

Natural Product Research

Formerly Natural Product Letters

ISSN: 1478-6419 (Print) 1478-6427 (Online) Journal homepage: www.tandfonline.com/journals/gnpl20

Isolation of new xanthonones and evaluation of antioxidant, antibacterial activities, and molecular docking of *Calophyllum soulattri* Burm.f. Stem bark

Mas Atikah Lizazman , Vivien Yi Mian Jong , Nor Hisam Zamakshshari ,
Yiizamy Suffian & Mohamad Izwan Bin Ismail

To cite this article: Mas Atikah Lizazman , Vivien Yi Mian Jong , Nor Hisam Zamakshshari , Yiizamy Suffian & Mohamad Izwan Bin Ismail (26 May 2026): Isolation of new xanthonones and evaluation of antioxidant, antibacterial activities, and molecular docking of *Calophyllum soulattri* Burm.f. Stem bark, Natural Product Research, DOI: [10.1080/14786419.2026.2674730](https://doi.org/10.1080/14786419.2026.2674730)

To link to this article: <https://doi.org/10.1080/14786419.2026.2674730>



View supplementary material [↗](#)



Published online: 26 May 2026.



Submit your article to this journal [↗](#)



Article views: 79



View related articles [↗](#)



View Crossmark data [↗](#)



Isolation of new xanthenes and evaluation of antioxidant, antibacterial activities, and molecular docking of *Calophyllum soulattri* Burm.f. Stem bark

Mas Atikah Lizazman^a, Vivien Yi Mian Jong^a, Nor Hisam Zamakshshari^b,
Yiizamy Suffian^b and Mohamad Izwan Bin Ismail^c

^aFaculty of Applied Sciences, Universiti Teknologi MARA, Kota Samarahan, Malaysia; ^bFaculty of Resource Sciences and Technology, Universiti Malaysia Sarawak, Kota Samarahan, Malaysia; ^cFaculty of Applied Sciences, Universiti Teknologi MARA, Mukah, Malaysia

ABSTRACT

Six new xanthenes (**1–6**), along with eight known xanthenes (**7–14**) were isolated from *C. soulattri* stem bark. Their structures were elucidated using 1D and 2D NMR, FTIR, and MS analyses. The phytochemical profiling, antioxidant, and antibacterial evaluations were conducted on the extracts, and the interaction of new compounds with PBP was explored through molecular docking analysis. Among the extracts, ethyl acetate and chloroform exhibited the highest TPC and TFC, respectively, whereas the methanol extract portrayed the highest antioxidant activity (IC_{50} 7.97 μ g/mL). In the antibacterial assay, the chloroform and ethyl acetate extracts exhibited the most significant inhibitory activity against all tested *A. baumannii* strains (MIC 0.225–0.440 mg/mL). Molecular docking study revealed that compound **6** displayed the strongest binding energy (–14.2 kJ/mol) towards penicillin-binding protein compared to the other isolated compounds.

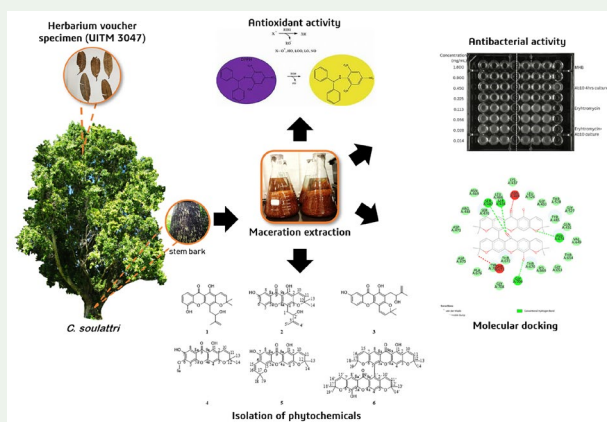
ARTICLE HISTORY

Received 5 October 2025

Accepted 12 May 2026

KEYWORDS

Calophyllum soulattri;
xanthone; molecular
docking; DPPH;
Acinetobacter baumannii



CONTACT Vivien Jong Yi Mian ✉ vivien@uitm.edu.my

b Supplemental data for this article can be accessed online at <https://doi.org/10.1080/14786419.2026.2674730>.

© 2026 Informa UK Limited, trading as Taylor & Francis Group

1. Introduction

Calophyllum soulattri Burm.f. is a flowering plant species that is native to Australia (Northern Territory), Brunei, Cambodia, Indonesia, India, Malaysia, the Philippines, Papua New Guinea, Singapore, Thailand, and Vietnam. Traditionally, the Indonesians fed the horses with the inner bark of the tree to keep them in good condition (Stevens 1980) and the root infusion was used to relieve rheumatic pain (Khan et al. 2002). The fresh bark of the shoot was used as a medicine in postpartum treatment in the Caroline Islands (Stevens 1980). The stem bark of *C. soulattri* has been reported to contain several phytochemicals, such as xanthenes and coumarins (Ee et al. 2011). In addition, previous studies have revealed that *C. soulattri* exhibited anti-inflammatory, antimicrobial, and cytotoxic activities (Chinthu et al. 2023; Abang Heilman et al. 2025). Nevertheless, thorough research on the Borneo stem bark of *C. soulattri* is still lacking, particularly regarding its xanthone composition and bioactivities.

Natural products are an important source of drug discovery due to their structural diversity (Karunakaran et al. 2016; Chaachouay and Zidane 2024). *C. soulattri* species may be a promising source of new bioactive compounds, considering the rising number of naturally occurring compounds being discovered (Cheng Lian Ee et al. 2011; Mah et al. 2011; Mah et al. 2012; Tanjung et al. 2018; Abang Heilman et al. 2025). Moreover, during the biotic and abiotic stresses, plants biosynthesise a considerable number of antioxidants which are capable of scavenging the reactive oxygen species that cause the oxidative stress, leading to harmful effects such as neurodegenerative and cardiovascular diseases. Therefore, the antioxidant agents are crucial to remediate the damage caused by the free radicals and balance the cellular redox reaction (Pammi et al. 2023). Besides the antioxidant properties of the natural compounds, they have gained more recognition for their antibacterial capabilities (Zaine et al. 2025). The emergence of antibiotic-resistant pathogens, such as *A. baumannii*, spotlights the urgency for the discovery of novel antimicrobial agents (Butler et al. 2019).

The present work aims to address the existing research gaps through a comprehensive investigation of the phytochemical composition of the extracts of *C. soulattri* stem bark, evaluating the biological potential of its extracts, and exploring the possible protein-ligand interactions through molecular docking as a preliminary *in silico* approach. By incorporating phytochemical profiling, biological activity assays, and *in silico* studies, this study intends to provide an in-depth understanding of the therapeutic potential of *C. soulattri* and provide preliminary data for future antibacterial research.

2. Results and discussion

2.1. Extraction and isolation of *C. soulattri* stem bark

The sequential maceration extraction of 1.5 kg *C. soulattri* stem bark has yielded oily light brown extract from *n*-hexane (CSH, 28.3 g), yellowish brown extract from dichloromethane (CSD, 30.2 g), yellowish-dark brown extract from chloroform (CSC, 12.3 g), reddish-brown extract from ethyl acetate (CSEA, 13.8 g), and reddish-black extract from methanol (CSM, 85.1 g). The isolation of the *n*-hexane extract of *C. soulattri* stem

bark has afforded six new xanthenes, soulaxanthone A (**1**), soulaxanthone B (**2**), soulaxanthone C (**3**), soulaxanthone D (**4**), 7-hydroxyvenuloxanthone (**5**), bispyranojacareubin (**6**), along with known xanthenes, brasilixanthone B (**7**) (Ee et al. 2004), caloxanthone I (**8**) (Zamakshshari et al. 2019), bracteaxanthone XII (**9**) (Seruji et al. 2024), brasixanthone B (**10**) (Mah et al. 2012; Seruji et al. 2023), caloxanthone C (**11**) (Lizazman et al. 2023), trapezifolixanthone (**12**) (Lizazman, Jong, et al. 2026b; Suffian et al. 2026), 7-O-demethylmangostanin (**13**) (Yang et al. 2017), and 9-hydroxycalabaxanthone (**14**) (Daud et al. 2021) as shown in Figure 1. The known xanthenes have been previously reported from other *Calophyllum* species (Table S1), supporting the chemotaxonomic consistency of this genus (Ito et al. 1996, 2002; linuma et al. 1997; Cheng et al. 2004; Ee et al. 2004; Yimdojo et al. 2004; Shen et al. 2005; Mah et al. 2011; Ee et al. 2012; Mah et al. 2012; Tanjung et al. 2018; Zamakshshari et al. 2018; Laopian et al. 2019; Daud et al. 2021; Haerani et al. 2021; Cao et al. 2022; Karunakaran et al. 2022; Lizazman et al. 2023; Seruji et al. 2024). Detailed structural elucidation was focused on the *n*-hexane extract due to its chemical richness and chromatographic tractability, while the remaining extracts were evaluated at the crude level for comparative biological screening.

2.2. Characterisation of new compounds (1-6)

Soulaxanthone B (**2**) was isolated as a yellow needle crystal with a melting point of 193–194 °C. The HR-LC-ESI-MS spectrum gave a quasi-molecular ion peak at m/z 395.1477 $[M+H]^+$ (calcd for $C_{23}H_{23}O_6^+$, 395.1489; $\Delta = -3.1$ ppm), which is in line with the molecular formula $C_{23}H_{22}O_6$. The IR spectrum displayed distinct absorptions at 3362 (OH group), <3000 (sp^3 C–H stretch), 1650 (conjugated C=O), 1483 (aromatic C=C), and 1208 (C–O) cm^{-1} . The proton NMR spectrum exhibited two deshielded singlet peaks resonating at δ_H 13.36 and δ_H 8.93, indicating the presence of two hydroxyl groups. Doublet resonances observed at δ_H 5.76 (10.0 Hz, 1H) and δ_H 6.72 (10.0 Hz, 1H), along with two sets of singlets integrating for three protons each (δ_H 1.52 and 1.53), formed the 2,2-dimethylpyrano system. The signals of olefinic protons of the terminal double bond (δ_H 4.64 and 4.72), hydroxy methine proton (δ_H 4.42, dd, 6.5, 7.0), a methylene proton (δ_H 3.05, dd, 7.0, 13.1, 1H; δ_H 3.09, dd, 6.5, 13.1, 1H), and a methyl group (δ_H 1.89, s, 3H) established a 2-hydroxy-3-methylbut-3-en-1-yl substituent. The aromatic protons at δ_H 7.38 (H-6), 7.53 (H-5), and 7.58 (H-8) were indicative of the xanthone scaffold. The carbon NMR spectrum, including DEPT (45, 90, 135) experiments, exhibited 23 carbon peaks, establishing $C_{23}H_{22}O_6$, and has concluded three methyls, two methylene, six methines, and twelve quaternary carbons. The assignment of the structure was supported with the 2D NMR (HSQC, HMBC and COSY). The cross-peaks of methylene protons H-1' resonating at δ_H 3.05 and 3.09, with C-3, C-4, and C-4a, indicate that the 2-hydroxy-3-methylbut-3-en-1-yl was substituted at quaternary carbon C-4 (δ_C 105.7). The 7-OH (δ_H 8.93) exhibited the HMBC interactions with C-6, C-7, and C-8, indicating the positioning of a hydroxyl group at aromatic carbon C-7.

Soulaxanthone A (**1**) and soulaxanthone C (**3**) are structural isomers of compound **2** and are obtained as yellow solids with respective melting points of 184–184 °C and 243–244 °C. The HR-LC-ESI-MS spectra of both compounds gave respective

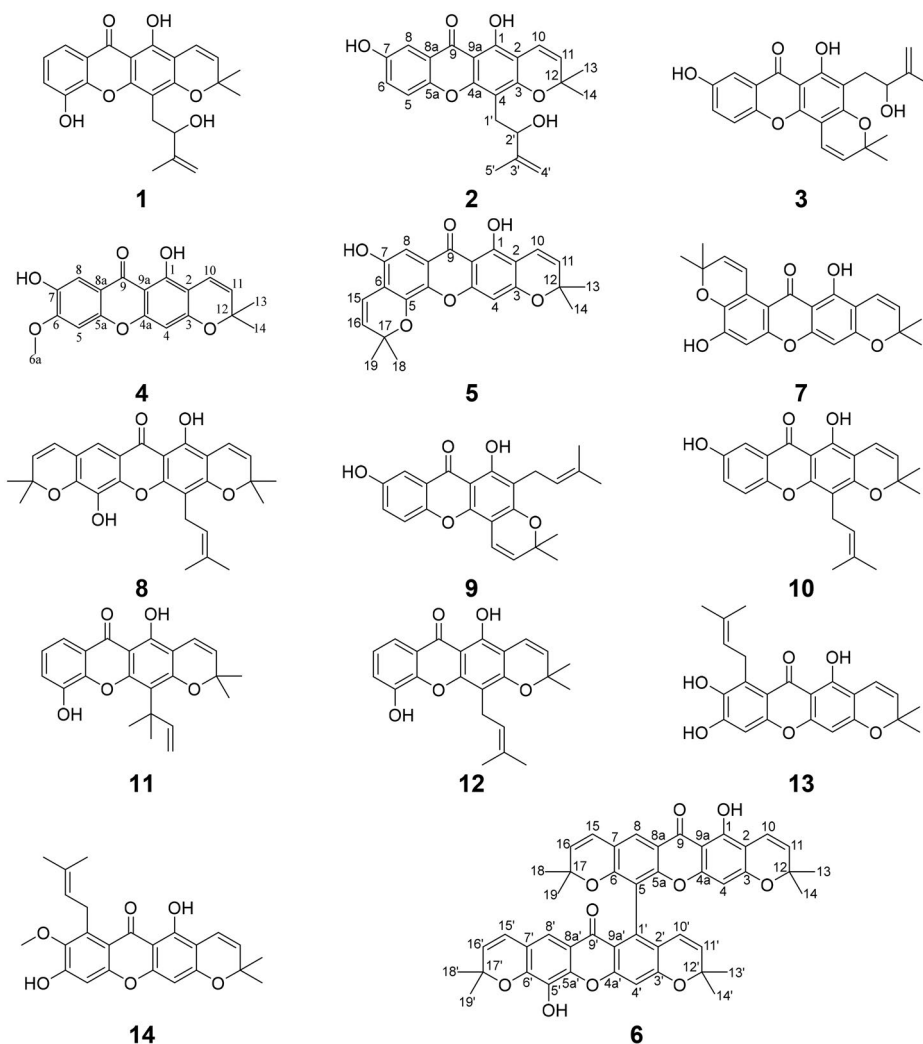


Figure 1. Structures of compounds **1–14**.

quasi-molecular ion peaks at m/z 395.1479 $[M+H]^+$ (calcd for $C_{23}H_{23}O_6^+$, 395.1489; $\Delta = -2.5$ ppm), and m/z 395.1500 $[M+H]^+$ (calcd for $C_{23}H_{23}O_6^+$, 395.1489; $\Delta = +2.8$ ppm), which is consistent with the molecular formula $C_{23}H_{22}O_6$. The IR spectrum exhibited absorptions at 3348 (OH group), <3000 (sp^3 C–H stretch), 1649 (conjugated C=O), 1582 (aromatic C=C), and 1126 (C–O) cm^{-1} for compound **1**. Meanwhile, the IR spectrum of compound **3** gave absorptions at 3334 (OH group), <3000 (sp^3 C–H stretch), 1651 (conjugated C=O), 1579 (aromatic C=C), and 1137 (C–O) cm^{-1} . Their NMR spectra exhibited similar proton and carbon resonances with significantly shifted chemical shifts. In comparison to compound **2**, the 5-OH (δ_H 9.26) in compound **1** was confirmed to be bonded to C-5 by comparison of the xanthone skeleton at C-5, C-6, C-7, and C-8 with that of the trapezifolixanthone skeleton (Lizazman et al. 2022). On the other hand, compound **3** gave the cross-peaks of H-10 (δ_H 6.90) with C-3 (δ_C 159.7), and H-11 (δ_H 5.76) with C-4 (δ_C 101.2) in the HMBC spectrum, indicating the pyrano

ring was fused to the xanthone skeleton at C-4 and C-3 through oxygen. The 2-hydroxy-3-methylbut-3-en-1-yl substituent of compound **3** was assigned to position C-2 based on HMBC correlations between the methylene proton H-1' (δ H 2.88 and 2.96) with C-1 (δ C 161.9), C-2 (δ C 109.5), and C-3 (δ C 159.7).

Soulaxanthone D (**4**) was obtained in the form of pale-yellow needle crystals with a melting point of 226–227°C. Based on the MS spectrum, the quasi-molecular ion peak was observed at m/z 341.1013 $[M+H]^+$ (calcd for $C_{19}H_{17}O_6^+$, 341.1020; $\Delta = -2.1$ ppm), which is consistent with the molecular formula $C_{19}H_{16}O_6$. The IR spectrum displayed distinct absorptions at 3269 (OH group), <3000 (sp^3 C–H stretch), 1606 (conjugated C=O), 1479 (aromatic C=C), and 1174 (C–O) cm^{-1} . The analysis of the ^1H NMR spectrum revealed a chelated hydroxyl group (δ H 13.57) and three aromatic protons (δ H 6.33, 6.95, and 7.55). The presence of two *ortho*-coupled doublets at δ H 5.74 and 6.68, along with a singlet integrating for six protons at δ H 1.47, indicated the existence of a 2,2-dimethyl-2*H*-pyrano ring. Additionally, a singlet at δ H 3.99 integrating for three protons confirmed the presence of a methoxyl group in the compound. Further analysis using ^{13}C NMR and DEPT 45 spectra revealed 23 carbon signals comprising five methines, three methyls, and eleven quaternary carbons, including a carbonyl that resonates at δ C 180.6. In the HMBC spectrum, cross-peaks between the chelated hydroxyl group and three aromatic carbons at δ C 103.7, 105.1, and 158.3 indicated its position at C-1 (δ C 158.9). Correlations between δ H 3.99 (H-6a) and δ C 146.8 (C-6) confirmed the methoxyl moiety at carbon 6. Meanwhile, aromatic proton H-5 (δ H 6.95) gave cross-peaks with δ C 155.4 (C-7), δ C 146.8 (C-6), δ C 153.4 (C-5a), δ C 113.4 (C-8a), confirming protons H-4 and H-5 belong to different parts of the ring system. On the other hand, the remaining aromatic proton resonating δ H 7.55 (H-8) appears as a singlet, suggesting it is in *para*-position relative to proton H-5, which also appears as a singlet. Moreover, the olefinic protons δ H 6.68 (H-10) were correlated with C-1 and C-3, and δ H 5.74 (H-11) gave a cross-peak with δ C 105.1 (C-2), indicating the pyrano ring was fused with the xanthone skeleton at C-2 and C-3.

7-Hydroxyvenuloxanthone (**5**) was isolated as a yellow needle crystal with a melting point of 244–245°C. HR-LC-ESI-MS showed a quasi-molecular ion peak at m/z 393.1324 $[M+H]^+$ (calcd for $C_{23}H_{21}O_6^+$, 393.1324; $\Delta = 0.0$ ppm), signifying a molecular formula of $C_{23}H_{20}O_6$. The IR spectrum showed absorptions at 3244 (OH group), <3000 (sp^3 C–H stretch), 1613 (conjugated C=O), 1466 (aromatic C=C), and 1125 (C–O) cm^{-1} . The ^1H NMR spectrum showed the presence of the proton signals of two singlets in the aromatic region at δ H 6.42 and 7.45 (each 1H), which suggests that compound **5** is a typical xanthone with six substituents. The presence of a chelated hydroxyl group at δ H 13.52 and a lone hydroxyl group at δ H 8.34 is assignable to the signals of 1-OH and 7-OH, respectively. The proton NMR also revealed the presence of two sets of 2,2-dimethylpyrano group, of which one of the groups was observed at δ H 6.95 (d, 10.1 Hz, 1H), δ H 5.95 (d, 10.1 Hz, 1H), and δ H 1.53 (s, 6H). Another ring was indicated by two doublets at δ H 6.69 and 5.74 with $J = 10.2$ Hz, along with a singlet resonance integrating for six protons (δ H 1.47). This suggestion was further confirmed by COSY, which exhibited the couplings of the doublets' protons with each other (H-10/H-11 and H-15/H-16). The ^{13}C NMR spectrum of **5** showed 23 carbon signals following the molecular formula. Meanwhile, the DEPT experiments (DEPT 45, 90, 135) gave four methyls, six methines and thirteen quaternary carbons, including a carbonyl carbon

resonating at δC 180.8. The HMBC correlations of 1-OH with three quaternary carbons (δC 103.7, 105.1, 158.4) show that the chelated hydroxyl group was bonded to C-1. The carbons resonating at δC 110.5, 148.3, and 147.0 showed cross-peaks with a proton (δH 6.69) belonging to one of the pyrano ring, showing that the group was fused at C-5 and C-6. Moreover, the doublets at δH 5.95 and 6.95 gave HMBC correlations with C-2, which indicates the attachment of another set of pyrano ring to C-2 and C-3.

Bispyranojacareubin (**6**) was discovered as a pale-yellow crystal with a melting point of 254–255 °C. The MS spectrum exhibited a quasi-molecular ion peak at m/z 749.2838 $[\text{M}-\text{H}]^-$ (calcd for $\text{C}_{46}\text{H}_{37}\text{O}_{10}^-$, 749.2838; $\Delta = -0.7$ ppm), consistent with the molecular formula $\text{C}_{46}\text{H}_{38}\text{O}_{10}$. The IR spectrum showed absorptions at 3446 (OH group), <3000 (sp^3 C–H stretch), 1637 (conjugated C=O), and 1462 (aromatic C=C) cm^{-1} . The ^1H NMR spectrum exhibited a downfield signal attributed to the chelated hydroxyl group resonating at δH 13.53 (1-OH). Another singlet peak (δH 8.58) in the proton spectrum indicated the presence of a hydroxyl group (5'-OH) as it gave no correlation with any carbon peak in the HSQC spectrum. Two sets of aromatic protons appeared as two pairs of doublets coupling with each other (δH 5.75/6.68, and δH 5.91/6.59) as shown in COSY, along with two methyl peaks (δH 1.48 and 1.50) indicating two pyrano systems. Meanwhile, the aromatic proton resonances at δH 6.38 and 7.44 were presumed to be in two different rings, as no coupling signals were detected in the COSY spectrum. Hence, compound **6** was predicted to have the xanthone skeleton with two ring systems fused to it. The proton spectrum generally portrayed similar chemical shifts to those of pyranojacareubin (Tee et al. 2018). Except for the singlet peaks of the hydroxyl groups (1- and 5'-OH), the protons integrated in the ^1H NMR spectrum of compound **6** were doubled, indicating the overlapping of proton signals. This suggests the presence of two dipyranoxanthone skeletons within the compound, which was supported by the presence of two downfield signals (δC 181.1 and 181.2) of typical carbonyl carbons within the xanthone skeleton. The ^{13}C NMR spectrum exhibited a total of 46 carbon peaks, including the overlapped carbon peaks with integration of 2, at δC 28.4, 28.5, 78.9, 79.0, 113.3, 122.1, and 132.6. The DEPT spectra (45, 90, 135) have concluded the presence of twelve methine, eight methyl, and twenty-six quaternary carbons. Further 2D NMR analyses were conducted to confirm the hypothesis. The HMBC spectrum revealed the cross-peaks of δH 13.53 (1-OH) with δC 103.7 (C-9a), 105.2 (C-2), and 158.6 (C-1), suggesting the position of the chelated hydroxyl at C-1. The singlet signal at δH 8.58 (5'-OH) gave ^2J correlations to the carbon signals at δC 146.8 (C-5a') and 146.8 (C-6'), indicating the hydroxyl group was bound to C-5' in another xanthone skeleton. Importantly, the long-range correlation between δH 7.44 (H-8) with δC 134.3 (C-1') has confirmed that the two xanthenes were connected by a C-5/C-1' bridge. Thus, compound **6** was concluded as a xanthone dimer, 5',12-dihydroxy-2,2,2',2',10,10,10',10'-octamethyl-2H,2'H,6H,6'H,10H,10'H-[5,12'-bidipyrano[3,2-b:2',3'-i] xanthene]-6,6'-dione.

The COSY and long-range HMBC correlations were consistent with compounds **1-6** (Supplementary Figure S1). The ^1H and ^{13}C NMR data for compounds **1-6** are reported herein for the first time (Supplementary Tables S2 and S3). The IR, MS, 1D, and 2D NMR spectra of xanthenes **1-6** were displayed in Figures S2–S43 in the supplementary information.

The 2D structures of new compounds **1-6** unveil a typical xanthone core distinguished by a tricyclic aromatic skeleton and a carbonyl (C=O) functionality, with a typical chelated hydroxyl group at C-1. Nevertheless, the main structural differences are observed in the patterns of substitution. Compounds **1-3** are positional isomers that possess similar functional groups such as hydroxyl groups, a 2-hydroxy-3-methylbut-3-en-1-yl chain, and a pyran ring. For example, the fusion of the pyran ring involves C-C linkage at C-2 and C-O-C linkage at C-3, while the bonding of the hydroxylated prenyl moiety is linked through C-C at C-4 in both compounds **1** and **2**. Meanwhile, the heterocyclic ring is fused at C-3 through oxygen and C-4 via a C-C bond, and a hydroxylated prenyl chain is bound to C-2 in compound **3**, transforming the compound into an angular pyranoxanthone. Moreover, compound **4** exhibits an additional methoxyl group attached at C-6, establishing ether functionality (C-O-C) with the absence of the amphiphilic 2-hydroxy-3-methylbut-3-en-1-yl side chain when compared with compound **2**. Compound **5** has a partial similarity in terms of tetracyclic scaffold with compound **4**, but also features an extra fused ring system at C-5 and C-6 through respective C-O-C and C-C linkages, forming an angular dipyranoxanthone. However, compound **6** possesses a pair of linear dipyranoxanthone scaffolds having a hydroxyl group each, establishing a xanthone dimer that connects through a C-C bridge between C-5 and C-1'. This suggests that a stronger pi-pi stacking can be formed due to the presence of multiple aromatic systems in comparison to the monomers **1-5**.

2.3. TPC of *C. soulattri* extracts

The total phenolic content (TPC) of the extracts was determined using the Folin-Ciocalteu (FC) method (Naves et al. 2019). The TPC varied significantly ($p < 0.05$) across the different extracts. The highest TPC was demonstrated by CSEA, followed by CSM with values 281.70 ± 9.19 and 279.20 ± 7.76 mg GAE/g extract, respectively. On the contrary, CSH portrayed the lowest TPC of 84.92 ± 6.83 mg GAE/g extract, showing no significant difference when compared to CSD and CSC. These results indicate that polar solvents extract higher phenolic content. These findings are consistent with previous reports on *C. soulattri* (Husni et al. 2020).

2.4. TFC of *C. soulattri* extracts

The total flavonoid content of the extracts was determined using the aluminium chloride calorimetric method (Sakai et al. 2022; Lizazman, Jong, et al. 2026b). The TFC of the extracts exhibited significant variation, ranging from 47.39 ± 0.89 to 166.7 ± 1.58 mg QE/g extract. CSC demonstrated the highest TFC, significantly ($p < 0.05$) surpassing that of the other extracts (166.7 ± 1.58 mg QE/g extract). Comparatively, CSD exhibited a high TFC of 139.3 ± 0.97 mg QE/g extract. Meanwhile, CSH, CSEA and CSM contained significantly lower amount of flavonoid compounds. Based on the results, flavonoids were more prevalent in the semi-polar solvents such as chloroform and dichloromethane. This is the first report on the flavonoid content of *C. soulattri* stem bark. The data is tabulated in Table S4.

2.5. 2,2-Diphenyl-1-picrylhydrazyl (DPPH•) antioxidant assay

The antioxidant activity of the extracts was evaluated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH•) radical scavenging assay (Lizazman, Mian, et al. 2026a). The result from the DPPH assay has demonstrated significant variations ($p < 0.05$) among the extracts. Among all the extracts, the highest radical scavenging activity was exhibited by CSM with an IC_{50} of $7.97 \pm 0.16 \mu\text{g/mL}$, which was comparable to that of quercetin (IC_{50} $6.33 \pm 0.34 \mu\text{g/mL}$). Similarly, CSEA also showed a strong antioxidant potential with an IC_{50} of $11.25 \pm 0.61 \mu\text{g/mL}$. On the other hand, CSD and CSH showed the weakest to no antioxidant activity. This is consistent with the higher TPC and TFC observed in polar extracts (Husni et al. 2020), where the highest antioxidant activity was detected in the most polar ethanol extract, followed by the butanol and ethyl acetate fractions, using ferric reducing antioxidant power (FRAP) assay.

2.6. Pearson's correlation between TPC, TFC, and antioxidant activity (DPPH•)

Pearson's correlation was conducted to evaluate the relationship between TPC, TFC, and antioxidant activity of the extracts. The coefficient (r) is a statistical measure to quantify the strength and direction of a linear relationship between two variables, and it ranges from -1 to $+1$. The relationship is considered strong if the values are close to -1 or 1 . A positive value means that the variables increase or decrease together, while a negative value means one variable increase while the other decreases. The result reveals a statistically non-significant negative correlation ($r = -0.626$, $p = 0.259$) between TPC and TFC, which suggests an inverse relationship. A negative correlation ($r = -0.438$) was noted between TPC and DPPH, suggesting that an increase in phenolic compounds may be connected to the increase in antioxidant activity. Nevertheless, the relationship was not significant ($p = 0.461$). Moreover, TFC gave a weak negative correlation ($r = 0.359$) with DPPH, suggesting that flavonoids may influence the antioxidant activity, even though it is not statistically significant ($p = 0.553$).

2.7. Antibacterial assay

The antibacterial activity of extracts from *C. soulattri* was assessed against nine bacterial strains of *A. baumannii* using the minimum inhibitory concentration (MIC) method (Noh and Jong 2020). The MIC values ranged from 0.225 to 0.450 mg/mL , and are available in the [supplementary information \(Supplementary Table S5, Figure S44–S53\)](#). The observed MIC values indicated a moderate antibacterial activity when compared to standard antibiotics such as colistin (MIC 0.125 – $0.5 \mu\text{g/mL}$) (El Mrimar et al. 2024; Nguyen et al. 2025), imipenem (MIC 16 – $32 \mu\text{g/mL}$) (Liu et al. 2014; Lasarte-Monterrubio et al. 2021), meropenem (MIC 16 – $16 \mu\text{g/mL}$) (Lasarte-Monterrubio et al. 2021), and tigecycline (MIC₉₀ $2 \mu\text{g/mL}$) (Falagas et al. 2018) against *A. baumannii* strains. For plant extracts, the MIC values between 100 and $500 \mu\text{g/mL}$ are considered moderate antibacterial activity, which is frequently mentioned as effective, even though not the most potent (Da Silva et al. 2022; Zouine et al. 2024). The results reveal that chloroform and ethyl acetate extracts exhibited the most consistent antibacterial effects across *A. baumannii* strains, with MIC values of 0.225 mg/mL . The antibacterial activity

observed in CSC and CSEA may be partially associated with their phenolic and flavonoid content. However, the contribution of individual constituents was not determined in this study. The polarity index of the solvents used, methanol (5.1), ethyl acetate (4.4), chloroform (4.1), and hexane (0.1), affects the bioactive compounds present in the extract (Xochicale-Santana et al. 2021). Both CSC and CSEA used semi-polar solvents that showed more effective inhibition to most bacterial strains with MIC values of 0.225 mg/mL. The moderate antibacterial activity in crude plant extracts could be attributed to the relatively low concentration of active compounds and the potential for synergistic or antagonistic interactions among the compounds (Tinrat 2022). However, the antibacterial efficacy may be improved through further isolation and purification of active compounds, thus lowering the antagonistic effects. The CSM extract also exhibited some antibacterial activity; however, its polarity likely limits its effectiveness (Scorciapino et al. 2017) compared to the more compatible semi-polar extracts (Lee et al. 2024). The methanol extract still showed better efficacy than the non-polar hexane extract, but the difference in polarity between methanol and the compounds most effective against *A. baumannii* may have reduced its potency. Among all the tested strains, Ab08 showed the least susceptibility to all extracts with a consistent MIC value of 0.450 mg/mL. This result suggests that Ab08 may possess resistance mechanisms, such as efflux pumps, biofilm formation, or enzymatic inactivation, which can reduce the effectiveness of plant-derived compounds (Kyriakidis et al. 2021). The comparison with existing literature values provides a useful benchmark in assessing the antibacterial potential, even though no standard antibiotic was included in the study. To the best of our knowledge, no prior research has examined the antibacterial properties of *C. soulattri* against *A. baumannii* strains. Thus, the current findings represent the first report showing that *C. soulattri* stem bark extracts have inhibitory activity against this clinically significant pathogen. Future investigation involving the isolated compounds and incorporation of standard antibiotics as positive controls is required to validate the antibacterial potential.

2.8. Molecular docking of the isolated compounds

The docking was performed using AutoDock vina (Eberhardt et al. 2021) with the root-mean-square deviation (RMSD) of 1.6691 Å. $\text{RMSD} < 3 \text{ Å}$ indicates the reliability of the docking method for the prediction of the binding orientation of ligands (Zaine et al. 2025). The molecular docking results indicate that bispyranojacareubin (**6**) showed the highest binding energy of -14.2 kcal/mol compared to the other compounds (Figure S54). Meanwhile, the others score binding energy ranging from -7.0 to 8.0 kcal/mol , suggesting a favourable binding interaction with penicillin-binding protein (PBP). The stronger binding affinity of compound **6** can be attributed to the formation of four hydrogen bonds between bispyranojacareubin and amino acid residues through oxygen element, along with van der Waals interactions. Furthermore, bispyranojacareubin was found to interact with specific amino acid residues, including ASN434, LYS669, THR670, THR672, and TYR707, which are also involved in the binding mechanism of β -lactam antibiotics such as penicillin G, imipenem, and aztreonam (Han et al. 2011). However, molecular docking does not validate the actual biological

activity, although it provides the predicted binding affinity. Thus, it is necessary to validate these findings through enzyme inhibition or antimicrobial assays. In addition, the correlation between the antibacterial activity and docking scores cannot be established as the extracts contain a mixture of compounds of varying concentrations with potential synergistic or antagonistic effects. Nonetheless, the docking results provide valuable insight into the potential mechanism of action of the docked compounds, with compound **6** appearing to play a key role in the overall antibacterial effect.

2.9. SAR study

The analysis of the structure–activity relationship (SAR) indicates a connection between the enhanced-binding affinity compound **6** and its complex dimeric xanthone framework. The extended pi-conjugated system throughout the aromatic fused rings enhances pi-pi and hydrophobic interactions within the PBP binding cleft. Moreover, the presence of polar hydrogen bond interaction with key amino acid residues is due to the presence of multiple oxygen-containing functional groups, such as hydroxyl and ether. Importantly, compound **6** possesses a larger molecular skeleton that provides a larger surface area for interaction within the binding site in comparison to the monomeric xanthenes **1–5**. The presence of two pairs of pyrano rings within the compound **6** scaffold further improves the structural rigidity, which enhances the binding stability through the promotion of optimal orientation within the active site. Conversely, the smaller monomeric compounds demonstrated less interaction with the residues, thus lower binding affinity. This observation aligns with the structural data, which shows compound **6** possesses a more intricate fused ring system than the simple xanthone derivatives.

3. Experimental

See [Supplementary Material](#).

4. Conclusion

The isolation of the stem bark of *C. soulattri* has afforded six new xanthenes **1–6**, and eight known xanthenes **7–14**. To the best of our knowledge, this is the first report of brasilixanthone B (**7**), caloxanthone I (**8**), bracteaxanthone XII (**9**), 7-O-demethylmangostanin (**13**), and 9-hydroxycalabaxanthone (**14**) from *C. soulattri*. The ethyl acetate extract showed the highest both TPC and antioxidant activity, while the highest TFC was demonstrated by the chloroform extract. The phytochemical study concluded that TPC was associated with the antioxidant activity of *C. soulattri* extracts. The extracts from *C. soulattri* showed moderate antibacterial activity against *A. baumannii*, with chloroform and ethyl acetate extracts exhibiting the most significant antibacterial activity across all strains tested, including the multidrug-resistant strains. These findings suggest that semi-polar solvents may be effective in extracting antibacterial agents from *C. soulattri*. However, future targeted studies are required

to elucidate their mechanisms of action. Molecular docking analysis indicated that bispyranojacareubin exhibited the strongest predicted binding affinity of all the isolated compounds. Overall, this study provides phytochemical and preliminary biological insights into *C. soulattri*.

Acknowledgements

The authors gratefully acknowledge UiTM Samarahan and UiTM Mukah, Sarawak, for providing the necessary facilities and resources that were essential for the successful completion of this research conducted on the genus *Calophyllum*. The support and encouragement from the institution have been invaluable throughout the study. The Sarawak Biodiversity Centre (SBC) is also acknowledged.

Author contributions statement

CRedit: **Mas Atikah Lizazman**: Data curation, Methodology, Writing – original draft, Writing – review & editing; **Vivien Yi Mian Jong**: Conceptualization, Data curation, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing; **Nor Hisam Zamakshshari**: Data curation, Methodology, Supervision, Writing – original draft, Writing – review & editing; **Yiizamy Suffian**: Data curation, Methodology, Writing – original draft, Writing – review & editing; **Mohamad Izwan Bin Ismail**: Data curation, Methodology, Writing – original draft, Writing – review & editing.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by a research grant from UiTM Sarawak [100-TNCPI/PRI 16/6/2 (020/2020)].

References

- Abang Heilman DNA et al. 2025. Soulaxanthone, a new xanthone derivative from *Calophyllum soulattri*. Nat Prod Res. 39(19):5502–5508. <https://doi.org/10.1080/14786419.2024.2345752>
- Butler DA et al. 2019. Multidrug resistant *Acinetobacter baumannii*: resistance by any other name would still be hard to treat. Curr Infect Dis Rep. 21(12):46. <https://doi.org/10.1007/s11908-019-0706-5>
- Cao TT et al. 2022. Xanthones from *Calophyllum polyanthum* Wallich ex Choisy with CYP1 enzymes inhibitory activity. Chem Biodivers. 19(6):e202200268. <https://doi.org/10.1002/cbdv.202200268>
- Chaachouay N, Zidane L. 2024. Plant-derived natural products: a source for drug discovery and development. DDC. 3(1):184–207. <https://doi.org/10.3390/ddc3010011>
- Cheng H et al. 2004. Pyranoxanthones from *Calophyllum inophyllum*. J Chin Chem Soc. 51(2):431–435. <https://doi.org/10.1002/jccs.200400066>
- Chinthu RV, Praveen Kumar BR, Raveendran M. 2023. A review on the genus *Calophyllum* (*Clusiaceae*): a potential medicinal tree species. Plant Sci Today. 10(3):1–5. <https://doi.org/10.14719/pst.1818>

- Da Silva RM, Da Silva IDMM, Estevinho MM, Estevinho LM. 2022. Anti-bacterial activity of *Annona muricata* Linnaeus extracts: a systematic review. Food Sci Technol. 42:e13021. <https://doi.org/10.1590/fst.13021>
- Daud S et al. 2021. Cytotoxicity and nitric oxide inhibitory activities of xanthenes isolated from *Calophyllum hosei* Ridl. Nat Prod Res. 35(24):6067–6072. <https://doi.org/10.1080/14786419.2020.1819273>
- Eberhardt J, Santos-Martins D, Tillack AF, Forli S. 2021. AutoDock Vina 1.2.0: new docking methods, expanded force field, and Python bindings. J Chem Inf Model. 61(8):3891–3898. <https://doi.org/10.1021/acs.jcim.1c00203>
- Ee GCL et al. 2004. A new pyranoxanthone inophyllin B from *Calophyllum inophyllum*. Nat. Prod. Sci. 10(5):220–222. <https://www.scopus.com/inward/record.uri?eid=2-s2.0-8444251316&partnerID=40&md5=8ddaafe3a112f00e6c6965207a4581e>
- Ee GCL et al. 2011. Soulamarin, a new coumarin from stem bark of *Calophyllum soulattri*. Molecules. 16(11):9721–9727. <https://doi.org/10.3390/molecules16119721>
- Ee GCL et al. 2012. A new xanthone from *Garcinia nitida*. Nat Prod Res. 26(9):830–835. <https://doi.org/10.1080/14786419.2011.559640>
- El Mrimar N, Belouad EM, Benaissa E, Maleb A, Elouennass M. 2024. Antimicrobial resistance of multidrug-resistant Enterobacterales and *Acinetobacter baumannii* isolates to colistin in a Moroccan hospital. Microbes Infect Dis. 5(3):1139–1146. <https://doi.org/10.21608/mid.2024.279217.1862>
- Falagas ME et al. 2018. Activity of TP-6076 against carbapenem-resistant *Acinetobacter baumannii* isolates collected from inpatients in Greek hospitals. Int J Antimicrob Agents. 52(2):269–271. <https://doi.org/10.1016/j.ijantimicag.2018.03.009>
- Haerani SN, Raksat A, Pudhom K. 2021. Two new xanthenes from the root of Thai *Calophyllum inophyllum* and their toxicity against colon and liver cancer cells. J Nat Med. 75(3):670–674. <https://doi.org/10.1007/s11418-021-01492-3>
- Han S et al. 2011. Distinctive attributes of β -lactam target proteins in *Acinetobacter baumannii* relevant to development of new antibiotics. J Am Chem Soc. 133(50):20536–20545. <https://doi.org/10.1021/ja208835z>
- Husni E, Dachriyanus D, Saputri VW. 2020. Penentuan kadar fenolat total, uji aktivitas antioksidan dan antibakteri dari ekstrak dan fraksi kulit batang bintangor (*Calophyllum soulattri* Burm. F). J Sains Farm Klin. 7(1):92. <https://doi.org/10.25077/jsfk.7.1.92-98.2020>
- linuma M et al. 1997. New linear pyranoxanthenes from *Calophyllum apetalum*. Heterocycles [Internet]. 45(2):299–307. <https://doi.org/10.3987/COM-96-7652>
- Ito C et al. 2002. Chemical constituents of *Calophyllum brasiliensis*: structure elucidation of seven new xanthenes and their cancer chemopreventive activity. J Nat Prod. 65(3):267–272. <https://doi.org/10.1021/np010398s>
- Ito C, Miyamoto Y, Rao KS, Furukawa H. 1996. A novel dibenzofuran and two new xanthenes from *Calophyllum panicflorum*. Chem Pharm Bull. 44(2):441–443. <https://doi.org/10.1248/cpb.44.441>
- Karunakaran T et al. 2016. A new coumarin from stem bark of *Mesua hexapetala*. Nat Prod Res. 30(14):1591–1597. <https://doi.org/10.1080/14786419.2015.1120727>
- Karunakaran T, Firouz NS, Santhanam R, Jong VYM. 2022. Phytochemicals from *Calophyllum macrocarpum* Hook.f. and its cytotoxic activities. Nat Prod Res. 36(2):654–659. <https://doi.org/10.1080/14786419.2020.1795658>
- Khan MR, Kihara M, Omoloso AD. 2002. Antimicrobial activity of *Calophyllum soulattri*. Fitoterapia. 73(7–8):741–743. [https://doi.org/10.1016/S0367-326X\(02\)00242-3](https://doi.org/10.1016/S0367-326X(02)00242-3)
- Kyriakidis I, Vasileiou E, Pana ZD, Tragiannidis A. 2021. *Acinetobacter baumannii* antibiotic resistance mechanisms. Pathogens. 10(3):373. <https://doi.org/10.3390/PATHOGENS10030373>
- Laopian F, Kaennakam S, Rassamee K, Siripong P, Tip-Pyang S. 2019. Calaxanthenes A-C, three new xanthenes from the roots of *Calophyllum calaba* and the cytotoxicity. Nat Prod Res. 33(11):1584–1590. <https://doi.org/10.1080/14786419.2018.1425849>

- Lasarte-Monterrubio C et al. 2021. Activity of imipenem, meropenem, cefepime, and sulbactam in combination with the β -Lactamase inhibitor LN-1-255 against *Acinetobacter* spp. *Antibiotics* (Basel). 10(2):210. <https://doi.org/10.3390/antibiotics10020210>
- Lee JE et al. 2024. The influence of solvent choice on the extraction of bioactive compounds from Asteraceae: a comparative review. *Foods*. 13(19):3151. <https://doi.org/10.3390/FOODS13193151/S1>
- Liu M, Li K, Yan P, Wang X, Ouyang X. 2014. Effect of aminoglycosides on reducing the mutant selective window of *Acinetobacter baumannii* in combination therapy. *Chin J Infect Chemother*. 14(4):334–337. <https://www.scopus.com/inward/record.uri?eid=2-s2.0-84996479819&partnerID=40&md5=d0b1ab5a09fcaccf84df046065398ed5>
- Lizazman MA, Mian VJY, Karunakaran T, Suffian Y, Zamakshshari NH, Nazeri AM, Nazri NZHBM, Ismail MIB, Singh KKB. 2026a. Phytochemical composition, antioxidant and antibacterial activities of *Calophyllum canum* Hook. f. ex T. Anderson extracts: molecular docking insights. *Chem Biodivers*. 23(4):e00773. <https://doi.org/10.1002/cbdv.202500773>
- Lizazman MA, Jong VYM, Zamakshshari NH, Suffian Y, Ismail MIB, Md Yusof EN, Seruji NMUB. 2026b. Phytochemical investigation of *Calophyllum sundaicum* P.F.Stevens: isolation, structure elucidation, and biological potential. *Nat Prod Res*. 1–11. <https://doi.org/10.1080/14786419.2026.2613276>
- Lizazman MA, Jong VYM, Chua PF, Lim WK, Karunakaran T. 2023. Phytochemicals from *Calophyllum canum* Hook f. ex T. Anderson and their neuroprotective effects. *Nat Prod Res*. 37(12):2043–2048. <https://doi.org/10.1080/14786419.2022.2116021>
- Lizazman MA, Karunakaran T, Jong VYM. 2022. Trapezifolixanthone as a common constituent in the genus *Calophyllum*: an insight review. *Biocatal Agric Biotechnol*. 44(9):102471. <https://doi.org/10.1016/j.bcab.2022.102471>
- Mah SH et al. 2011. A new pyranoxanthone from *Calophyllum soulattri*. *Molecules*. 16(5):3999–4004. <https://doi.org/10.3390/molecules16053999>
- Mah SH et al. 2011. A new pyranoxanthone from the stem bark of *Calophyllum inophyllum*. *Lett Org Chem* [Internet]. 8(6):447–449. <https://doi.org/10.2174/157017811796064430>
- Mah SH et al. 2012. Phylatrin, a new cytotoxic xanthone from *Calophyllum soulattri*. *Molecules*. 17(7):8303–8311. <https://doi.org/10.3390/molecules17078303>
- Naves VML et al. 2019. Antimicrobial and antioxidant activity of *Garcinia brasiliensis* extracts. *S Afr J Bot*. 124:244–250. <https://doi.org/10.1016/j.sajb.2019.05.021>
- Nguyen THN et al. 2025. Trends of colistin MIC among *Acinetobacter baumannii* and *Pseudomonas aeruginosa* at a first-class hospital in Vietnam. *J Trop Med*. 2025(1):6165665. <https://doi.org/10.1155/jotm/6165665>
- Noh IA, Jong VYM. 2020. Phytochemicals, antimicrobials and antioxidants studies of the stem bark extract from *Calophyllum ferrugineum*. *Sci Res J*. 17(2):1–12. <https://doi.org/10.24191/srj.v17i2.6917>
- Pammi SSS, Suresh B, Giri A. 2023. Antioxidant potential of medicinal plants. *J Crop Sci Biotechnol*. 26(1):13–26. <https://doi.org/10.1007/s12892-022-00159-z>
- Sakai FD, Khong HY, Nyokat N. 2022. Phytochemicals contents and antibacterial properties of different solvent extracts from barks and leaves of *Ostodes pauciflora* Merr. *Med Plants*. 14(2):312–322. <https://doi.org/10.5958/0975-6892.2022.00036.3>
- Scorciapino MA et al. 2017. Rationalizing the permeation of polar antibiotics into Gram-negative bacteria. *J Phys Condens Matter*. 29(11):113001. <https://doi.org/10.1088/1361-648X/AA543B>
- Seruji NMU et al. 2023. 8-Dihydroxy-2,2-dimethyl-12-(3-methylbut-2-enyl)pyrano[3,2-b]xanthen-6-one (brasixanthone B). *IUCrdata*. 8(1):x221198. <https://doi.org/10.1107/S2414314622011981>
- Seruji NMU et al. 2024. Molecular docking studies and in-vitro cholinesterase inhibitory activities of chemical constituents of *Calophyllum gracilentum*. *Phytochem Lett*. 63:93–100. <https://doi.org/10.1016/j.phytol.2024.08.007>
- Shen YC, Wang LT, Khalil AT, Chiang LC, Cheng PW. 2005. Bioactive pyranoxanthones from the roots of *Calophyllum blancoi*. *Chem Pharm Bull* (Tokyo). 53(2):244–247. <https://doi.org/10.1248/cpb.53.244>

- Stevens PF. 1980. A revision of the old world species of *Calophyllum* (Guttiferae). J. Arnold Arbor. 61:117–424. <https://doi.org/10.2307/1222522>
- Suffian Y et al. 2026. Isolation of phytochemicals from *Calophyllum nodosum* and in silico evaluation of their drug-likeness and DNA gyrase inhibition potential. J. Sci. Math. Lett. 14(1):1–14. <https://doi.org/10.37134/jsml.vol14.1.1.2026>
- Tanjung M et al. 2018. Airlanggins A-B, two new isoprenylated benzofuran-3-ones from the stem bark of *Calophyllum soulattri*. Nat Prod Res. 32(13):1493–1498. <https://doi.org/10.1080/14786419.2017.1380027>
- Tee KH et al. 2018. Natural products from stem bark of *Calophyllum andersonii*. Pertanika J Trop Agric Sci. 41(2):759–768.
- Tinrat S. 2022. Phytochemical screenings, antibacterial and anti-biofilm activities of *Garcinia cowa* Roxb. leaves extracts and its synergistic effect with antibiotic. Pharm Sci Asia. 49(6):556–567. <https://doi.org/10.29090/psa.2022.06.22.280>
- Xochicale-Santana L, Vidyasagar CC, Muñoz-Flores BM, Pérez VMJ. 2021. Microwave assisted organic syntheses (MAOS): the green synthetic method. In: Handbook of greener synthesis of nanomaterials and compounds: volume 1: fundamental principles and methods. Elsevier. p. 491–542. <https://doi.org/10.1016/B978-0-12-821938-6.00015-3>
- Yang R et al. 2017. Xanthones from the pericarp of *Garcinia mangostana*. Molecules. 22(5):1–10. <https://doi.org/10.3390/molecules22050683>
- Yimdjo MC et al. 2004. Antimicrobial and cytotoxic agents from *Calophyllum inophyllum*. Phytochemistry. 65(20):2789–2795. <https://doi.org/10.1016/j.phytochem.2004.08.024>
- Zaine NFZ, Abd Halim AN, Saat R, Mian VJY, Zamakshshari NH. 2025. Antibacterial activity of *Garcinia* spp. by molecular docking simulations: an overview. Phytochem Rev. 24(4):2587–2628. <https://doi.org/10.1007/s11101-024-09997-x>
- Zamakshshari NH, Ee GCL, Daud S, Teh SS, Mah SH. 2018. Phytochemicals from *Calophyllum depressinervosum*. Asian J Chem. 30(5):975–978. <https://doi.org/10.14233/ajchem.2018.21045>
- Zamakshshari NH, Ee GCL, Ismail IS, Ibrahim Z, Mah SH. 2019. Cytotoxic xanthones isolated from *Calophyllum depressinervosum* and *Calophyllum buxifolium* with antioxidant and cytotoxic activities. Food Chem Toxicol. 133:110800. <https://doi.org/10.1016/j.fct.2019.110800>
- Zouine N, Ghachtouli NE, Abed SE, Koraichi SI. 2024. A comprehensive review on medicinal plant extracts as antibacterial agents: factors, mechanism insights and future prospects. Sci Afr. 26:e02395. <https://doi.org/10.1016/j.sciaf.2024.e02395>