [52]. There is considerable variability in the classification of prenylated xanthones; in fact, it is possible to observe the presence of the prenyl group in different positions of the basic structure. These groups can have carbon chains consisting of a single prenyl group, composed of five carbons or geranyl group, composed of 10 carbons (e.g., 1,3,5,8-tétrahydroxy-2-(3-méthybut-2-ényl)-4-(3,7-diméthyloct-2,6-diényl)xanthone (**39**) [53]. The prenylated xanthone group contains the largest number of natural xanthone derivatives, such as α-mangostin (**12**), caloxanthone (**13**), and calozeylxanthone (**14**), as shown in Fig. 10.2.

Bisxanthones

Bisxanthones are quite rare, and only around 12 xanthone dimers have been reported so far. Their chemical structure consists of a 9*H*-xanthen-9-one dimer with several substituent groups. The first isolated xanthone dimer was swertipunicoside (**15**) obtained from the whole plant of *Swertia punicea* in 1992. Swertipunicoside (**15**) and phomoxanthone A (**16**) are two examples of xanthone dimers, shown in Fig. 10.2.

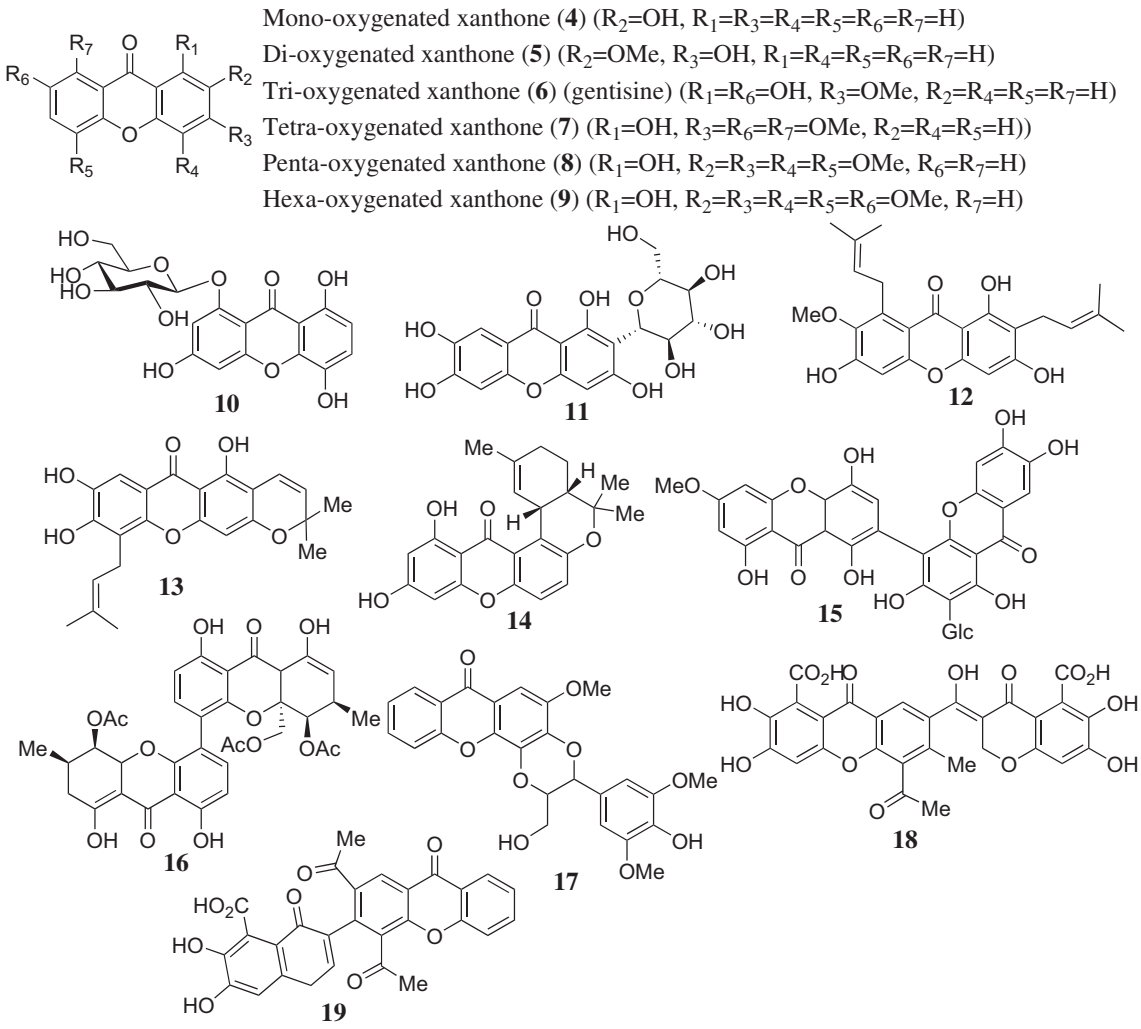

FIGURE 10.2 Classification of xanthone derivatives with some examples for each group [49].

Xantholignoids

Natural xanthonolignoids are characterized by a connection between xanthone and lignin (coniferyl alcohol) frameworks. The building blocks of xanthonolignoids are simple *ortho*-dioxygenated xanthones and a C_6-C_3 unit represented by cinnamyl alcohol [54]. The number of xanthonolignoids is also limited. The isolated xanthonolignoids have been reported from *Guttiferae*, such as cadensin D (**17**) as shown in Fig. 10.2.

Miscellaneous xanthones

Miscellaneous xanthones are defined for all xanthone derivatives that could not be classified into the other groups, such as xanthofulvin (**18**) and vinaxanthone (**19**), and their chemical structures are shown in Fig. 10.2. They are found in the kingdom of plants and fungi.

Isolation, structural elucidation, and biosynthesis pathway for xanthone

Though methods of isolation and structure elucidation of xanthones have been covered in previous reviews [3,54,55], Bo and Liu have recently reviewed separation methods used for pharmacologically active xanthones with emphasis on new capillary electrophoresis techniques [56]. An increasing number of bioactive xanthones have been isolated by bioassay-guided fractionation methods. Among the biological activities used to monitor the isolation of bioactive xanthones, the mains are antibacterial [57], antifungal [58], antiviral [59,60], trypanocidal [61,62] activities, and cytotoxicity against human carcinoma cell lines [63–66]. Some specific activities such as potentiation of nerve growth factor (NGF) action in the PC12D cell [67] and secreted aspartic protease (SAP) of *Candida albicans* [68] have also been used to monitor the isolation of several bioactive prenylated xanthones.

^{1}H and ^{13}C NMR spectroscopic methods continue to be the most useful tools in the structure elucidation of naturally occurring xanthones. However, several 2D NMR techniques such as COSY, NOESY, HSQC, and HMBC have been widely used to elucidate unambiguously structures of the more complex xanthones, especially prenylated [51,61,63,64,68–74] and bisxanthones [75–77]. Other NMR techniques such as SINEPT [78], NOEDIFF [71–73,79,80], ROESY [69,81,82], TOCSY [80,83], and INADEQUATE [84] have also found use in structure elucidation of some xanthones.

Isolation

It has been shown that xanthones are present in nonpolar or medium-polar extracts of the plant′s materials. The efficiency of the extraction procedure has been tested by using different techniques and by sequentially varying the composition of the solvents, such as methanol, 70% methanol, and ethanol. It has been shown that undiluted methanol yielded more benzophenones and xanthones than aqueous methanol [85]. The amounts of the compounds extracted by constant stirring at room temperature and by ultrasonic extraction were compared for the majority of the assayed analytes, and the highest extraction efficiency was achieved by stirring with methanol. For xanthones, it was found that ultrasonic extraction and extraction with ethanol gave comparable quantities. Xanthones are commonly separated by classical, such as silica gel, chromatography using different solvent mixtures. Sephadex LH-20 is a very useful stationary phase for the separation of xanthones [86]. HPLC has been proven as the best technique for the separation, identification, and quantification of xanthones. Several HPLC methods have been developed for naturally occurring xanthones using microporous chemically bonded silica gel (Micropak CN column), solvent hexane-chloroform (13:7, v/v), isooctane-$CHCl_3$ (3:17, v/v), or dioxane-dichloromethane (1: 9) detected at 254 nm by UV detector [87]. An increasing number of bioactive xanthones have been isolated by bioassay-guided fractionation methods. Bo and Liu [56] have reviewed separation methods used for pharmacologically active xanthones with an emphasis on new capillary electrophoresis techniques.

HPLC analytical methods have demonstrated excellent selectivity and resolution for xanthone compounds, in relatively short runs of approximately 30 min. Extraction with a mixture of 80:20 acetone/water is an efficient, robust method for the preferential extraction of xanthones from their natural sources [88]. A rapid ion-pair HPLC method was developed and validated for the determination of polyprenylated xanthones [89]. The simultaneous analysis of naturally occurring xanthones is a quantitative determination conducted by RP-HPLC with a photodiode array detector (PDA) [90].

Polar aglycones, as well as glycosides of xanthones, are also resolved on a reversed-phase column (C8 and C18) using acetonitrile-water as a mobile phase [91]. High-speed countercurrent chromatography (HSCCC) and high-performance centrifugal partition chromatography (HPCPC) were also used for the separation and isolation of some xanthones, for example, mangiferin and neomangiferin from an extract of *Anemarrhena asphodeloides* [92] and α-mangostins and γ-mangostins from mangosteen pericarp, respectively [93].

Structural elucidation

Detailed structural information of xanthone structures is essential for understanding the wide range of biological and pharmacological activities described for these compounds.

The structure of xanthones has been established based on ultraviolet (UV), infrared (IR), mass spectrometry MS, and nuclear magnetic resonance (NMR) data [94]. Mass spectroscopy (MS) and nuclear magnetic resonance (NMR) spectroscopy are the most powerful structure elucidation techniques. 2D-NMR techniques, such as COSY, NOESY, HSQC, and HMBC, are used to unambiguously elucidate structures of more complex xanthones, especially prenylated and bisxanthones. Other successfully used techniques include X-ray diffraction analysis for structure elucidation and confirmation of the stereochemistry. Table 10.2 displays a summary of the structural elucidation of xanthones using spectroscopy techniques.

Ultraviolet-visible spectroscopy

The UV spectrum of xanthone reflects the absorption characteristics of xanthone chromophores in the ultraviolet region. This technique is useful for locating free hydroxyl groups in xanthones. In particular, the OH group at position 3 is easily detected by the addition of NaOAc which results in a bathochromic shift of the 300−330 nm bands with increased intensity. Three or four bands of maximum absorption are always found in the region 200−400 nm and it is noteworthy that all bands show high intensity. Most of the substances show a marked absorption in the 400 nm regions, which accounts for their yellow color [95].

Infrared spectroscopy

The carbonyl group in xanthones is always easily detectable in IR spectra as a strong band (stretching frequency) in the region of 1657 cm^{-1} [96]. The presence of a hydroxyl group in the 1 or 8 position lowers the frequency to about 1650 cm^{-1} by hydrogen bonding. Substituents in the three or six position of the xanthone nucleus may have a marked effect on the carbonyl stretching frequency [97].

Mass spectrometry

The molecular weight of xanthone can be determined from its MS spectrum. The unsaturation degree of xanthone, as well as halogen substituents, are mostly determined from the MS spectrum. The core structure of the xanthone has one pyran structure, two aromatic rings, and 1 C═O double bond; thus, the xanthone core itself has an unsaturation degree of 10. In the mass spectrum of *O*-glycosides, no discernible molecular ion peak can be observed, but an important fragment ion peak due to the aglycone moiety appears, followed by further fragmentation. Significant fragment ions from the loss of OH, H_2O, and CHO are typical for xanthones and related compounds with a methoxy substituent peri to the carbonyl group [96]. The halogen substituent can be indicated by its isotopic effect on the MS spectra. Chloro- and bromo-substituted xanthones commonly give two molecular ion fragments with m/z of $[M]^+$ and $[M+2]^+$ in 3:1 and 1:1 ratios, respectively. In contrast, elucidation of fluoro- and iodo-substituted xanthones from their MS spectrum is difficult, as both halogen atoms are only found as a single isotope. Therefore, fluoro- and bromo-substituents in xanthones can be observed using the ^{19}F-NMR and ^{127}I-NMR techniques, respectively.

Proton nuclear magnetic resonance spectroscopy

1D and 2D-NMR spectra (^{1}H, ^{13}C, DEPT, COSY, TOCSY, HROESY, HSQC, HMBC, and NOESY) have been used for the characterization of the xanthones. The ^{1}H-NMR spectrum appears predominantly in the range of

TABLE 10.2 A summary of the structure elucidation of xanthones using spectroscopy techniques.

Structure	IR (cm^{-1})	UV (nm)	^{1}H-NMR (ppm)	^{13}C-NMR (ppm)
C_{sp^2} – H	3000−3100	–	6−9	–
C═O	1650−1720	200−400	–	176
C═C aromatic	1450−1600		–	126 (C-1) 124 (C-2) 135 (C-3) 118 (C-4) 156 (C-4a) 121 (C-8a)
C−O−C	1000−1200	–	–	–
O−H	3300−3500	–	9-10 (C-2 or C-7) 9-11 (C-4 or C-5) 10-11 (C-3 or C-6) 12-14 (C-1 or C-8)	

0−12 ppm downfield from the reference signal of TMS. The integral of the signals is proportional to the number of protons present. ^{1}H-NMR gives information about the substitution pattern on each ring. Acetylated derivatives have been utilized in the structure determination of glycosides [98]. The number and relative position of acetyl and methoxy groups can be determined by observing the shift in the position of absorption for the aromatic protons which occurs upon replacing the methoxy group with an acetyl group. Signals between δ 2.40−2.50 are indicative of acetylation at peri-position to the carbonyl group (1 or 8 positions) since for other positions the acetyl signals fall between δ 2.30 and 2.35. In nonacetylated xanthones, the presence of hydrogen-bonded OH at δ 12−13 also confirms hydroxyl substitution at 1 or 8. But when these positions are unsubstituted, then absorption for the aromatic protons appears at δ 7.70−8.05 [99]. Tetraoxygenated xanthones, namely, 1,3,7,8- and 1,3,5,8-, showed two meta and two ortho-coupled protons in the ^{1}H NMR spectrum. They can also be distinguished by the fact that the presence of the ortho-coupled proton in the 1,3,7,8-system appears at a lower field [100] than that for 1,3,5,8-(bellidifolin) system [101]. The signals of 2″-O-acetyl methyl protons of 8-C-glucosyl flavone acetate are found at a higher field than those of corresponding 6-C-glucosyl flavone acetate [102]. Similarly, 2-C and 4-C isomeric glycosyl xanthones can be distinguished.

Carbon nuclear magnetic resonance spectroscopy

The number of signals in the ^{13}C NMR spectrum indicates the number of different types of C atoms. It gives information about the total number of the C atoms present in the molecule. It is particularly diagnostic for determining the sugar linkage in di- or polysaccharides; the signal of the carbon carrying the primary alcohols appears at δ 62 in glucose. This signal is shifted to δ 67 in disaccharides possessing a 1−6 linkage [87,103]. The chemical shift for carbonyl carbon is δ 184.5 when positions 1 and 8 are substituted by hydroxyl groups. But when one of these positions is occupied either by a methoxy or a sugar moiety, the carbonyl signal is shifted upfield by about 4 ppm. If both positions are occupied by a methoxy group or sugar moieties, the upfield shift is about 10 ppm. When methoxy groups are located in position 1 or 8, the corresponding absorption appears at δ 60−61, whereas they appear at about δ 56 when the methoxy group is located in the remaining positions on the xanthone nucleus [96].

X-ray

The advances in molecular biology and a breakthrough in structure elucidation methods have made possible a high throughput screening of many new natural products from different sources. It is worth mentioning that X-ray crystallography has played an important role in the determination of the three-dimensional structure, including the absolute configuration of many new natural products. As we said above, xanthones are secondary metabolites that occur in some higher plant families, lichens, and fungi. Although there are several hundreds of synthesized and natural xanthones in the literature, only 50 crystal structures from 47 chemically different xanthone derivatives have been described [3]. The xanthone molecules stack in the crystals along the axis, with significant interactions. In addition, O−H - ⋯ O hydrogen bonds link the molecules into a long chain [104,105].

The crystal structure of 9*H*-xanthen-9-one (**3**) was first reported in 1982 [106] and redetermined 8 years later using more accurate experimental data [107]. The compound has two benzenoid and one pyranoid ring. The molecule is essentially planar except for the O(11) atom, which deviates 0.13 Å from the plane. The least squares planes containing the aromatic rings form angles of 3.7° and 2.0° with the plane of the pyranoid ring and the three-ring system adopts a very flattened boat conformation. The deviation of O(11) from the plane is not a general feature of the crystallographic structure of xanthone derivatives; it probably results from the crystallographic packing of compound 1, which may lead to repulsion between the atom O(11) from one molecule and C(6) of an adjacent molecule [107].

The central pyranoid ring has a partial aromatic character. The C(4a)-O(10)-C(10a) angle is 119.4(6)° and the C(4a)- O(10) and C(10a)-O(10) bond lengths are 1.35(1) Å and 1.37(1) Å, which are values slightly shorter than those observed for diaryl ethers (Car-O-Car): 1.384(14) Å [108]. Also, the C(8a)-C(9) and the C(9)-C(9a) bonds are shorter than the corresponding bonds in acetone. Thus, it appears that the pz electrons of atoms O(10) and C(9) are used for conjugation in the central ring and this conjugation makes the skeleton of the molecule planar. The two benzene rings are not regular hexagons in shape, but these distortions seem to be symmetric and the whole molecule has approximate C2v symmetry.

The introduction of substituents on the xanthone molecule may cause slight alterations in the structure of its skeleton. Frequently, the three-ring system is slightly twisted along its longitudinal axis taking a propeller-like form due to steric factors associated with the substituents. Also, the C═O bond length, which is 1.22 Å in the xanthen-9-one, may be larger (1.24−1.28 Å) when the carbonyl is involved in hydrogen bonding [109].

A summary of the chemical elucidation of xanthones using spectroscopy techniques is presented in Table 10.2 [49]. In this chapter, we presented an example of structural elucidation of isolated xanthone identified as 3-diméthyl-2-

géranyl-4-prénylbellidifolin. 3-diméthyl-2-géranyl-4-prénylbellidifolin is obtained in the form of a yellow powder in a Hex/CH_2Cl_2 (7:3) mixture. It gives a positive reaction with ferric chloride characteristic of phenolic compounds. The analysis of its electronic impact mass spectrum (Fig. 10.3) allows attributing to it the crude formula $C_{28}H_{32}O_6$ deduced from the molecular ion [M^+] at m/z 464 and containing 13 degrees of unsaturation. This high degree of unsaturation argues in favor of an aromatic structure. The UV and IR spectra of 3-diméthyl-2-géranyl-4-prénylbellidifolin are shown in Figs. 10.4 and Fig. 10.5.

The analysis of its ^{1}H-NMR spectrum (600 MHz; $CDCl_3$) combined with that of the COSY and HSQC spectra shows that 3-diméthyl-2-géranyl-4-prénylbellidifolin (known) and 1,3,5,8-tétrahydroxy-2-(3-méthybut-2-énYl)-4-(3,7-diméthyloct-2,6-diényl)xanthone (new) both isolated from *Garcinia smeathmannii*, are isomers. The only difference between the two compounds is the position of the geranyl and γ,γ-dimethylallyl moieties on the A ring of the xanthone backbone. The ^{1}H-NMR, ^{13}C-NMR, and DEPT spectra of 3-diméthyl-2-géranyl-4-prénylbellidifolin are shown, respectively, in Figs. 10.6—10.8.

The interpretation of all its spectroscopic data (MS, ^{1}H-NMR, ^{13}C-NMR, DEPT, and HMBC) and their comparison with those noted in the literature [110] led us to attribute the structure **39** below to this xanthone (Fig. 10.9).

To decide between the structures of the two compounds, we used the HMBC spectrum. Indeed, for the compound 1,3,5,8-tétrahydroxy-2-(3-méthybut-2-énYl)-4-(3,7-diméthyloct-2,6-diényl)xanthone, while the correlations observed between the protons at δ_H 3.47(H-1′) of geranyl and the carbons C-1(158.0); C-2(109.2);C-3(161.8); C-2′(120.8); C-3′(140.4) show that the geranylated fragment is attached to the C-2(109.2) carbon of the xanthonic ring; The proton at δ_H 3.50(1H, d, $J = 7.0$ Hz) correlating with carbons C-2′(122.0); C-3(161.8); C-3′(133.6) and C-4(106.1); C-4a (152.5) shows that the γ,γ-dimethylallyl group is attached to the C-4 (106.1) carbon.

For the compound 3-dimethyl-2-geranyl-4-prenylbellidifolin, the proton at δ_H 3.68(2H, d, J = 7.1 Hz)/δ C 22.2 of geranyl presents correlation spots with the carbons at δ_C 107.7(C-4); 122.8(C-2′); 136.7(C-3′); 153.6(C-4a); 162.3(C-3) thus showing that the geranylated fragment is fixed in position 4 of the xanthone skeleton while that at δ_H 3.45 (2H, d, J = 7.1 Hz)/δ_C 22.0 of the γ fragment, γ-dimethylallyl shows correlation spots with carbons at δ_C 111.6(C-2); 122.7(C-2″); 132.7(C-3″); 158.8(C-1); 162.3(C-3) showing that it is fixed in position 4.

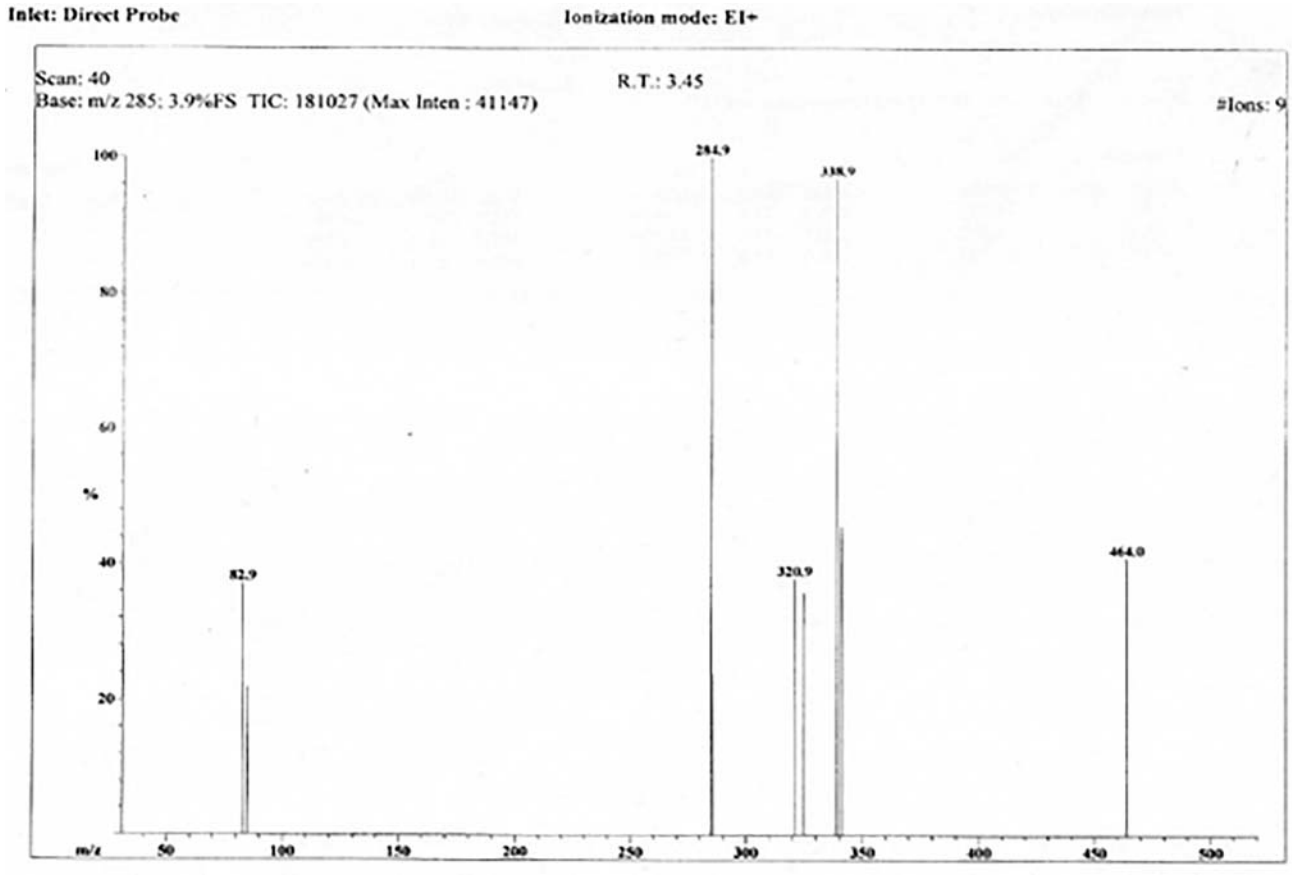

FIGURE 10.3 EI mass of 3-dimethyl-2-géranyl-4-prenylbellidifolin.

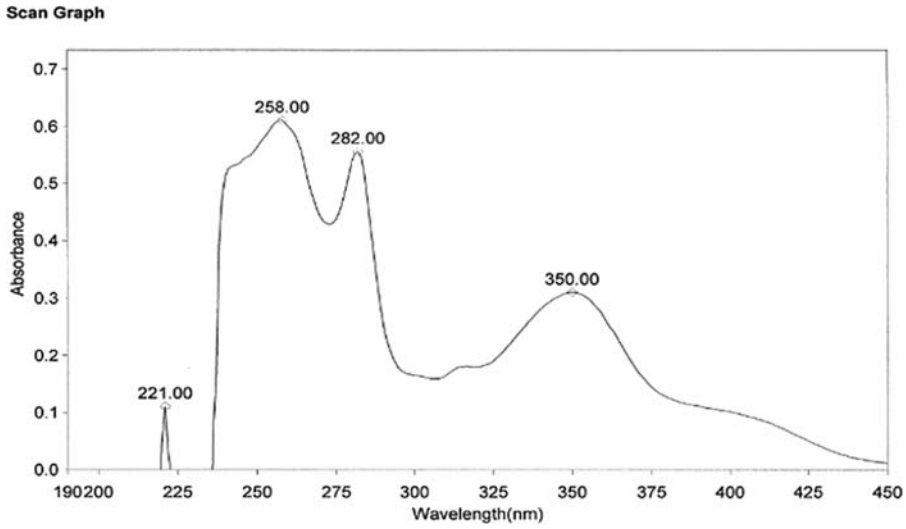

FIGURE 10.4 UV spectrum of 3-diméthyl-2-geranyl-4-prénylbellidifolin.

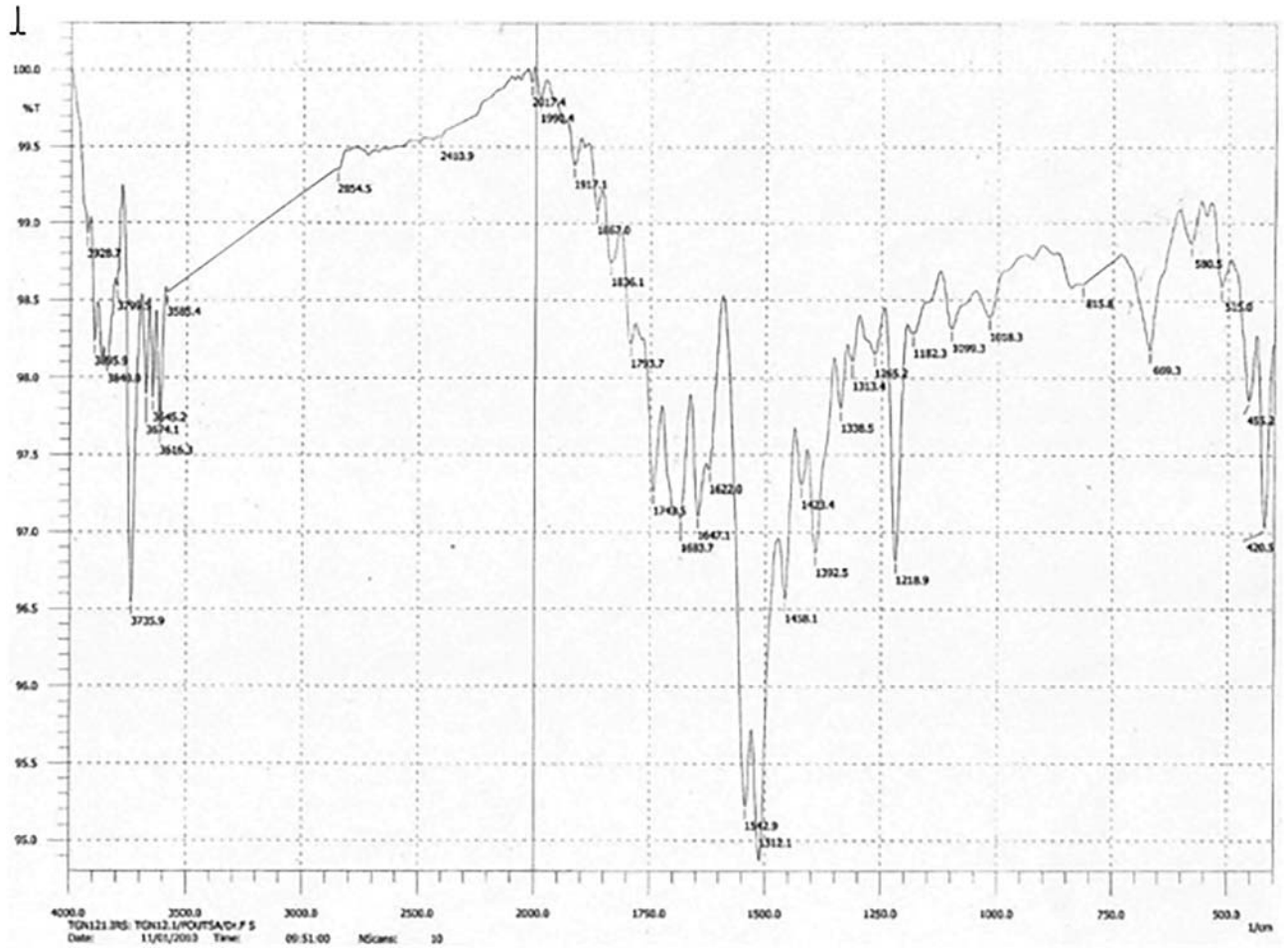

FIGURE 10.5 IR spectrum of 3-dimethyl-2-géranyl-4-prenylbellidifolin.

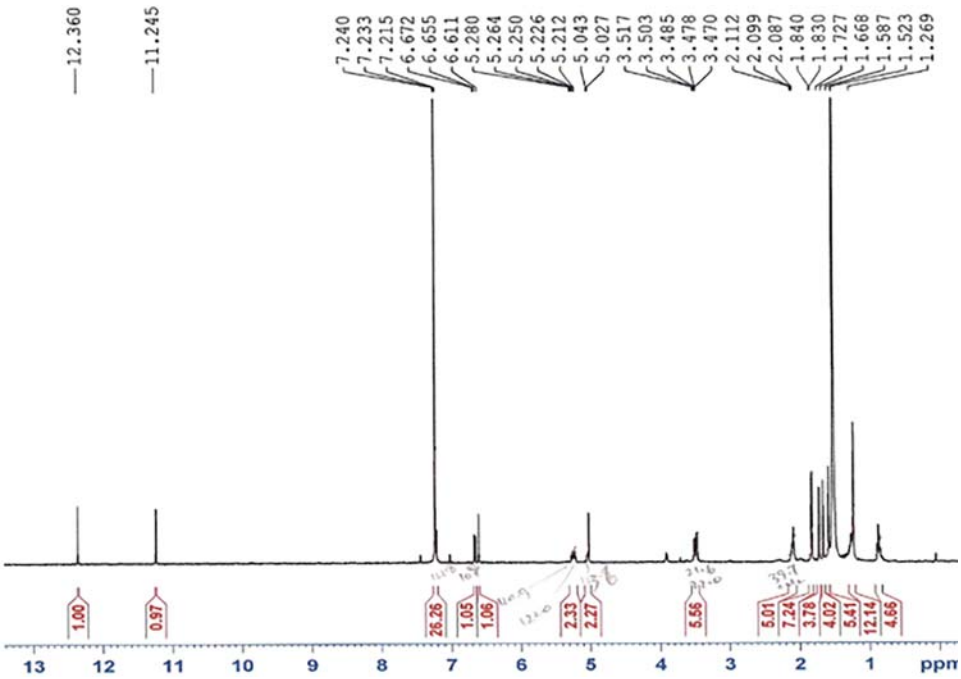

FIGURE 10.6 ^{1}H-NMR of 3-dimethyl-2-géranyl-4-prénylbellidifolin.

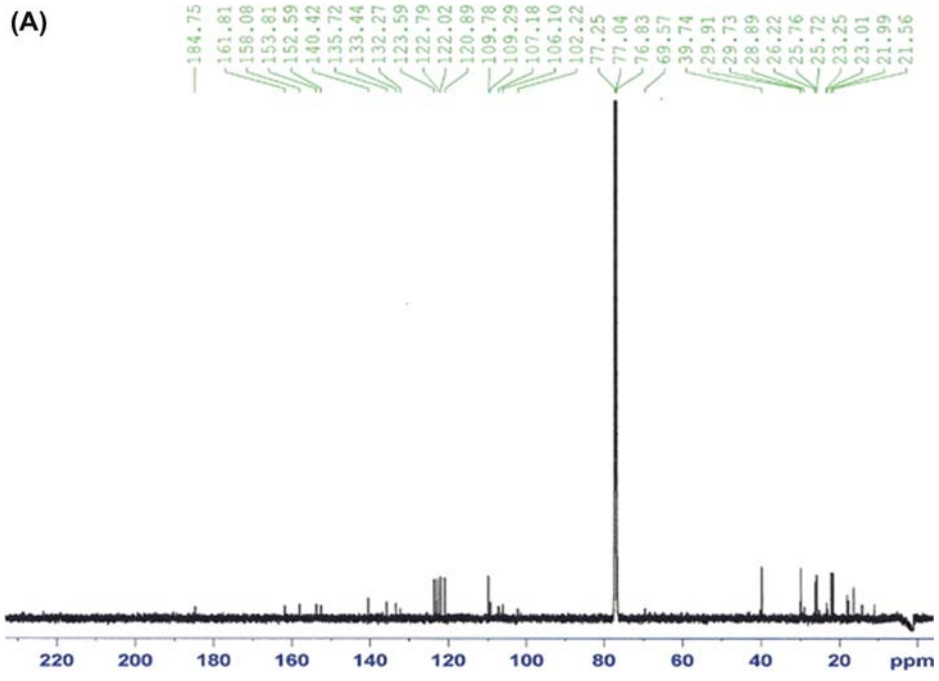

FIGURE 10.7 13C-NMR of 3-dimethyl-2-geranyl-4-prénylbellidifolin.

All this information allowed us to assign to the isolated compound, the above structure which corresponds to 3-dimethyl-2-geranyl-4-prenylbellidifolin. It is a compound that was first isolated by Ricaldez et al. [110], in 2000 from *Rheedia gardneriana*. The ^{1}H-NMR and ^{13}C-NMR spectral data (600, 125 MHz, $CDCl_3$) of 3-dimethyl-2-geranyl-4-prenylbellidifolin are shown in Table 10.3.

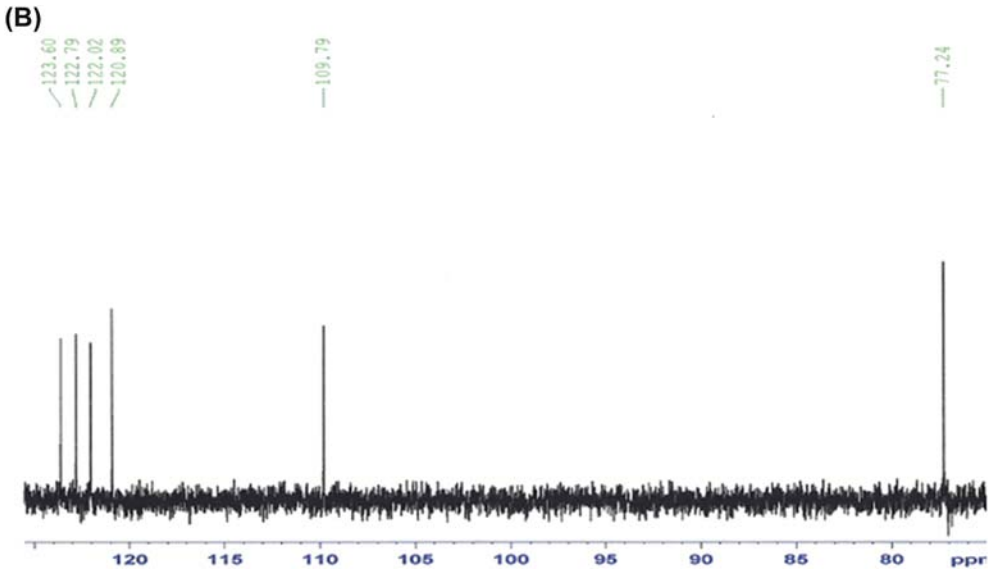

FIGURE 10.7 cont'd

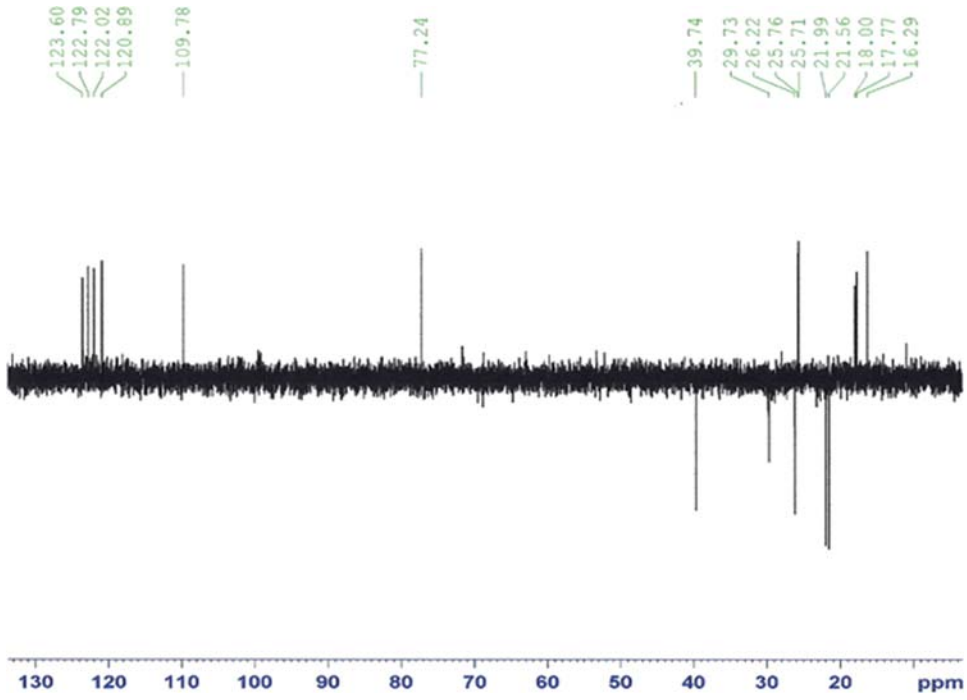

FIGURE 10.8 DEPT of 3-dimethyl-2-géranyl-4-prénylbellidifolin.

Xanthone biosynthesis in plants

Shikimate pathway

Xanthones are synthesized in plants via the shikimate pathway with the contribution of the acetate (or polyketide) pathway. Shikimate links carbohydrate metabolism, glycolysis, and pentose phosphate pathway, to aromatic compound biosynthesis (Fig. 10.10). The shikimate pathway occurs in green and nongreen plastids, thus dependently or independently from light [111]. However, it is known that nonphotosynthetic tissues are partially supplied with amino acids transported by the phloem, so production does not occur exclusively within the cell; it can also occur in other tissues or organs, and then transport to other locations [112]. Moon and Mitra [113] showed that shikimate dehydrogenase (SKD) and shikimate kinase

FIGURE 10.9 The proton spectrum (600 MHz; $CDCl_3$) of the compound 1,3,5,8-tétrahydroxy-2-(3-méthybut-2-ényl)-4-(3,7-diméthyloct-2,6-diényl) xanthon.

TABLE 10.3 ^{1}H-NMR and ^{13}C-NMR spectral data (600, 125 MHz, $CDCl_3$) of compound 3-dimethyl-2-geranyl-4-prenylbellidifolin.

Position	^{13}C	^{1}H(m, J(Hz))	HMBC
1	158,0	–	
2	109,2	–	
3	161,8	–	
4	106,1	–	
4a	152,5	–	
10a	140,4	–	
5	135,7	–	
6	122,7	7,22(1H, d, $J = 8,5$ Hz)	135,7; 153,8; 140,4
7	109,7	6,66(1H, d, $J = 8,5$ Hz)	135,7; 153,8; 106,1
8	153,8	–	
8a	107,1	–	
9	184,7	–	
9a	102,2	–	
1′	21.,5	3,47(2H, d, $J = 8,5$ Hz)	109,2; 120,8; 140,4; 158,0; 161,8
2′	120,8		16,29; 21,56; 39,74
3′	140,4	–	
4′	18,0	1,83	140,4; 120,8; 39,7

Continued

TABLE 10.3 ^{1}H-NMR and ^{13}C-NMR spectral data (600, 125 MHz, $CDCl_3$) of compound 3-dimethyl-2-geranyl-4-prenylbellidifolin.—cont'd

Position	^{13}C	^{1}H(m, J(Hz))	HMBC
5′	39,7	–	
6′	26,2	2,08	140,4; 122,7; 25,7
7′	123,5	–	
8′	132,2	–	
9′	17,7	1,66	132,2; 122,7
10′	25,7	1,58	132,2; 122,7
1″	21,9	5,22	152,5; 106,1; 161,8; 133,4; 122,0
2″	122,0	–	
3″	133,4	–	
4″	16,2	1,84	133,4; 122,0
5″	25,7	1,72	133,4; 122,0
1-OH	–	12,36(1H, s)	102,2; 109,2; 158,0
–	–	6,61(1H, s)	
5-OH	–	5,03(1H, s)	
8-OH	–	11,24(1H, s)	107,1; 109,2; 158,0

(SK), key enzymes of the shikimate pathway, are activated after elicitation by a Ca^{2+}-mediated H_2O_2 generation, leading to a consequent increase in the xanthone biosynthesis, giving further confirmation to the role of xanthones as defense metabolites as described by numerous articles on the subject [114]. This study revealed for the first time the link between ROS and the pathways involved in xanthone biosynthesis.

After the shikimate pathway, xanthone biosynthesis can proceed with an L-phenylalanine-dependent pathway, as in *Hypericum androsaemum* L. [116], *G. mangostana*, and *G. Lutea* [117] or an L-phenylalanine-independent pathway, as in *Swertia chirata* Buch. -Ham. ex Wall. [118], *C. erythraea* [119,120], and *Hoppea fastigiata* Griseb. [118]. Both the phenylalanine-dependent and phenylalanine-independent pathways pass through the production of 2,3′,4,6-tetrahydroxybenzophenone (2,3′,4,6-THB), which is therefore a central intermediate in the biosynthesis of xanthones (Fig. 10.10).

Phenylalanine-dependent pathway

In the phenylalanine-dependent pathway, shikimate forms the amino acid phenylalanine through numerous reactions occurring in two different cell compartments, plastid, and cytosol [121] (Fig. 10.10). Phenylalanine is biosynthesized from chorismate, the final product of the shikimate pathway. In plastids, chorismate is converted to prephenate which in turn is transaminated producing arogenate. This compound is then dehydrated/decarboxylated to phenylalanine which is then transported to cytosol by the plastidial cationic amino acid transporter (pCAT) [122]. In plants, the arogenate pathway is the predominant route for phenylalanine biosynthesis although another pathway, more common in microorganisms [123], has been described. This route, which has yet to be clarified, involves phenylpyruvate, another product downstream of prephenate. Phenylpyruvate may originate from prephenate in plastids by the action of arogenate dehydratases (ADTs) [124] or in the cytosol, requiring a cytosolic pool of prephenate supposedly formed by the action of a cytosolic chorismate mutase (CM) from chorismate previously synthesized in the plastid and then transported to the cytosol [122]. Indeed, as described by Yoo and coworkers [125] in *Petunia hybrida* E.Vilm, prephenate seems to be produced in the plastid but converted to phenylalanine in the cytosol by a phenylpyruvate aminotransferase (PPY-AT), which preferentially uses prephenate as a substrate, suggesting that this alternative route to phenylalanine biosynthesis is also active in the plants. Once in the cytosol, the amino acid is converted to trans-cinnamic acid by the action of the enzyme phenylalanine ammonia-lyase (PAL), which catalyzes the deamination. Trans-cinnamic acid is the substrate of cinnamate-CoA ligase (CNL), which leads to cinnamoyl-CoA. Cinnamoyl-CoA is an intermediate from

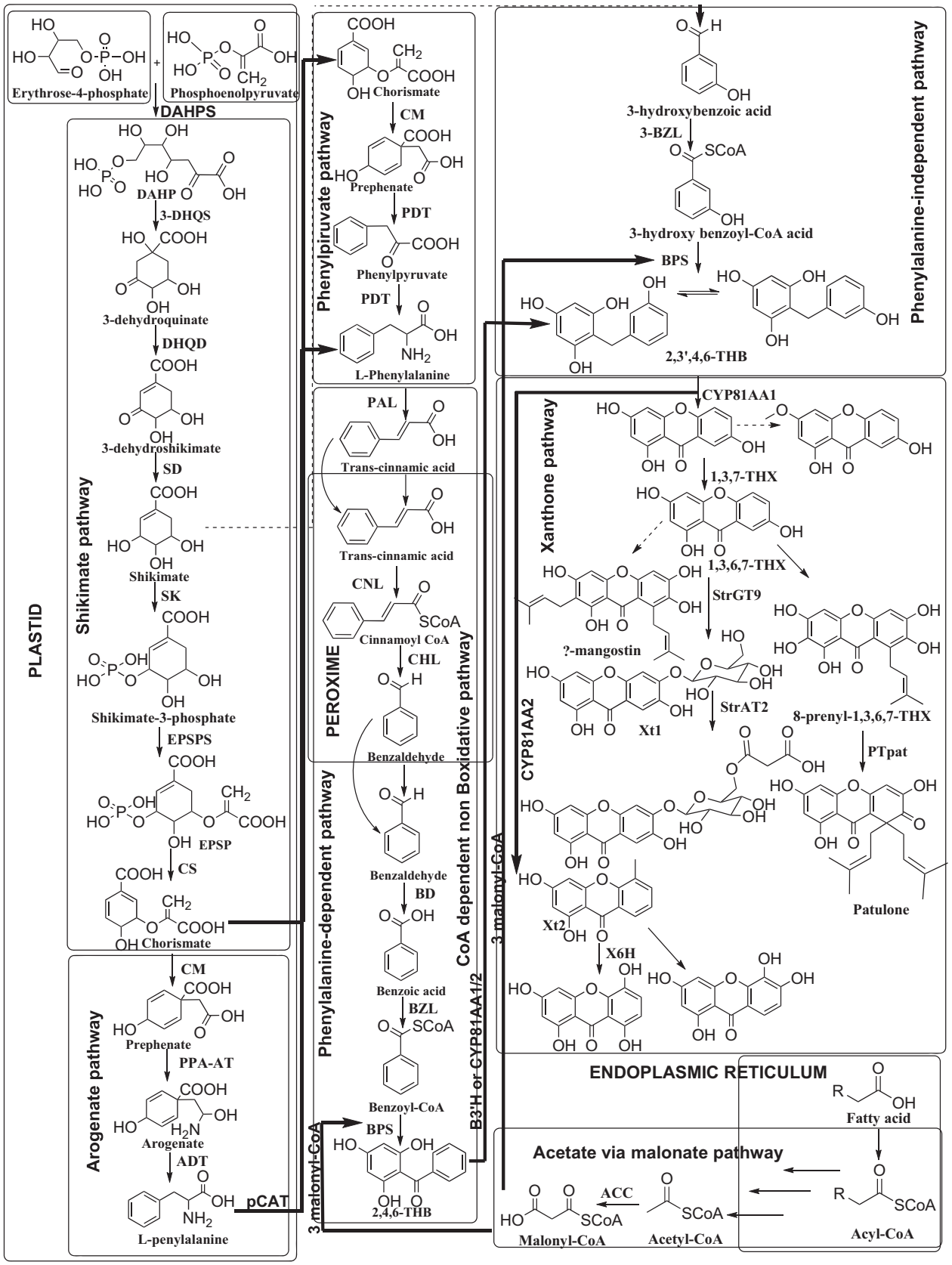

FIGURE 10.10 Pathways involved in xanthone biosynthesis in plants: Unknown proteins [115]. *1,3,5,6-THX*, 1,3,5,6-tetrahydroxyxanthone; *1,3,5,8-THX*, 1,3,5,8-Tetrahydroxyxanthone; *1,3,5-THX*, 1,3,5-Trihydroxyxanthone; *1,3,6,7-THX*, 1,3,6,7-THX-tetrahydroxyxanthone; *1,3,7-THX*, 1,3,7-Trihydroxyxanthone; *2,3′,4,6-THB*, 2,3^{0},4,6-Tetrahydroxybenzophenone; *2,4,6-THB*, 2,4,6-Trihydroxybenzophenone; *3-BZL*, 3-Benzoate-CoA ligase; *3-DHQS*, 3-Dehydroquianate synthase; *8-prenyl-1,3,6,7-THX*, 8-Prenyl-1,3,6,7-tetrahydroxyxanthone; *ACC*, acetyl-CoA carboxylase; *ADT*, arogenate dehydratase; *B3′H*, benzophenone 3′-hydroxylase; *BD*, benzaldehyde dehydrogenase; *BPS*, Benzophenone synthase; *BZL*, Benzoate-CoA ligase; *CHL*, cinnamoyl-CoA hydratase/lyase; *CM*, chorismate mutase; *CNL*, cinnamate-CoA ligase; *CoASH*, coenzyme A; *CS*, chorismate synthase; *CYP81AA1/2*, Cytochrome P450 oxidase 81AA1/2; *DAHP*, 3-Deoxy-D-arabino-heptulosonate-7-phosphate; *DAHPS*, DAHP synthase; *DHQD*, 3-Dehydroquinase dehydratase; *EPSP*, 5-enolpyruvylshikimate 3-phosphate; *EPSPS*, EPSP synthase; *PAL*, phenylalanine ammonia lyase; *pCAT*, Plastidial cationic amino acid transporter; *PDT*, Prephenate dehydratase; *PPA-AT*, Prephenate aminotransferase; *PPP*, Pentose phosphate pathway; *PPY-AT*, phenylpyruvate aminotransferase; *PT8PX*, 8-Prenylxanthone-forming prenyltransferase; *PTpat*, Patulone-forming prenyltransferase; *SD*, shikimate 5-dehydrogenase; *SK*, shikimate kinase; *StrAT2*, malonyl-CoA acyltransferase; *StrGT9*, norathyriol 6-O-glucosyltransferase; *X6H*, xanthone-6-hydroxylases; *Xt1*, norathyriol 6-O-glucoside; *Xt2*, norathyriol-6-O-(6′-O-malonyl)-glucoside.

which benzoyl-CoA is formed as a result of three reactions that are catalyzed by the enzymes cinnamoyl-CoA hydratase/lyase (CHL), benzaldehyde dehydrogenase (BD), and benzoate-CoA ligase (BZL). BZL expression has been demonstrated to increase before xanthone biosynthesis, when the plant is exposed to elicitation, suggesting its role in the biosynthetic pathway upstream of xanthones. Singh and co-workers [126] have shown in *Hypericum calycinum* L. that BZL is localized in both peroxisomes and cytosol, indicating the activation of the CoA-dependent non-β-oxidative pathway for benzoyl-CoA production. The activation of this pathway was previously demonstrated at the biochemical level in *Hypericum androsaemum* L. cell cultures [127]. Furthermore, it is hypothesized that the enzyme is purely involved in the phenylalanine-dependent pathway having benzoic acid as a preferential substrate.

The subsequent reaction is catalyzed by benzophenone synthase (BPS), a type III polyketide synthase, which condenses the benzoyl-CoA molecule with three malonyl-CoAs originating 2,4,6-trihydroxybenzophenone (2,4,6-THB). BPS in *H. androsaemum* and *G. mangostana* has benzoyl-CoA as a specific substrate, suggesting that the phenylalanine-dependent pathway is the one followed for xanthone production in these species [116]. CYP81AA, a cytochrome P450 (CYP) monooxygenase that possesses benzophenone 3′hydroxylase (B3′H) activity, converts 2,4,6-THB to 2,3′,4,6-THB. Thus, these compounds are the precursors of various benzophenones and xanthones. The two main precursors of xanthones are formed from 2,3′,4,6-THB ring closure. 1,3,5-trihydroxyxanthone (1,3,5-THX) and 1,3,7-trihydroxyxanthone (1,3,7-THX) originate from oxidative phenol coupling reaction that occurs either at the ortho or para position of the 3′-OH group, respectively. Cyclization to 1,3,5-THX and 1,3,7-THX depends on the species [128,129]. These reactions are catalyzed by two xanthone synthases belonging to the CYP oxidases [130]. They are now known as 1,3,5-THX synthase (CYP81AA2) and 1,3,7-THX synthase (CYP81AA1), respectively [129,131]. One of the two pathways could be used preferentially by a species, but it has been shown from transcriptome databases of *Hypericum* spp. that genes for both CYPs are present, so both isomers of the enzyme could be synthesized in a species in response to certain signals [117,129]. Kitanov and Nedialkov [132] proposed that 1,3,7-THX is generated from 2,4,5′,6-tetrahydroxybenzophenone-2′-O-glucoside (hypericophenonoside) in *H. annulatum* first removing the glucoside group by hydrolysis before cyclization. Many different xanthones will then be produced from these precursors, although to date the biosynthetic pathways of many of them are only assumed.

Phenylalanine-independent pathway

In the phenylalanine-independent pathway, the biosynthetic pathway originates from shikimate to produce 3-hydroxybenzoic acid in the cytoplasm without the involvement of phenylalanine (Fig. 10.10). To date, how shikimate leaves plastids and which enzymes are responsible for the conversion to 3-hydroxybenzoic acid is unknown. The 3-hydroxybenzoic acid is then thioesterified by 3-hydroxybenzoate-CoA ligase (3-BZL) to form 3-hydroxybenzoyl-CoA, and subsequent condensation by BPS leads to the formation of 2,3′,4,6-THB. In *Centaurium* species, 3-BZL enzyme has been shown to have 3-hydrobenzoic acid rather than benzoic acid as a preferred substrate, suggesting that the phenylalanine-independent pathway is the one followed in these species [133]. The biosynthetic pathway continues as described for the phenylalanine-dependent route.

Although the phenylalanine-dependent pathway is more studied and it is assumed that most xanthones are produced downstream of phenylalanine or indistinctly by both the phenylalanine-dependent and independent pathways, some xanthones such as 1,3,5,8-tetrahydroxy xanthone and 1,5,7-trihydroxy-3-methoxy xanthone appear to be produced only through the phenylalanine-independent pathway [124] (Fig. 10.10).

Xanthone derivatives of 1,3,5-trihydroxyxanthone

Xanthone-6-hydroxylases (X6H), a CYP-dependent monooxygenase, has been shown to hydroxylate 1,3,5-THX to 1,3,5,6-tetrahydroxyxanthone (1,3,5,6-THX) in *H. androsaemum* and *C. erythraea* [134]. In *S. chirata*, the hydroxylation of 1,3,5-THX occurs at the C-8 position of the ring, originating 1,3,5,8-tetrahydroxyxanthone (1,3,5,8-THX) [135]. On the contrary, Beerhues and Berger [119], studied the elicited cell cultures of *C. erythraea* and *C. littorale* proposing a direct formation of 1,5-dihydroxy-3-methoxyxanthone from 1,3,5-THX. Moreover, the authors proposed a biosynthetic pathway downstream 1,3,5-THX in the cell cultures of these species which produce xanthones such as 1,5-dihydroxy-3-methoxyxanthone, 1-hydroxy-3,5,6,7-tetramethoxyxanthone, and 1,8-dihydroxy-3,5-dimethoxyxanthone. However, the enzymes involved in these reactions have not been identified [119].

Xanthone derivatives of 1,3,7-trihydroxyxanthone

Many more xanthones derive from 1,3,7-THX. X6H is also involved in the formation of 1,3,7-THX derivatives [134]. Indeed, the hydroxylation of 1,3,7-THX forms

1,3,6,7-tetrahydroxyxanthone (1,3,6,7-THX) in *H. androsaemum* and *G. Mangostana* [134] and potentially resides in the endoplasmic reticulum [129].

1,3,7-THX is proposed to be a precursor compound for prenylated xanthones, such as rubraxanthone from *Garcinia* [136] and *Calophyllum* species [11], and scortechinone B from *Garcinia scortechinii* King [137,138], as well as simple xanthones, such as 1,7-dihydroxy-3-methoxyxanthone (gentisin) and 1,3-dihydroxy-7-methoxyxanthone (isogentisin) from *G. lutea* [139]. In *G. mangostana*, γ-mangostin is proposed to be generated by prenylation of the 1,3,6,7-tetrahydroxyxanthones, and α-mangostin by the subsequent O-methylation [140,141]. Another pathway that produces patulone, hyperxanthone E, and hyperixanthone A starting from 1,3,6,7-tetrahydroxyxanthones has been reported in *Hypericum* spp. [142,143]. Two enzymes involved in these reactions are known: 8-prenylxanthone-forming prenyltransferase (PT8PX) and patulone-forming prenyltransferase (PTpat). The former has prenylation activity and is mainly localized at the envelope of the chloroplast [143] (Fig. 10.10). The latter is also a prenyltransferase which prenylates the reaction product of the previous reaction, 8-prenyl-1,3,6,7-tetrahydroxyxanthone, and produces patulone [142,143]. Other xanthones are supposed to be formed from this route, such as hyperxanthone A and E, but the enzymes involved are unknown [142,143].

Among the glycosylated xanthones, norathyriol 6-O-glucoside (tripteroside or Xt1) and norathyriol-6-O-(6′-O-malonyl)-glucoside (Xt2) have recently been characterized at the molecular level [48]. The enzymes responsible for the reaction that produces these xanthones from 1,3,6,7-THX are norathyriol 6-O-glucosyltransferase (StrGT9) and malonyl-CoA acyltransferase (StrAT2). StrGT9 glucosylates 1,3,6,7-THX to Xt1, which in turn is malonylated in the presence of malonyl-CoA to Xt2 by StrAT2. Badiali and his co-worker [115] have provided a summary of the biosynthetic pathway of xanthone as displayed in Fig. 10.10. Mangiferin is a well-studied C-glucoside xanthone. A route for its biosynthesis was proposed by Fujita and Inoue [144] and Chen and co-workers [145] in *Anemarrhena asphodeloides* Bunge and *M. indica*, respectively, and reviewed by Ehianeta and co-workers [146]. The results suggest that mangiferin and related xanthone C-glycosides are produced through an intermediate, maclurin 3-C-glucoside, which is converted to mangiferin and isomangiferin by C-glycosyltransferase (CGT).

Xanthones isolated from the African plants from 2013 to 2023

Within 2013-2023, as many as 29 new xanthone derivatives have been isolated from African plants. Among the families from which xanthones belong, Polygalaceae and Clusiaceae are more representative. Xanthones can be found in other families like Hypericacae, Celestraceae, Asphodelaceae, and Hyacinthaceae.

Several research studies on the isolation of new xanthone derivatives from African plants are highlighted in this chapter. In 2013, Waller et al. [147] reported the isolation of 1,6-Dihydroxy-2,3,5-trimethoxy-8-methyl-9H-xanthen-9-one (**23**) from bulbs of *Ledebouria ovatifolia* (Hyacinthaceae) in South Africa. In the same year in Cameroon, Tala et al. [148] successfully isolated from leaves of *Pentadesma butyracea* one new prenylated xanthone named butyraxanthone F (**26**), while adamaxanthone (**42**) was isolated by Tsaffack et al., from barks and fruits of *Psorospermum adamauense* (Engl). Dibwe et al. [149] also reported the isolation of five new xanthones: 1,6,8-Trihydroxy-2,3,4,5-tetramethoxyxanthone (**43**), 1,6-Dihydroxy-2,3,4,5,8-pentamethoxyxanthone (**44**), 8-Hydroxy-1,4,5,6-tetramethoxy-2,3-methylenedioxyxanthone (**45**), 4,6,8-Trihydroxy-1,2,3,5-tetramethoxyxanthone (**46**) and 4,8-Dihydroxy-1,2,3,5,6-pentamethoxyxanthone (**47**) from roots of *Securidaca longepedunculata* in Democratic Republic of Congo (DRC). Finally, in 2013, Abd El-Kader et al. [150] reported the isolation of one glycosylated xanthone, 1,8-Dihydroxy-3,6-dimethoxy-xanthone-5-O-[a-L-rhamnopyranosyl-(1″→2′)]-b-D-glucopyranoside (**48**) from *Polygonum bellardii* All., in Egypt.

In 2014, Dibwe et al. reported the successful isolation from DRC roots of *Securidaca longepedunculata* of eight new xanthones: Muchimangin E (**21**) and Muchimangin F (**22**); Muchimangin G (**33**), Muchimangin H (**34**), Muchimangin I (**35**), and Muchimangin J (**36**); Muchimangin L (**37**), and Muchimangin K (**38**) [151]. In Cameroon, a prenylated xanthone named banganxanthone C (**21**) was isolated from the leaves of *Garcinia polyantha* [152]. In Kenya, the isolation of one new xanthone, from the roots of *Bulbine frutescens*: 8-Hydroxy-6-methylxanthone-1-carboxylic acid (**27**) has been reported [153].

In 2015, two new xanthones were isolated from two Cameroonian plants. Hyperixanthone (**20**), a new oxygenated xanthone was isolated from leaves of *Hypericum riparium* by Tala et al. [154], while a prenylated xanthone named 1,3,5,8-tetrahydroxy-2-(3-methylbut-2-enyl)-4-(3,7-dimethyloct-2,6-dienyl) xanthone (**39**) was isolated from stem bark of *Garcinia smeathmannii*, by Fouotsa et al. Another prenylated xanthone, Banfoxanthone (**41**), was isolated from the stem bark of *Garcinia ovalifolia* [155]. In Madagascar, Elieaxanthone (**29**) was isolated from the root bark of *Eliea articulata* Cambess [156]. In 2018, Mountessou et al. [157] reported the isolation from the stem bark of *Allanblackia floribunda*, of two new oxygenated xanthones: 2-(3-hydroxy-3,3-dimethyldihydroallyl)-dihydro-6-deoxyisojacareubin (**24**), and dihydro-6-deoxyjacareubin (**25**). In 2020, a new oxygenated xanthone named

roeperone A (**32**) was isolated from leaves of *Hypericum roeperianum* Schimp. [158]. In the same year, Fouotsa et al. [159] reported the isolation of mboudiexanthone (**30**), a prenylated xanthone from leaves of *Garcinia nobilis* Engl. In 2022, Wedajo et al. [160] successfully isolated from the root bark of *Securidaca longipedunculata*, 3,8-dihydroxy-1,2,4,5,6-pentamethoxyxanthone (**31**), a new oxygenated xanthone. A summary of the new compounds isolated in African plants from 2013 to 2023 is given in Table 10.4, while their chemical structures are shown in Fig. 10.11. The chemical structures of known xanthones isolated within the same period are shown in Fig. 10.12.

Pharmacological activities of xanthones isolated from African medicinal plants from 2013 to 2023

Xanthones are a class of oxygen-containing heterocyclic compounds with a broad range of biological activities, and

TABLE 10.4 New xanthones isolated from the African plants from 2013 to 2023.

Common name (Chemical name)	Plant origin (family), country	Separation methods	Spectral analysis	Physical properties	References
Simple oxygenated xanthones					
Monooxygenated					
8-Hydroxy-6-methylxanthone-1-carboxylic acid (**27**)	*Bulbine frutescens* (Asphodelaceae), Kenya	QCC, SiO_2 CC & Sephadex LH-20 CC	UV, IR, HRESIMS, ^{1}H- & ^{13}C-NMR	Yellow crystalline solid m.p. 267 −268 °C	[153]
Trioxygenated					
Hyperixanthone (**20**)	*Hypericum riparium* (Hypericaceae), Cameroon	SiO_2 CC & HPLC	UV, EI-HR-MS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[154]
Tetraoxygenated					
l-Hydroxy-2,5-dimethoxyxanthone (**28**)	*Garcinia nobilis* (Guttiferae), Cameroon	QCC & SiO_2 CC	UV, IR, HR-EI-MS, ^{1}H- & ^{13}C-NMR, X-ray analysis	Yellow crystal; mp 175−176 °C	[161]
Roeperone A (**32**)	*Hypericum roeperianum* Schimp.(Hypericaceae), Cameroon	SiO_2 CC & Sephadex LH-20 CC	UV, IR, HRESIMS, ^{1}H- & ^{13}C-NMR, COSY, HMBC	Yellow powder	[158]
Pentaoxygenated					
1,6-Dihydroxy-2,3,5-trimethoxy-8-methyl-9*H*-xanthen-9-one (**23**)	*Ledebouria ovatifolia* (Hyacinthaceae), South Africa	SiO_2 CC	IR, HRESIMS, ^{1}H- & ^{13}C-NMR, COSY, NOESY, HMBC	Yellow powder	[162]
Heptaoxygenated					
3,8-Dihydroxy-1,2,4,5,6-pentamethoxyxanthone (**31**)	*Securidaca longipedunculata* Fresen (Polygalaceae), Ethiopia	SiO_2 CC, Sephadex LH-20 CC	UV, IR, HRESIMS, ^{1}H- & ^{13}C-NMR, NOE, HMBC	Yellow solid	[160]
1,6,8-trihydroxy-2,3,4,5-tetramethoxyxanthone (**43**)	*Securidaca longepedunculata* (Polygalaceae), DRC	SiO_2 CC	HREIMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[163]
1,6-dihydroxy-2,3,4,5,8-pentamethoxyxanthone (**44**)	*Securidaca longepedunculata* (Polygalaceae), DRC	SiO_2 CC	HRFABMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[163]
8-hydroxy-1,4,5,6-tetramethoxy-2,3-methylenedioxyxanthone (**45**)	*Securidaca longepedunculata* (Polygalaceae), DRC	SiO_2 CC	HRFABMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[163]

Continued

TABLE 10.4 New xanthones isolated from the African plants from 2013 to 2023.—cont'd

Common name (Chemical name)	Plant origin (family), country	Separation methods	Spectral analysis	Physical properties	References
4,6,8-trihydroxy-1,2,3,5-tetramethoxyxanthone (**46**)	*Securidaca longepedunculata* (Polygalaceae), DRC	SiO_2 CC	HRFABMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[163]
4,8-dihydroxy-1,2,3,5,6-pentamethoxyxanthone (**47**)	*Securidaca longepedunculata* (Polygalaceae), DRC	SiO_2 CC	HRFABMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[163]
Prenylated and related xanthones					
2-(3-Hydroxy-3,3-dimethyldihydroallyl)-dihydro-6-deoxyisojacareubin (**24**)	*Allanblackia floribunda* Oliv. (Guttiferae), Cameroon	SiO_2 CC, Sephadex LH-20 & prep. HPLC	UV, IR, EIMS, ^{1}H- & ^{13}C-NMR, HMBC, DEPT & COSY	Yellow solid (m.p. 186 −187 °C)	[157]
Dihydro-6-deoxyjacareubin (**25**)	*Allanblackia floribunda* Oliv. (Guttiferae), Cameroon	SiO_2 CC, Sephadex LH-20 & prep. HPLC	UV, IR, HRESIMS, ^{1}H- & ^{13}C-NMR, HMBC, DEPT & COSY	Orange solid (m.p. 190 −192 °C)	[157]
Butyraxanthone F (**26**)	*Pentadesma butyracea* (Guttiferae), Cameroon	SiO_2 CC, Sephadex LH-20	UV, IR, HRESIMS, ^{1}H- & ^{13}C-NMR	Yellow amorphous solid	[164]
Elieaxanthone (**29**)	*Eliea articulata* Cambess (Hypericaceae), Madagascar	SiO_2 CC	^{1}H- & ^{13}C-NMR, HSQC, COSY, NOESY, HMBC	–	[156]
Mboudiexanthone (**30**)	*Garcinia nobilis* Engl. (Guttiferae), Cameroon	SiO_2 CC, Sephadex LH-20	UV, IR, HRESIMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow powder	[159]
1,3,5,8-Tetrahydroxy-2-(3-methylbut-2-enyl)-4-(3,7-dimethyloct-2,6-dienyl) xanthone (**39**)	*Garcinia smeathmannii* (Guttiferae), Cameroon	QCC, SiO_2 CC	UV, IR, HR-EI-MS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow powder	[53]
Banganxanthone C (**40**)	*Garcinia polyantha* (Guttiferae), Cameroon	SiO_2 CC	UV, IR, HR-MS, ^{1}H- & ^{13}C-NMR, HMBC, HSQC	Yellow powder	[152]
Banfoxanthone (**41**)	*Garcinia ovalifolia* (Guttiferaceae), Cameroon	SiO_2 CC	UV, IR, HREIMS, ^{1}H- & ^{13}C-NMR, HMBC, HSQC, HMQC, NOESY, COSY, TLC.	Yellow needle crystals	[155]
Adamaxanthone (**42**)	*Psorospermum adamauense* (Engl) (Hypericaceae), Cameroon	SiO_2 CC	UV, IR, HR-ESI-TOF-MS and HR-ESI-TOF-MS/MS, ^{1}H- & ^{13}C-NMR, HMBC, HSQC, HMBC, NOESY, COSY, TLC	Plates, MP: 218°C	[165]
Glycosylated xanthone					
1,8-dihydroxy-3,6-dimethoxy-xanthone-5-*O*-[a-L-rhamnopyranosyl-(1″→2′)]-b-D-glucopyranoside (**48**)	*Polygonum bellardii* All (Polygalaceae), Egypt	VLC, SiO_2 CC, Sephadex LH-20	FAB-MS, ^{1}H- & ^{13}C-NMR, HMBC	Yellowish needles	[166]
Miscellaneous xanthones					
Muchimangin E (**21**)	*Securidaca longepedunculata* (Polygalaceae), Congo	SiO_2 MPLC	HRFABMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[167]

Continued

TABLE 10.4 New xanthones isolated from the African plants from 2013 to 2023.—cont'd

Common name (Chemical name)	Plant origin (family), country	Separation methods	Spectral analysis	Physical properties	References
Muchimangin F (**22**)	*Securidaca longepedunculata* (Polygalaceae), Congo	SiO_2 MPLC	HRFABMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[167]
Muchimangin G (**33**)	*Securidaca longepedunculata* Fresen. (Polygalaceae), DRC	SiO_2 MPLC, RP prep. TLC	HR-EI-MS, ^{1}H- & ^{13}C-NMR, HMBC, X-ray analysis	Yellow amorphous solid	[168]
Muchimangin H (**34**)	*Securidaca longepedunculata* Fresen. (Polygalaceae), DRC	SiO_2 MPLC, RP prep. TLC	HRFABMS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[168]
Muchimangin I (**35**)	*Securidaca longepedunculata* Fresen. (Polygalaceae), DRC	SiO_2 MPLC, RP prep. TLC	HR-EI-MS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[168]
Muchimangin J (**36**)	*Securidaca longepedunculata* Fresen. (Polygalaceae), DRC	SiO_2 MPLC, RP prep. TLC	HR-EI-MS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[168]
Muchimangin L (**37**)	*Securidaca longepedunculata* Fresen. (Polygalaceae), DRC	SiO_2 MPLC, RP prep. TLC	HR-EI-MS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[151]
Muchimangin K (**38**)	*Securidaca longepedunculata* Fresen. (Polygalaceae), DRC	SiO_2 MPLC, RP prep. TLC	HR-FAB-MS, ^{1}H- & ^{13}C-NMR, HMBC	Yellow amorphous solid	[151]

they have prominent significance in the field of medicinal chemistry, where they have attracted researchers in the last decade. Numerous naturally occurring and synthetic xanthone derivatives have been reported in the literature with several beneficial heterogeneous pharmacological activities. Given the importance of xanthone derivatives in medicinal chemistry, we have summarized the different biological activities of xanthones isolated from African plants and reported in the literature over the last decade (Table 10.5).

In 2013, Kokotkiewicz et al. [170] reported the isolation of mangiferin (**30**) and isomangiferin (**31**) from the stems and leaves of *Cyclopia genistoides*. Both compounds exhibited pro-apoptotic activity on TNF-α-stimulated synovial cells isolated from rheumatoid arthritis patients. In the same year, Tala et al. [147] successfully isolated two xanthones, named globuxanthone (**32**) and allanxanthone A(**33**) from the leaves of *Pentadesma butyracea*. These isolated compounds exhibited antiproliferative activity on BGC-823 cancer cells. Dibwe et al. [148] reported the isolation of 1,6,8-trihydroxy-2,3,4,5-tetramethoxyxanthone (**24**) and 1,6-dihydroxy-2,3,4,5,8-pentamethoxyxanthone (**25**) from the roots of *Securidaca longepedunculata*. These oxygenated xanthones exhibited cytotoxic activity with the preferential cytotoxicity (PC_{50}) of 22.8 and 17.4 μM, respectively. Still, in 2013, Fouotsa et al. [171] reported the isolation from the stem bark of *Garcinia nobilis*, of 3-dimethyl-2-geranyl-4-prenylbellidifolin (**37**), a prenylated xanthone exhibiting an antibacterial activity with MIC value of 8 μg/mL against *M. tuberculosis* ATCC 27,294 and *M. tuberculosis* clinical MTCS2 strains. The isolation from *Polygonum bellardii* All, of 1,8-Dihydroxy-3,6-dimethoxy-xanthone-5-*O*-[a-L-rhamnopyranosyl-(1″→2′)]-b-D-glucopyranoside (**29**), a glycosylated xanthone showing significant antioxidant potential by DPPH scavenging activity technique has been reported [149].

In 2014, Kuete et al. [29] reported the isolation of three xanthones: 8-hydroxycudraxanthone G (**38**) and morusignin I (**39**) from twigs of *Garcinia nobilis* Engl., and cudraxanthone I (**40**) from the root of *Milicia excelsa*. These compounds exhibited cytotoxic activity with the IC_{50} value ranging from 7.15 μM (against CCRF-CEM cells) to 53.85 μM [against human glioblastoma U87MG.ΔEGFR cells] for compound **39**, and from 2.78 μM (against breast cancer MDA-MB231 BCRP cells) to 22.49 μM (against U87MG cells) for compound **41**. Compound **40** was active on 8/9 cell lines with the IC_{50} values ranging from 16.65 μM (against leukemia CCRF-CEM cells) to 70.38 μM (against hepatocarcinoma HepG2 cells). In the

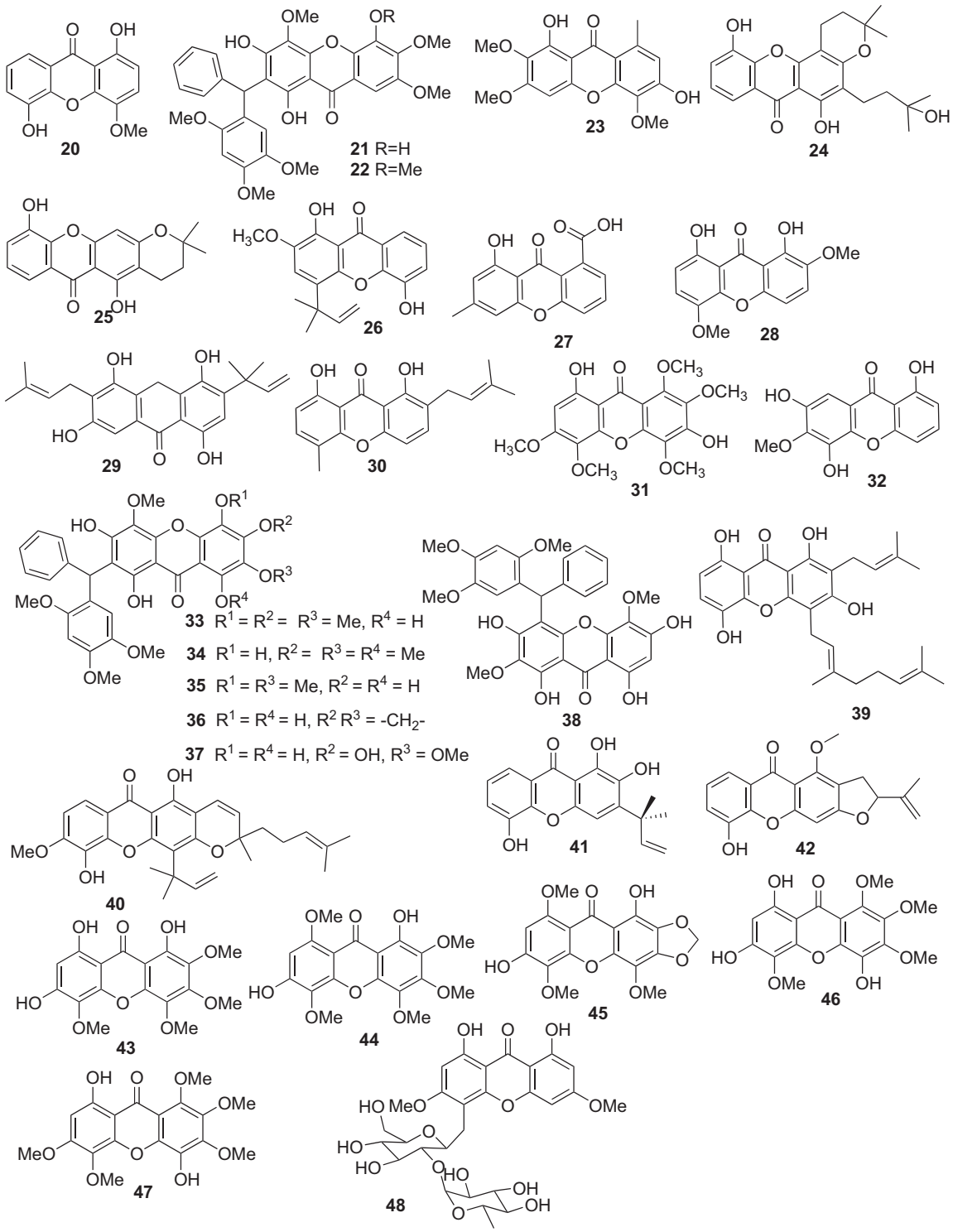

FIGURE 10.11 **New xanthones isolated from the African plants from 2013 to 2023.** Hyperixanthone (**20**); muchimangin E (**21**); muchimangin F (**22**); 1,6-dihydroxy-2,3,5-trimethoxy-8-methyl-9*H*-xanthen-9-one (**23**); 2-(3-hydroxy-3,3-dimethyldihydroallyl)-dihydro-6-deoxyisojacareubin (**24**); Dihydro-6-deoxyjacareubin (**25**); butyraxanthone F (**26**); 8-hydroxy-6-methylxanthone-1-carboxylic acid (**27**); l-hydroxy-2,5-dimethoxyxanthone (**28**); elieaxanthone (**29**); mboudiexanthone (**30**); 3,8-dihydroxy-1,2,4,5,6-pentamethoxyxanthone (**31**); roeperone A (**32**); muchimangin G (**33**); muchimangin H (**34**); muchimangin I (**35**); muchimangin J (**36**); muchimangin L (**37**); muchimangin K (**38**); 1,3,5,8-tetrahydroxy-2-(3-methylbut-2-enyl)-4-(3,7-dimethyloct-2,6-dienyl)xanthone (**39**); banganxanthone C (**40**); banfoxanthone (**41**); adamaxanthone (**42**); **24**: 1,6,8-Trihydroxy-2,3,4,5-tetramethoxyxanthone (**43**); 1,6-dihydroxy-2,3,4,5,8-pentamethoxyxanthone (**44**); **26:** 8-hydroxy-1,4,5,6-tetramethoxy-2,3-methylenedioxyxanthone (**45**); 4,6,8-trihydroxy-1,2,3,5-tetramethoxyxanthone (**46**); 4,8-dihydroxy-1,2,3,5,6-pentamethoxyxanthone (**47**); 1,8-dihydroxy-3,6-dimethoxy-xanthone-5-**O**-[a-L-rhamnopyranosyl-(1″ → 2′)]-b-D-glucopyranoside (**48**).

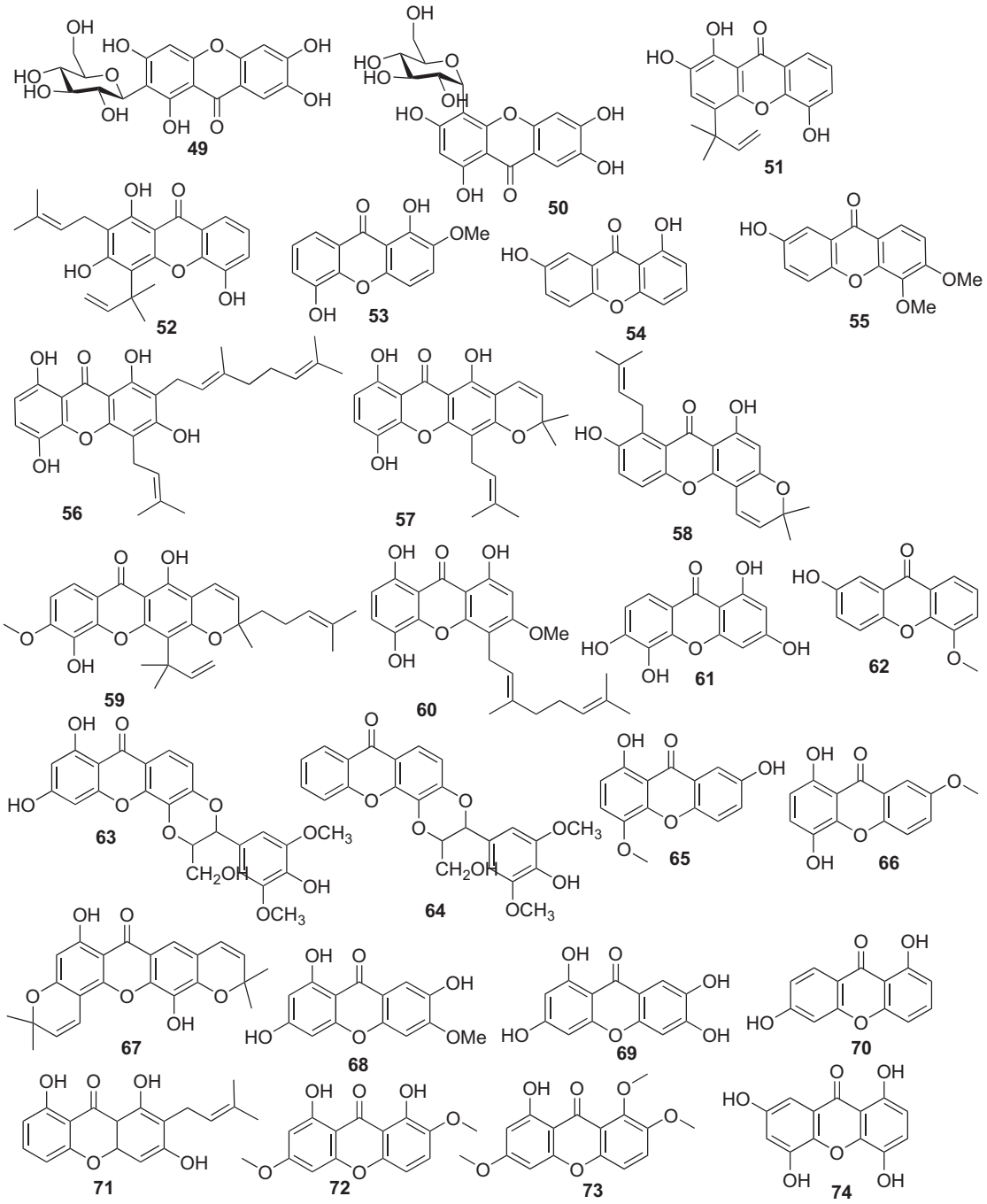

FIGURE 10.12 Known pharmacological xanthones isolated from African medicinal plants from 2013 to 2023. mangiferin (**49**); isomangiferin (**50**); globuxanthone (**51**); allanxanthone A (**52**); 1,5-dihydroxy-2-methoxyxanthone (**53**); euxanthone (**54**); 3,4-dimethoxy-7-hydroxyxanthone (**55**); 3-dimethyl-2-geranyl-4-prenylbellidifolin (**56**); 8-hydroxycudraxanthone G (**57**); morusignin I (**58**); cudraxanthone I (**59**); 4-[(2**E**)-3,7-dimethylocta-2,6-dien-1-yl]-1,5,8- trihydroxy-3-methoxy-9*H*-xanthen-9-one (**60**); 1,3,5,6-tetrahydroxyxanthone (**61**); 2-hydroxy-5-methoxyxanthone (**62**); 3′-hydroxymethyl-2′-(4″-hydroxy-3″,5″-dimethoxyphenyl)-5′,6′:5,6-(6,8-dihydroxyxanthone)-1′,4′-dioxane (**63**); 3′-hydroxymethyl-2′-(4″-hydroxy-3″,5″-dimethoxyphenyl)-5′,6′:5,6-(xanthone)-1′,4′-dioxane (**64**); 1,7-dihydroxy-4-methoxyxanthone (**65**); 1,4-dihydroxy-7-methoxyxanthone (**66**); rheediaxanthone A (**67**); Isoathyriol (**68**); Norathyriol (**69**); 1,6-dihydroxyxanthone (**70**); 1,3,7-trihydroxy-2-isoprenylxanthone (**71**); Swertiaperenin (**72**); Decussatin (**73**); 1,4,5,7-tetrahydroxyxanthone (**74**).

same year, Lannang et al. [152] reported the isolation of two prenylated xanthones from leaves of *Garcinia polyantha*, exhibiting cytotoxic activity on cancer cell lines. These compounds are named Banganxanthone C (**21**) and 4-[(2*E*)-3,7-dimethylocta-2,6-dien-1-yl]-1,5,8- trihydroxy-3-methoxy-9*H*-xanthen-9-one (**41**).

TABLE 10.5 Pharmacological activities of xanthones isolated from African medicinal plants in the period 2013-2023

Common Name (Chemical Name)	Plant Origin (families), Country	Plant parts	Activities (IC_{50} in μM)	References
Simple xanthones				
Dioxygenated				
Euxanthone (**54**)	*Garcinia nobilis* Engl. *(Clusiaceae)*, Cameroon	Leaves	Antiproliferative: IC50 2.91 μM (MCF-7)	[159]
1,6-dihydroxyxanthone(**70**)	*Hypericum lanceolatum* Lam (Hypericaceae), Cameroon	Stem bark and twigs	Antiplasmodial: IC_{50} 33.6 μg/mL (*Pf* 3D7); cytotoxic: IC_{50} 17.6 μg/mL (P388)	[169]
2-hydroxy-5-methoxyxanthone (**62**)	*Hypericum roeperianum* (Clusiaceae), Cameroon	Bark	Cytotoxic: IC50 52.95 μM (CEM/ADR5000); IC50 16.80 μM (CCRF-CEM)	[170]
Trioxygenated				
1,5-dihydroxy-2-methoxyxanthone (**53**)	*Hypericum riparium* (Hypericaceae), Cameroon	Leaves	Cytotoxic (IC_{50} 18.50 μM on *S. aureus*)	[154]
3,4-dimethoxy-7-hydroxyxanthone (**55**)	*Securidaca longipedunculata* (Polygalaceae), Ethiopia	Root bark	Antibacterial: inhibition zone diameter 15 mm (*B. subtilis*)	[171]
1,7-dihydroxy-4-methoxyxanthone **(65)**	*Securidaca longipedunculata* (Polygalaceae), Ethiopia	Root bark	Cytotoxic: IC_{50} 0.38 μM (KB-3-1 cell line)	[160]
1,4-dihydroxy-7-methoxyxanthone **(66)**	*Securidaca longipedunculata* (Polygalaceae), Ethiopia	Root bark	Cytotoxic: IC_{50} 52 μM (KB-3-1 cell line)	[160]
Tetraoxygenated				
Isoathyriol (**68**)	*Hippocratea Africana* (Willd.) Loes. ex. Engl. (Celastraceae), Nigeria	Roots	anti-inflammatory, analgesic, and antioxidant	[172]
Norathyriol (**69**)	*Hippocratea Africana* (Willd.) Loes. ex Engl. (Celastraceae), Nigeria	Roots	anti-inflammatory, analgesic, and antioxidant	[172]
1,3,5,6-tetrahydroxyxanthone (**61**)	*Hypericum roeperianum* (Guttiferae), Cameroon	Bark	Cytotoxic Cytotoxic: IC_{50} 38.46 μM (CEM/ADR5000); IC_{50} 38.58 μM (CCRF-CEM)	[170]
Swertiaperenin (**72**)	*Anthocleista schweinfurthii* Gilg (Loganiaceae), Cameroon	Leaves	Antibacterial, antioxidant	[169]
Decussatin (**73**)	*Anthocleista schweinfurthii* Gilg (Loganiaceae), Cameroon	Leaves	Antibacterial, antioxidant	[169]
1,4,5,7-tetrahydroxyxanthone (**74**)	*Psorospermum adamauense* (Hypericaceae), Cameroon	Barks and Fruits	Antimicrobial: MIC 4 μg/mL (*E. coli*)	[165]
Prenylated and related xanthones				
Globuxanthone (**51**)	*Pentadesma butyracea* (Guttiferae), Cameroon	Leaves	Antiproliferative: IC_{50} 16.90 μgM (BGC-823); IC_{50} 59.28 μM (HeLa); IC_{50} 23.81 μM (A549)	[164]
Allanxanthone A (**52**)	*Pentadesma butyracea* (Guttiferae), Cameroon	Leaves	Antiproliferative: IC_{50} 68.31 μgM (BGC-823); IC_{50} 15.83 μM (HeLa)	[164]

Continued

TABLE 10.5 Pharmacological activities of xanthones isolated from African medicinal plants in the period 2013-2023—cont'd

Common Name (Chemical Name)	Plant Origin (families), Country	Plant parts	Activities (IC_{50} in μM)	References
3-dimethyl-2-geranyl-4-prenylbellidifolin (**56**)	*Garcinia nobilis* (Clusiaceae), Cameroon	Stem bark	Antibacterial: MIC 8 μg/ml (*M. tuberculosis* ATCC 27294 and the clinical MTCS2 strains)	[161]
8-hydroxycudraxanthone G (**57**)	*Garcinia nobilis* Engl.(Clusiaceae), Cameroon	Twigs	Cytotoxic: IC_{50} 16.65 μM (leukemia CCRF-CEM cells) to IC_{50} 70.38 μM (hepatocarcinoma HepG2 cells)	[29]
Morusignin I (**58**)	*Garcinia nobilis* Engl.(Clusiaceae), Cameroon	Twigs	Cytotoxic: IC_{50} 7.15 μM (CCRF-CEM cells) to IC_{50} 53.85 μM (U87MG.ΔEGFR cells)	[29]
Cudraxanthone I (**59**)	*Milicia excelsa* (Moraceae), Cameroon	Roots	Cytotoxic: IC_{50} 2.78 μM (MDA-MB231 BCRP cells) to IC_{50} 22.49 μM (U87MG.ΔEGFR cells)	[29]
4-[(2*E*)-3,7-dimethylocta-2,6-dien-1-yl]-1,5,8- trihydroxy-3-methoxy-9*H*-xanthen-9-one (**60**)	*Garcinia polyantha* (Clusiaceae), Cameroon	Leaves	Antiproliferative: IC_{50} 2.8 μg/mL (TPH-1)	[152]
Rheediaxanthone A **(67)**	*Garcinia epunctata* Stapf (Guttiferae), Cameroon	Stem bark	Cytotoxic: IC_{50} 3.15 μM (Caco-2 cells); SI 35.49	[28]
1,3,7-trihydroxy-2-isoprenylxanthone (**71**)	*Garcinia goudotiana* (Clusiaceae), Madagascar	Leaves	Antimicrobial: MIC 39 μg/mL (*E. Faecalis* C159-6); MIC 39 μg/mL (*M. Smegmatis* 5003); MIC 78 μg/mL (*S. lugdunensis* T26A3)	[170]
Xanthonolignoids				
3′-hydroxymethyl-2′-(4″-hydroxy-3″,5″-dimethoxyphenyl)-5′,6′:5,6-(6,8-dihydroxyxanthone)-1′,4′-dioxane (**63**)	*Hypericum roeperianum* (Clusiaceae), Cameroon	Bark	Cytotoxic: IC_{50} 54.04 μM (CEM/ADR5000); IC_{50} 23.28 μM (CCRF-CEM)	[170]
3′-hydroxymethyl-2′-(4″-hydroxy-3″,5″-dimethoxyphenyl)-5′,6′:5,6-(xanthone)-1′,4′-dioxane (**64**)	*Hypericum roeperianum* (Clusiaceae), Cameroon	Bark	Cytotoxic: IC_{50} 43.47 μM (CEM/ADR5000); IC_{50} 16.31 μM (CCRF-CEM)	[170]
Glycosylated xanthone				
Mangiferin (**49**)	*Cyclopia genistoides* (Fabaceae), South-Africa	stems and leaves	Pro-apoptotic: 67% of annexin-V positive CD3− synovial cells	[171]
Isomangiferin (**50**)	*Cyclopia genistoides* (Fabaceae), South-Africa	stems and leaves	Pro-apoptotic: 75% of annexin-V positive CD3− synovial cells	[171]

In 2015, Fouotsa et al. [53] reported the isolation of 1,3,5,8-tetrahydroxy-2-(3-methylbut-2-enyl)-4-(3,7-dimethyloct-2,6-dienyl) xanthone (**20**), from *Garcinia smeathmannii*. This prenylated xanthone exhibited antibacterial activity against gram-positive *Enterococcus faecalis* with a minimal inhibitory concentration value of 8 μg/mL, and antioxidant activity, showing the capacity to scavenge free radicals. In the same year, 1,5-dihydroxy-2-methoxyxanthone (**34**), an oxygenated cytotoxic xanthone against the human gastric cell line (BGC-823) with an IC_{50} value of 18.50 μM, was isolated from the leaves of *Hypericum riparium* by Tala et al. [154].

In 2018, Kuete et al. [28] reported the isolation of rheediaxanthone A (**48**) from the stem bark of *Garcinia epunctata* Stapf. This prenylated xanthone displayed cytotoxicity toward Caco-2 cells with an IC_{50} value of 3.15 μM.

Tikisa et al. [171] reported the isolation of 3,4-dimethoxy-7-hydroxyxanthone (**36**) from the root bark of *Securidaca longipedunculata*, displaying antibacterial activity against *Bacillus subtilis* with an inhibition zone diameter of 15 mm, comparable to that of the reference drug (gentamycin).

In 2020, Fouotsa et al. [159] isolated two xanthones named mboudiexanthone (**11**) and Euxanthone (**35**) from the leaves of *Garcinia nobilis* Engl. Both compounds exhibited an antiproliferative activity with IC_{50} values of 35.26 and 32.91 mM, respectively. In the same year, Damen et al. [158] isolated a new xanthone, roeperone A (**13**) from leaves of *Hypericum roeperianum* Schimp., exhibiting an antibacterial activity against a panel of eight bacterial strains with MIC values ranging from 64 to 128 μg/mL. Guefack et al. [170] reported the isolation from bark of *Hypericum roeperianum*, of five xanthones named norathyriol (**23**), 1,3,5,6-tetrahydroxyxanthone (**42**), 2-hydroxy-5-methoxyxanthone (**43**), 3′-hydroxymethyl-2′-(4″-hydroxy-3″,5″-dimethoxyphenyl)-5′,6′:5,6-(6,8-dihydroxyxanthone)-1′,4′-dioxane (**44**), and 3′-hydroxymethyl-2′-(4″-hydroxy-3″,5″-dimethoxyphenyl)-5′,6′:5,6-(xanthone)-1′,4′-dioxane (**45**). The four xanthones exhibited a cytotoxicity activity toward the tested cancer cell lines.

In 2021, Umoh et al. [172] isolated from the root of *Hippocratea africana* (Willd.) two oxygenated xanthones named isoathyriol (**49**) and norathyriol (**50**), which demonstrated good anti-inflammatory, analgesic, and antioxidant properties compared with the standards used in each assay.

In 2022, Wedajo et al. [160] reported the isolation of 1,7-dihydroxy-4-methoxyxanthone (**46**) and 1,4-dihydroxy-7-methoxyxanthone (**47**), from the root bark of *Securidaca longipedunculata*. Both oxygenated xanthones (**46** and **47**) showed cytotoxic activities with IC_{50} values of 0.38 μM and 52 μM, respectively, against the human cervical cancer, KB-3-1 cell line. The IC_{50} values of all tested compounds are reported in Table 10.5.

Conclusion

Xanthone derivatives are an important group of natural products and due to their privileged structure can interact with different types of drug targets. They have gradually risen to great importance because of their medicinal properties. During the last decade, 29 new xanthones have been isolated for the first time from a plant distributed as simple oxygenated xanthones (1 mono-, 1tri-, 2 tetra-, 1 penta-, and 6 heptaoxgyenated xanthones), nine prenylated xanthones, one glycosylated xanthone, and eight miscellaneous xanthones. This review focuses on the types, isolation, characterization, biological applications, and biosynthesis of naturally occurring xanthones isolated so far. Different physicochemical and instrumental methods such as liquid−solid and liquid−liquid extraction, TLC, flash chromatography, column chromatography, IR, 1 HNMR and 13 CNMR spectroscopy, GLC, HPLC, GC, and LC-MS have been widely used for isolation and structural elucidation of xanthones. Some biological activities with values of IC_{50} of naturally occurring xanthones have been reported.

List of abbreviations

^{13}C NMR Carbon-13 Nuclear Magnetic Resonance
1D One dimensional (NMR)
^{1}H NMR Proton Nuclear Magnetic Resonance
2D Two dimensional (NMR)
AcOEt Ethyl acetate
AcOH Acetic acid
AH6809 isopropoxy-9-oxoxanthene-2-carboxylic acid
CC Column Chromatography
$CHCl_3$ Trichloromethane
COSY Correlation Spectroscopy
CPC Centrifugal Partition Chromatography
DEPT Distortionless Enhancement by Polarization Transfer
DMXAA 5,6-dimethylxanthenone-4-acetic acid
GC Gas chromatography
GLC Gas-liquid chromatography
GPC Gel Permeation Chromatography
H_2O Water
H_2SO_4 Sulfuric Acid
HIV/AIDS Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
HMBC Heteronuclear Multiple Bond Correlation
HPCPC High-performance centrifugal partition chromatography
HPLC High-performance liquid chromatography
HROESY High-Rotating-Frame Overhauser Effect Spectroscopy
HSCCC High-speed counter-current chromatography
HSQC Heteronuclear Single Quantum Coherence
IC_{50} Inhibitory Concentration 50 (concentration of a compound required for 50% inhibition)
INADEQUATE Incredible Natural Abundance DoublE QUAntum Transfer Experiment
IUPAC International Union of Pure and Applied Chemistry
KOH Potassium hydroxyl
LC-DAD Liquid chromatography—Photodiode array detector
LC−MS Liquid chromatography−mass spectrometry
MeOH Methanol
MPLC Medium Pressure Liquid Chromatography
NADPH Nicotinamide Adenine Dinucleotide Phosphate Hydrogene
NaOAc Sodium acetate
NMR Nuclear magnetic resonance
NOEDIFF Nuclear Overhauser effect difference spectroscopy
NOESY Nuclear Overhauser Effect Spectroscopy
OH Hydroxyl group
PKSs polyketide synthases
QCC Quick Column Chromatography
ROESY Rotating Overhauser Effect Spectroscopy
RP-CC Reversed-Phase Column Chromatography
RP-HPLC Reversed-Phase High-Performance Liquid Chromatography

SINEPT Selective Insensitive Nuclei Enhancement by Polarization Transfer
SiO2 Silica gel
THPA 2,3′,4,6-tetrahydroxybenzophenone
TLC Thin-layer chromatography
TMS Tetramethylsilane
TOCSY Total Correlation Spectroscopy
VLC Vacuum liquid chromatography

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