Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Antioxidant Potential of *Calophyllum canum* P. F. Stevens*:* Xanthones, Phenolics, and Radical Scavenging Activity

Mas Atikah Lizazman
Universiti Teknologi MARA, Kota Samarahan, Sarawak, Malaysia
Vivien Jong Yi Mian
vivien@uitm.edu.my

Universiti Teknologi MARA, Kota Samarahan, Sarawak, Malaysia

Research Article

Keywords: Calophyllum canum, extract, canumolactone, xanthone, TPC, TFC, DPPH.

Posted Date: April 30th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-4336474/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: The authors declare no competing interests.

Abstract

The isolation and purification of the ethyl acetate of *C. canum* stem bark have yielded a new *α,β*-unsaturated *δ*-lactone compound, canumolactone **(8)**, along with known xanthones, 1-hydroxy-7-methoxyxanthone **(1)**, caloxanthone C **(2)**, trapezifolixanthone **(3)**, ananixanthone **(4)**, euxanthone **(5)**, gentisin **(6)**, 2-hydroxyxanthone **(7)**, and *α*-mangostin **(9)**. In this study on *C. canum* extracts, the total phenolic content (TPC), total flavonoid content (TFC), and radical scavenging activity (RSA) were investigated to assess the antioxidant potential. The extraction of *C. canum* stem bark yielded various crude extracts, with the ethyl acetate extract showing the highest RSA (97.14 ± 0.24 %) and TPC (277.33 ± 9.65 mg GAE/g extract). The TFC values varied across extracts, with the dichloromethane extract displaying the highest TFC (117.96 ± 3.35 mg QE/g extract). A strong positive correlation was observed between TPC and RSA, indicating the significant role of phenolic compounds in the antioxidant activity of the extracts. Conversely, the relationship between TFC and RSA was weak, suggesting a minor contribution of flavonoids to the antioxidant potential of the extracts. These findings highlight the importance of phenolic compounds in determining the antioxidant activity of *C. canum* extracts.

1. Introduction

Calophyllum canum, commonly known as 'bintangor merah', stands as a prominent subject of investigation within the domain of natural product research. This large evergreen tree, towering up to 36 meters, thrives in diverse ecosystems, ranging from well-drained mixed dipterocarp forests to peat swamps, exhibiting its adaptability up to altitudes of 1200 meters. Widely distributed across Malaysia, Sumatera, and Northwestern Borneo, this species is integral to the local landscape (Taher et al. 2020).

The distinctive attributes of *C. canum* encompass a non-buttress trunk, the absence of spurs, and a yellowish outer bark adorned with closely spaced lines of lenticels (Aminudin et al. 2021). Recognizable features include a plump terminal bud, leaf blades exhibiting undulate margins and brown-vinaceous surfaces, and a midrib that gracefully narrows from the base (Stevens 1980). Local communities, particularly in Sarawak, recognize the significance of the plant as a vital source of timber, with its wood serving diverse purposes. Moreover, the latex extracted from *C. canum* finds traditional use in tuba fishing (Lizazman et al. 2023). The species derives its name from the grayish look of the entire inflorescence, with the epithet 'canum' signifying 'hoary' or 'gray'. Notably, *Calophyllum borneense* Vesque serves as a synonym for this species (Stevens 1980).

Beyond its botanical allure, *C. canum* has captured attention for its chemical composition. Phytochemical studies have revealed the presence of xanthones, triterpenoids, and flavonoids, offering potential avenues for pharmaceutical exploration (Carpenter et al. 1969; Lim et al. 2016; Taher et al. 2020; Aminudin et al. 2021; Lizazman et al. 2023). Biological studies further highlight the diverse activities of *C. canum*, including anti-bacterial (Susanti et al. 2011; Alkhamaiseh et al. 2012), anti-oxidant (Ramli et al. 2019), cytotoxic (Lim et al. 2016; Taher et al. 2020), and neuroprotective properties (Lizazman et al. 2023).

In the ongoing quest to combat a myriad of diseases and health challenges, humanity has embraced a diverse array of strategies. Noteworthy among these approaches is the use of medicinal plants for treating various ailments, now recognized as a complementary and alternative therapy when integrated with conventional treatments (Nwozo et al. 2023). Emerging as key players in this therapeutic landscape are free radicals, reactive and unstable oxygen/nitrogen species (ROS/RNS), such as the superoxide anion radical, hydrogen peroxide, hydroxyl radical, and singlet oxygen. These entities can trigger chain reactions leading to cellular damage, with the aerobic system naturally producing RNS and ROS as byproducts. Elevated production of ROS and RNS gives rise to oxidative and nitrosative stress, respectively, culminating in tissue damage and cell death through the impairment of proteins, lipids, and DNA (Zafar et al. 2023).

Recent studies have elucidated the pivotal role of antioxidants in this intricate dance, scavenging free radicals and protecting the body from oxidative stress by removing radical intermediates and undergoing oxidation themselves (Nwozo et al. 2023; Pammi et al. 2023). The significance of this delicate balance between oxidants and antioxidants, collectively known as oxidative stress, has been underscored in recent scientific inquiries. Imbalances in this equilibrium have been implicated in the development and progression of various diseases, encompassing cancer, neurological disorders, metabolic syndrome, cardiovascular diseases, and inflammatory conditions (Nwozo et al. 2023; Pammi et al. 2023; Zafar et al. 2023). This compelling interplay sheds light on the underlying mechanisms contributing to the pathogenesis of a spectrum of illnesses, further highlighting the potential of medicinal plants and antioxidant therapies in this ongoing medical narrative.

Plants, adept at responding to both biotic and abiotic stress conditions, manifest a robust defense mechanism through the synthesis of a diverse array of antioxidants. These natural antioxidants, classified as secondary metabolites, play a pivotal role in mitigating oxidative stress induced by reactive oxygen species, safeguarding plant cells against damage and cellular oxidation (Pammi et al. 2023). Moreover, the intricate interplay of oxidants and antioxidants derived from food exerts a profound influence on the body's oxidative stress homeostasis, yielding beneficial effects in preventing cancer and mitigating aging processes (Pammi et al. 2023). Emanating from the essential role these chemicals play in sustaining plant life, their consumption by humans translates into health benefits, particularly in terms of modulating the oxidative stress homeostasis within the human body (Nwozo et al. 2023; Zafar et al. 2023). External sources of antioxidants are predominantly found in foods rich in vitamins A, E (alpha tocopherol), C (ascorbic acid), minerals, and polyphenols, with a notable prevalence in plant-derived compounds (Nwozo et al. 2023).

In the vast landscape of bioactive compounds, polyphenols stand out with over 8000 variants identified in plants and fruits, approximately 500 of which exhibit biological activity and can be sourced from natural origins, industrial food, or juices (Marcucci et al. 2023). Polyphenols are a well-known group of phenolic systems defined by at least two phenyl rings and one or more hydroxyl groups (Saparbekova et al. 2023). These secondary metabolites display an impressive array of properties, including highly effective free radical scavenging, inhibition of hydrolytic and oxidative enzymes, and anti-inflammatory

action (Nwozo et al. 2023). The phenolic compounds are distributed across plant tissues and their types and quantities are vary significantly based on plant varieties, maturity, seasons, and regions. Notably, their exceptional antioxidant potential arises from high redox reactivity, enabling the reduction of free radicals and prevention of destructive cascade reactions (Lyu et al. 2023).

Polyphenols, found predominantly in glycosidic form, can be broadly classified into flavonoids and non-flavonoids, with flavonoids showcasing diverse beneficial abilities ranging from their ability to scavenge a wide range of oxygen, chlorine and nitrogen species such as hydroxyl ions, peroxynitrous acid, superoxide, reactive oxygen, peroxylradicals and hypochlorious acid to their ability to chelate ions by decreasing the metal ions pro-oxidant capacity. (Nwozo et al. 2023; Marcucci et al. 2023). This subgroup includes over 4000 types, further categorized into flavonols, flavanones, flavones, catechins, isoflavones, anthocyanidins, dihydroflavonols, and chalcones. Notably, flavonols like quercetin, abundant in vegetables, fruits, and tea, exhibit powerful natural antioxidant and cytotoxic properties (Azeem et al. 2023). Beyond flavonoids, non-flavonoid phenolic compounds, such as phenolic acids, xanthones, tannins, and stilbenes, bring their antioxidant-related benefits to the table. Phenolic acids feature a carboxyl group linked to a benzene ring, while xanthones, stilbenes, tannins, and lignans contain at least two aromatic rings fused or linked by C–C single or double bonds (Marcucci et al. 2023).

The close connection between antioxidants from plants and their positive impact on human health aligns with the growing concern over health problems attributed to oxidative stress (Zafar et al. 2023). Exploring the bioactive potential of traditional medicinal herbs emerges as a promising avenue for developing therapeutic and management techniques that target essential cellular pathways related to chronic illnesses. The World Health Organization's assertion that 80% of individuals globally rely on traditional medicine underscores the significance of antioxidant phytochemicals derived from medicinal plants as a primary source of treatment for various therapeutic purposes (Zafar et al. 2023). With their robust pharmacological effects, low toxicity, and economic feasibility, plants have become integral in global scientific endeavors to uncover therapeutic qualities for medicinal purposes. Despite the continued utilization of medicinal plants for biomolecules in novel medications, the vast potential of numerous plant species worldwide remains largely untapped. Recent research trends emphasize the preference for natural antioxidants over synthetic counterparts, driven by their enhanced efficiency (Pammi et al. 2023). These bioactive constituents play a crucial role in maintaining health and serve as a vital link between the food and pharmaceutical industries (Nwozo et al. 2023). The exploration of the diverse plant species and their antioxidant potential holds promise for advancing therapeutic interventions and addressing the growing global burden of chronic illnesses.

In this study, we examined the total phenolic content (TPC), total flavonoid content (TFC), and radical scavenging activity (RSA) using DPPH method of *C. canum* extracts. Additionally, the current investigation reports the isolation of compounds from from the ethyl acetate of *C. canum* extract.

2. Result and discussion

2.1 Extraction and isolation of C. canum stem bark

The extraction of the *C. canum* stem bark has yielded oily yellowish-brown *n*-hexane (22.0 g), light brown dichloromethane (15.1 g), dark brown chloroform (24.8 g), reddish-brown ethyl acetate (10.9 g), and reddish-black methanol (21.3 g) crude extracts. The percentage yield of the crude extracts was tabulated in Table 1. The compounds from the hexane and chloroform extracts have been previously reported (Lizazman et al. 2023).

Meanwhile, the isolation of ethyl acetate extract has identified l-hydroxy-7-methoxyxanthone **(1)** (Charoensup et al. 2022), caloxanthone C **(2)** (Lizazman et al. 2023), trapezifolixanthone **(3)** (Lizazman et al. 2022), ananixanthone **(4)** (Karunakaran et al. 2020), euxanthone **(5)** (Lim et al. 2019), gentisin **(6)** (Zheng et al. 2014), 2-hydroxyxanthone **(7)** (Amanatie et al. 2017), canumolactone **(8)**, α-mangostin **(9)** (Morelli et al. 2015; Abate et al. 2022) as shown in Figure 1. The structural elucidation of the compounds was achieved using 1D, 2D NMR, and comparison of the spectral data with the previous literature. The spectral data for compounds **1-9** and the flow chart of the isolation works were reported in the supplementary data (3.4.1-3.4.9) and Figure S1 respectively. The 1D and 2D NMR spectra of canumolactone **(8)** were also reported (Figure S4-S8).

Table 1. Extraction yield of *C. canum* extracts

Crude extracts	Dry yield (g)	Percentage yield (%)
n-hexane	22.0	2.20
dichloromethane	15.1	1.51
chloroform	24.8	2.48
ethyl acetate	10.9	1.09
methanol	21.3	2.13

2.2 Antioxidant assay

The antioxidant activity of the extracts was determined using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay (Trinh et al. 2014). The radical scavenging activity (RSA), which indicates the ability of the extracts to neutralize free radicals, varied notably across the extracts. The RSA percentages were ranged from 2.65 to 97.14 % as tabulated in Table 2. The ethyl acetate extract exhibited the highest RSA (97.14 ± 0.24 %), followed closely by the methanolic extract (86.89 ± 0.12 %). The lowest activity was demonstrated by the *n*-hexane extract with 2.65 ± 1.19 %. Meanwhile, comparable radical scavenging activity was exhibited by chloroform extract (19.46 ± 1.26 %) and dichloromethane extract (15.83 ± 2.15 %). These findings suggest that certain extracts possess superior antioxidant capabilities, potentially due to the presence of specific bioactive compounds. The results were tabulated in Table 2.

2.3 Total phenolic content

The total phenolic content of the extracts was determined using the Folin-Ciocalteu (FC) method (Naves et al. 2019). The total phenolic content (TPC) of the crude extracts was quantified using the established standard calibration curve of gallic acid depicted in Figure S2 ($y = 0.0079x - 0.0773$, $R^2 = 0.9697$). The result obtained revealed significant differences among the extracts, and expressed as milligrams of gallic acid equivalent per gram of dried weight extract (mg GAE/ g extract). The TPC was ranged from 83.07 to 277.33 mg GAE/g extract as tabulated in Table 2. The ethyl acetate extract contained the highest concentration of phenolic compounds (277.33 ± 9.65 mg GAE/g extract), followed by the methanolic extract (223.48 ± 12.88 mg GAE/g extract). The chloroform, dichloromethane, and *n*-hexane extracts displayed progressively lower concentrations, with values of 96.06 ± 2.64 mg GAE/g extract, 92.35 ± 3.43 mg GAE/g, and 83.07 ± 1.84 mg GAE/g extract, respectively. Phenolic compounds are well-known for their antioxidant properties, and the higher TPC values observed in certain extracts align with their enhanced RSA. The results were tabulated in Table 2.

2.4 Total flavonoid content

The total flavonoid content of the extracts was determined using the aluminium chloride calorimetric method (Sakai et al. 2022). The total flavonoid content (TFC) of the crude extracts was quantified using the established standard calibration curve of quercetin depicted in Figure S3 ($y = 0.0321x - 0.0703$, $R^2 = 0.9548$). The result highlighted considerable variability across the extracts, and expressed as milligrams of quercetin equivalent per gram of dried weight extract (mg QE/ g extract). The TFC ranging from 11.55 to 139.56 mg QE/ g extract as tabulated in Table 2. The highest TFC was found in the chloroform extract (139.56 ± 3.19 mg QE/g extract), followed by the dichloromethane extract (117.96 ± 3.35 mg QE/g extract). Subsequently, the *n*-hexane extract exhibited a falovonoid content of 11.55 ± 0.32 mg QE/g extract, while the ethyl acetate and methanolic extracts showed values of 87.66 ± 0.36 mg QE/g extract and 43.51 ± 2.22 mg QE/g extract, respectively. Flavonoids, like phenolic compounds, possess notable antioxidant properties, contributing to the overall RSA of the extracts. The results were tabulated in Table 2.

Table 2. Radical scavenging activity, total phenolic content, and total flavonoid content of the *C. canum* crude extracts

Crude extracts	Radical scavenging activity (%)	Total phenolic content (mg GAE/ g extract)	Total flavonoid content (mg QE/ g extract)
n-hexane	2.65 ± 1.19	83.07 ± 1.84	11.55 ± 0.32
dichloromethane	15.83 ± 2.15	92.35 ± 3.43	117.96 ± 3.35
chloroform	19.46 ± 1.26	96.06 ± 2.64	139.56 ± 3.19
ethyl acetate	97.14 ± 0.24	277.33 ± 9.65	87.66 ± 0.36
methanol	86.89 ± 0.12	223.48 ± 12.88	43.51 ± 2.22

An intriguing correlation between RSA and phytochemical content of the *C. canum* crude extracts was observe as in Figure 2. Notably, there appears to be a consistent trend between the levels of certain phytochemicals and the antioxidant potential of the extracts. When examining the RSA (%), we found that extracts with higher TPC (mg GAE/g extract) tended to exhibit greater RSA. This suggests that the presence of phenolic compounds may contribute significantly to the antioxidant potential of the extracts. On the other hand, the relationship between RSA (%) and TFC (mg QE/g extract) appeared less pronounced, indicating that flavonoid content may not play as substantial a role in determining the antioxidant activity of the extracts compared to phenolic compounds.

Based on the Pearson correlation coefficient (r) and the associated significance levels (p-values), the relationship between RSA (%) and TPC exhibits contrasting patterns (Table 3). The strong positive correlation coefficient of 0.9875 ($p<0.05$) suggests a highly significant linear relationship between RSA (%) and TPC. These findings support the notion that phenolic compounds contribute significantly to the antioxidant activity exhibited by *C. canum* extracts, with higher levels of phenolic content corresponding to enhanced RSA. However, the correlation coefficient of 0.1338 ($p>0.05$) between RSA (%) and TFC suggests a weak and statistically insignificant linear relationship. This indicates a negligible linear relationship between the antioxidant potential and the concentration of flavonoids in the extracts. While flavonoids are recognized for their antioxidant properties, the results suggest that, in the context of *C. canum* extracts, phenolic compounds may play a more significant role in determining the antioxidant activity compared to flavonoids.

Table 3. Pearson correlation coefficients between radical scavenging activity (%) and phytochemical content

Phytochemical content	Pearson correlation coefficient (r)	Significant level (p-value)
TPC	0.9875	0.002
TFC	0.1338	0.830

2.5 Discussion

Xanthones are commonly found in *Calophyllum* plants, known for their diverse biological activities. Previous studies on *C. canum* have identified several xanthones from different parts of plant. For instance, (Carpenter et al. 1969) isolated osajaxanthone, 2- (3,3-dimethylallyl) -1,3,7- trihydroxyxanthone, and 2- (3,3-dimethylallyl) -1,3,5,6-tetrahydroxyxanthone from the heartwood, while (Taher et al. 2020; Lizazman et al. 2023) reported biscaloxanthone, trapezifolixanthone A, 5-methoxytrapezifolixanthone, 5-methoxyananixanthone, 1,5-dihydroxy -3- methoxy-4 -isoprenylxanthone, and 6-deoxyisojacareubin from the stem bark. The current study focused on isolating compounds from the ethyl acetate extract of *C. canum*, resulting in the identification of 1-hydroxy-7-methoxyxanthone **(1)**, caloxanthone C **(2)**, trapezifolixanthone **(3)**, ananixanthone **(4)**, euxanthone **(5)**, gentisin **(6)**, 2-hydroxyxanthone **(7)**, canumolactone **(8)**, and *α*-mangostin **(9)**.

In terms of radical scavenging activity (RSA), the *n*-hexane extract exhibited the lowest activity (2.65 ± 1.19 %) consistent with previous findings indicating a higher half response concentration (RC_{50} 85 ± 4.35 µg/mL) compared to the methanol extract (Alkhamaiseh et al. 2012). (Susanti et al. 2011) also reported weak antioxidant (IC_{50} 0.26 mg/mL) for the *n*-hexane extract of *C. canum* stem bark. Similarly, the dichloromethane portrayed weak RSA with 15.83 ± 2.15 % which is comparable with the previous study indicating RC_{50} 91.6 ± 6.65 µg/mL. In contrast, the methanolic extract displayed high RSA (86.89 ± 0.12 %), supported by its low IC_{50} 11.89 ± 0.74 µg/mL (Ramli et al. 2019) and RC_{50} < 31.25 µg/mL (Alkhamaiseh et al. 2012).

Additionally, the *n*-hexane, dichloromethane, and chloroform extracts exhibited similarly low total phenolic content (TPC), with the *n*-hexane extract displaying the lowest TPC at 83.07 ± 1.84 mg gallic acid equivalents per gram (GAE/g) of extract. This finding is consistent with a previous report (Alkhamaiseh et al. 2012), which indicated a TPC of 1.292 ± 0.001 µg gallic acid per 10 mg of extract. Notably, the TPC of the extracts increased with the polarity of the solvents used for extraction. The dichloromethane extract (92.35 ± 3.43 mg GAE/g extract) exhibited a higher TPC than the *n*-hexane extract, as observed in previous research (1.992 ± 0.002 µg gallic acid/10 mg extract) (Alkhamaiseh et al. 2012). However, the chloroform extract demonstrated a slightly higher TPC value than that of the dichloromethane extract. The ethyl acetate extract displayed the highest TPC, followed by the methanolic extract (223.48 ± 12.88 mg GAE/g extract). In comparison with previous research (Alkhamaiseh et al. 2012), our results align with the observation that methanol yielded the highest TPC, with 3.517 ± 0.017 µg gallic acid/10 mg extract. However, another study reported a lower TPC for the methanolic extract at 77.11 ± 2.78 mg GAE/g of extract (Ramli et al., 2019).

Moreover, the *n*-hexane extract exhibited the lowest amount of total flavonoid compounds, measuring 11.55 ± 0.32 mg quercetin equivalents per gram (QE/g) of extract. This finding aligns with a previous report by (Alkhamaiseh et al. 2012), which indicated a total flavonoid content (TFC) of 5.040 ± 0.184 µg quercetin per 10 mg of extract. In contrast, the dichloromethane extract displayed the highest TFC value at 117.96 ± 3.35 mg QE/g extract. However, (Alkhamaiseh et al. 2012) reported a significantly lower TFC for the dichloromethane extract at 11.201 ± 2.446 µg quercetin per 10 mg of extract, indicating a substantial difference in the observed TFC. Furthermore, our study revealed that the methanolic extract showcased a TFC of 43.51 ± 2.22 mg QE/g extract. This contrasts with the findings of the previous report, which documented a TFC of 14.643 ± 1.222 µg quercetin per 10 mg of extract (Alkhamaiseh et al. 2012). These inconsistencies in TFC values between our study and previous reports emphasize the importance of methodological differences, plant variability, and extraction techniques, which can significantly influence the quantification of bioactive compounds in natural extracts. Importantly, the antioxidant activity, TPC and TFC of the chloroform and ethyl acetate extracts is reported here for the first time.

According to the Pearson's correlation analysis, the statistical data indicate a positive relationship between high total phenolic content (TPC) and strong antioxidant activity within the extracts. This suggests that phenolic compounds play a significant role in the antioxidant activity measured by the

DPPH method. Antioxidant compounds possess varying polarities, leading to differences in their concentrations depending on the solvent used for extraction or isolation. Solvents can generally be categorized as polar (such as ethanol, methanol, and aqueous solutions) or nonpolar (including acetone, ethyl acetate, and hexane), based on their ability to form ions in solution (Nwozo et al. 2023).

3. Experimental

See supplementary data.

4. Conclusion

The investigation into the antioxidant capacity of *C. canum* stem bark extracts revealed a notable correlation between elevated phenolic content and potent antioxidant efficacy. Notably, this study presents the first discovery of canumolactone. Additionally, various xanthone compounds were identified in the extract, with the ethyl acetate extract exhibiting the highest levels of radical scavenging activity and total phenolic content. The presence of these bioactive constituents highlights the therapeutic potential of *C. canum* in addressing oxidative stress-related diseases.

Declarations

Acknowledgment

The authors would like to acknowledge the Sarawak Research Development Council (SRDC) (RDCRG/CAT/2019/11) and Universiti Teknologi MARA for financial assistance and support given throughout the research conducted on genus *Calophyllum* by MAL and VJYM. The Sarawak Biodiversity Centre (SBC) is also acknowledged.

Authors Contribution

MAL has contributed to writing-original draft preparation resources, VJYM conceptualization writing-review, supervision, and funding acquisition,

Disclosure Statement

The authors declare no conflict of interest.

Funding

The research project conducted by VJYM, MAL was funded by Sarawak Research Development Council (SRDC) (RDCRG/CAT/2019/11).

References

1. Abate M, Pagano C, Masullo M, Citro M, Pisanti S, Piacente S, Bifulco M. 2022. Mangostanin, a xanthone derived from Garcinia mangostana fruit, exerts protective and reparative effects on oxidative damage in human keratinocytes. Pharmaceuticals. 15(1). https://doi.org/10.3390/ph15010084
2. Alkhamaiseh SI, Taher M, Ahmad F, Qaralleh H, Althunibat OY, Susanti D, Ichwan SJA. 2012. The phytochemical content and antimicrobial activities of Malaysian Calophyllum canum (stem bark). Pak J Pharm Sci. 25(3):555–563.
3. Amanatie A, Jumina J, Mustofa M, Hanafi M, Kadidae LO, Sahidin I. 2017. Synthesis of 2-hidroxyxanthone from xanthone as a basic material for new antimalarial drugs. Asian J Pharm Clin Res. 10(12):242–246. https://doi.org/10.22159/ajpcr.2017.v10i12.19858
4. Aminudin NI, Norazhar NA, Ahmad F. 2021. Development of a HPLC method for quantification of amentoflavone in leaf extracts of three Calophyllum species. Malaysian J Chem. 23(2):33–39. https://doi.org/10.55373/mjchem.v23i2.996
5. Azeem M, Hanif M, Mahmood K, Ameer N, Chughtai FRS, Abid U. 2023. An insight into anticancer, antioxidant, antimicrobial, antidiabetic and anti-inflammatory effects of quercetin: A review. Polymer Bulletin. 80(1):241–262. https://doi.org/10.1007/s00289-022-04091-8
6. Carpenter I, Locksley HD, Scheinmann F. 1969. Extractives from Guttiferae. Part X. The isolation and structure of four xanthones from Calophyllum canum Hook F. J Chem Soc C Org.(3):486–488. https://doi.org/10.1039/j39690000486
7. Charoensup R, Egoh M, Suthiphasilp V, Phukhatmuen P, Maneerat T, Duangyod T, Laphookhieo S. 2022. Antidiabetic properties of garciniacowone L, a new xanthone with an unusual 5,5,8a-trimethyloctahydro-2H-1-benzopyran moiety, and other xanthones from the twig extract of Garcinia cowa Roxb. ex Choisy. J King Saud Univ Sci [Internet]. 34(6):102201. https://doi.org/10.1016/j.jksus.2022.102201
8. Karunakaran T, Firouz NS, Santhanam R, Jong VYM. 2020. Phytochemicals from Calophyllum macrocarpum Hook.f. and its cytotoxic activities. Nat Prod Res [Internet]. 36(2):1–6. https://doi.org/10.1080/14786419.2020.1795658
9. Lim CK, Gan SY, Jong VYM, Leong CO, Mai CW, Chee CF. 2019. Cytotoxic activity of phytochemicals from the stem bark of Calophyllum castaneum. Pak J Pharm Sci. 32(5):2183–2187.
10. Lim CK, Hemaroopini S, Gan SY, Loo SM, Low JR, Jong VYM, Soo HC, Leong CO, Mai CW, Chee CF. 2016. In vitro cytotoxic activity of isolated compounds from Malaysian Calophyllum species. Med Chem Res. 25(8):1686–1694. https://doi.org/10.1007/s00044-016-1606-y
11. 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 [Internet]. 37(12):2043–2048. https://doi.org/10.1080/14786419.2022.2116021
12. Lizazman MA, Karunakaran T, Jong ViYM. 2022. Trapezifolixanthone as a common constituent in the genus Calophyllum: An insight Review. Biocatal Agric Biotechnol [Internet]. 44(9):102471. https://doi.org/10.1016/j.bcab.2022.102471

13. Lyu X, Agar OT, Barrow CJ, Dunshea FR, Suleria HAR. 2023. Phenolic compounds profiling and their antioxidant capacity in the peel, pulp, and seed of Australian grown avocado. Antioxidants. 12(1):185. https://doi.org/10.3390/antiox12010185
14. Marcucci G, Domazetovic V, Nediani C, Ruzzolini J, Favre C, Brandi ML. 2023. Oxidative stress and natural antioxidants in osteoporosis: Novel preventive and therapeutic approaches. Antioxidants. 12(2):373. https://doi.org/10.3390/antiox12020373
15. Morelli CF, Biagiotti M, Pappalardo VM, Rabuffetti M, Speranza G. 2015. Chemistry of α-mangostin. Studies on the semisynthesis of minor xanthones from Garcinia mangostana. Nat Prod Res. 29(8):750–755. https://doi.org/10.1080/14786419.2014.986729
16. Naves VML, dos Santos MH, Ribeiro IS, da Silva CA, Silva NC, da Silva MA, da Silva GA, Dias ALT, Ionta M, Dias DF. 2019. Antimicrobial and antioxidant activity of Garcinia brasiliensis extracts. S Afr J Bot [Internet]. 124:244–250. https://doi.org/10.1016/j.sajb.2019.05.021
17. Nwozo OS, Effiong EM, Aja PM, Awuchi CG. 2023. Antioxidant, phytochemical, and therapeutic properties of medicinal plants: A review. Int J Food Prop. 26(1):359–388. https://doi.org/10.1080/10942912.2022.2157425
18. 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
19. Ramli SN, Aminudin NI, Ahmad F, Susanti D. 2019. Comparison of extraction techniques for three Calophyllum species and their antioxidant activity. Malaysian J Anal Sci. 23(4):586–594. https://doi.org/10.17576/mjas-2019-2304-04
20. 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
21. Saparbekova AA, Kantureyeva GO, Kudasova DE, Konarbayeva ZK, Latif AS. 2023. Potential of phenolic compounds from pomegranate (Punica granatum L.) by-product with significant antioxidant and therapeutic effects: A narrative review. Saudi J Biol Sci. 30(2). https://doi.org/10.1016/j.sjbs.2022.103553
22. Stevens PF. 1980. A revision of the Old World species of Calophyllum (Guttiferae). J Arnold Arbor. 61(2):117–424. https://doi.org/10.2307/1222522
23. Susanti D, Taher M, Attoumani N, Ahmad F. 2011. Free radical scavenging and antibacterial activities of Malaysian Guttiferae plants. J Med Plant Res. 5(31):6714–6718. https://doi.org/10.5897/jmpr11.678
24. Taher M, Salleh WMNHW, Alkhamaiseh SI, Ahmad F, Rezali MF, Susanti D, Hasan CM. 2020. A new xanthone dimer and cytotoxicity from the stem bark of Calophyllum canum. Z Naturforsch C. 76(1–2):87–91. https://doi.org/10.1515/znc-2020-0089
25. Trinh DH, Ha LD, Tran PT, Nguyen LHD. 2014. Isoprenylated xanthone and benzophenone constituents of the pericarp of garcinia planchonii. Nat Prod Commun. 9(12):1737–1740. https://doi.org/10.1177/1934578X1400901219

26. Zafar F, Asif HM, Shaheen G, Ghauri AO, Rajpoot SR, Tasleem MW, Shamim T, Hadi F, Noor R, Ali T, et al. 2023. A comprehensive review on medicinal plants possessing antioxidant potential. Clin Exp Pharmacol Physiol. 50(3):205–217. https://doi.org/10.1111/1440-1681.13743
27. Zheng HH, Luo CT, Chen H, Lin JN, Ye CL, Mao SS, Li YL. 2014. Xanthones from Swertia mussotii as multitarget-directed antidiabetic agents. ChemMedChem. 9(7):1374–1377. https://doi.org/10.1002/cmdc.201300507

Figures

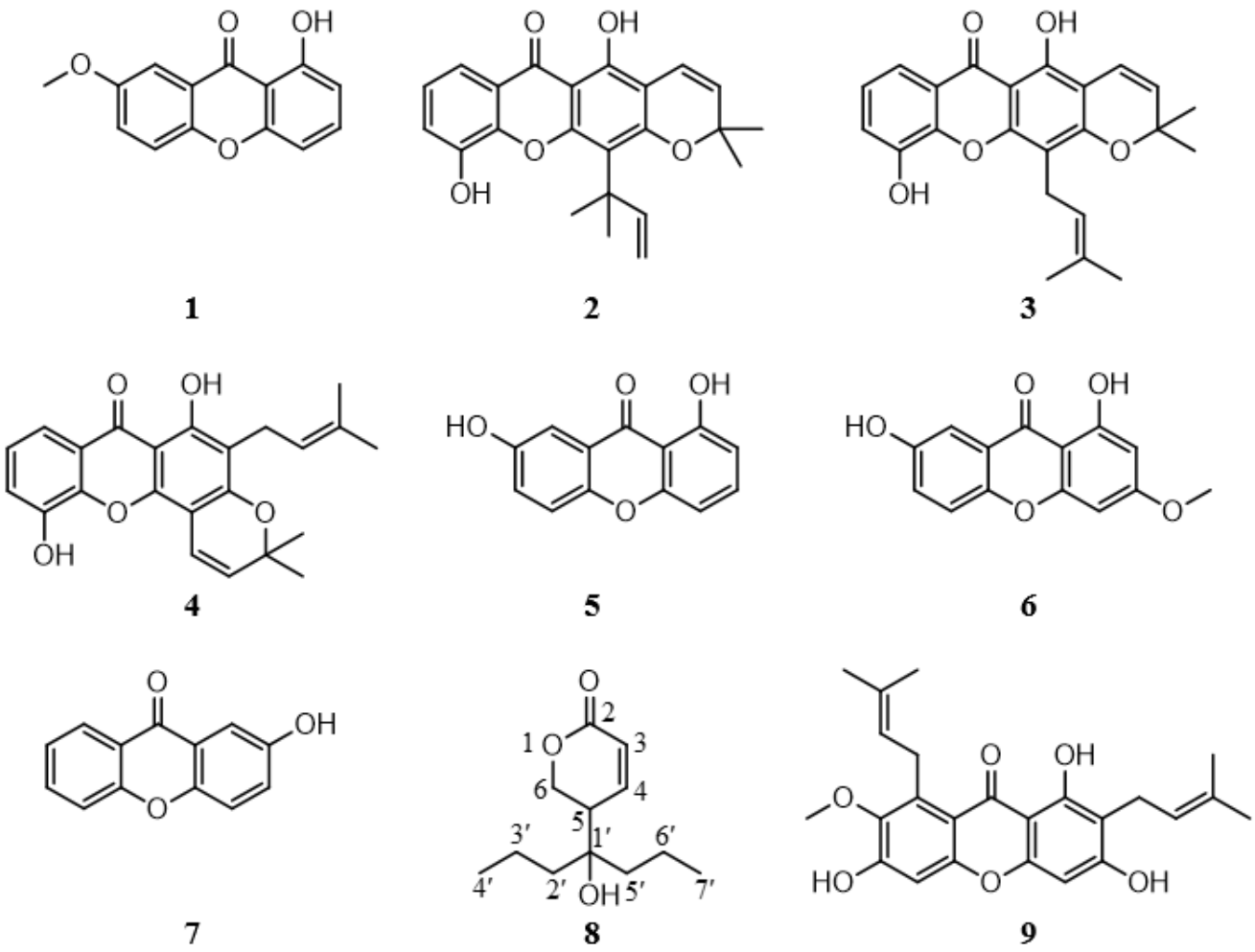


Figure 1

Structure of compounds **1-9**.

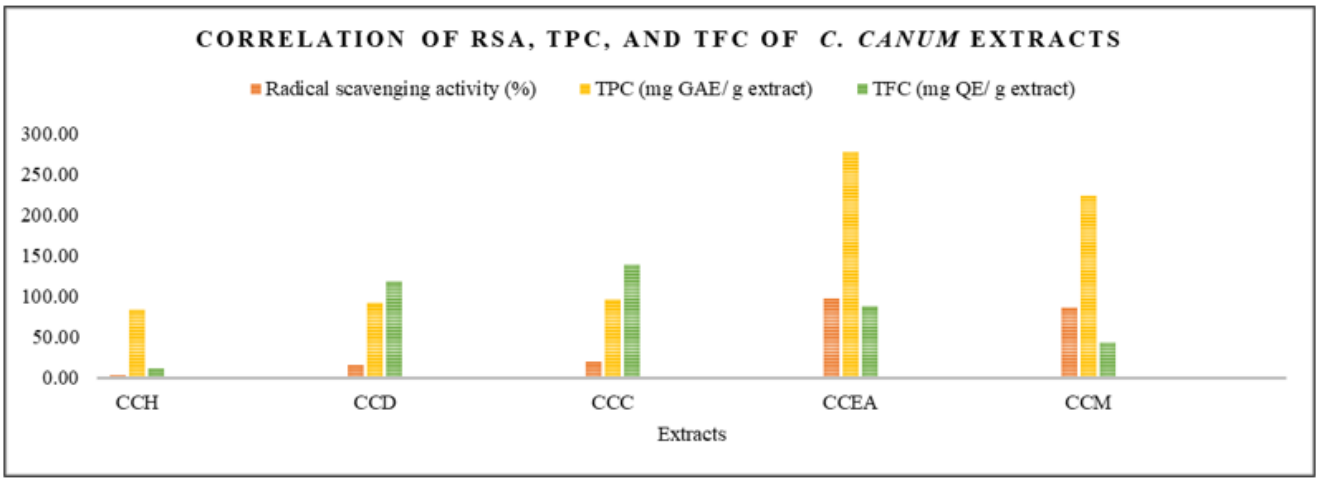


Figure 2

Correlation of radical scavenging activity, total phenolic content, and total flavonoid content of *C. canum* extracts.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 0c20240310SUPPLEMENTARYWRITEUPCcanumTPCTFCDPPH.docx