Chemical Constituents of Excoecaria cochinchinensis Exhibiting Cytotoxic, Antioxidant, Antityrosinase, and α-Glucosidase Inhibitory Activities

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Short Report

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Abstract

Eleven known compounds, including four triterpenoids (**1**–**4**), four sterols (**5**–**8**), two phenolic compounds (**9**–**10**), and a dipeptide (**11**), were isolated from *Excoecaria cochinchinensis*. Their structures were confirmed through spectroscopic analysis and compared with the existing literature. Eight compounds (**1**, **2**, **5**–**8**, **10**–**11**) have been identified in this species for the first time. The cytotoxicity of isolated compounds against MCF-7, A549, and HeLa cancer cell lines, antioxidant, *α*-glucosidase, and tyrosinase inhibitory activities were evaluated. The results revealed moderate cytotoxic effects against MCF-7 cells (**2**–**4**), A549 cells (**1**–**4**), and HeLa cells (**1**–**5**), while compounds **6**–**8**, **10**, and **11** showed no activity in any of the cell lines tested. Compound **1** exhibited more potent antioxidant activity and tyrosinase inhibitory properties than the positive control. Meanwhile, compound **4** showed a significant inhibitory effect on the *α*-glucosidase. In *silico* study, the molecular docking simulation of compound **1** to antioxidant (3RP8) and tyrosinase proteins (2Y9X), and of compound **4** to MCF-7 (1H7K), A549 cells (4ZXT), and *α*-glucosidase proteins (MAL32) were performed to calculate their binding affinities and to identify the ligand-binding sites.

Introduction

The Euphorbiaceae family is a large group of higher plants that contains around 300 genera and 7,500 species. This family is primarily found in tropical regions (Vasas and Hohmann 2014). One notable genus within this family is *Excoecaria*, which comprises about 40 species in tropical Africa, Asia, and the Western Pacific (Karamsetty and Aluri 2018).

In recent years, natural products derived from medicinal plants have attracted increasing attention as promising sources of therapeutic agents, particularly for cancer treatment and metabolic disorders (Rojas-Castano et al. 2024; Manjia et al. 2024). *Excoecaria cochinchinensis* Lour., belonging to the Euphorbiaceae family, is prevalent across Vietnam and was recognized as a traditional medicine plant to treat furuncles, pruritus, prolonged diarrhoea, urethrorrhagia, and dysentery (Giang et al. 2005; Hieu et al. 2020). The phytochemical studies on *E. cochinchinensis* have confirmed the presence of diverse secondary metabolites such as megastigmanes (Giang et al. 2005), diterpenoids (Yang et al. 2005), triterpenoids (Chen and Wang 2015), lignans (Hieu et al. 2020; Le et al. 2025), flavonoids (Li 2006), and steroids (Wang et al. 2009).

Researchers have focused on the biological activities of extracts from this plant. In particular, ethanol extract from the leaves of *E. cochinchinensis* has been shown to inhibit the growth of MKN45 gastric cancer cells (Hung 2021), while the methanol extract has demonstrated potential antibacterial activity (Nurhasana et al. 2023). Additionally, water and ethanol extracts exhibited notable anti-inflammatory properties (Jiangcun et al. 2020). Our previous studies reported a series of enzyme inhibitions of lignans and flavonoids from the ethyl acetate extract of this plant (Le et al. 2025). The current work reports the isolation and biological activities of eleven known compounds (**1**–**11**) from *E. cochinchinensis*. Their structures were determined through comprehensive spectroscopic analysis and comparison with

structures reported in the previous data. All the compounds were identified as triterpenoids, sterols, phenolic compounds, and dipeptides.

Materials and Methods

The aerial parts of *E. cochinchinensis* were collected and identified as detailed in our previous report (Le et al. 2025). The aerial parts of *E. cochinchinensis* (20.0 kg) were air-dried and ground into powder, which was then extracted with methanol (50 L, three times) at room temperature. After evaporating the solvent under vacuum, the residues were combined and suspended in water. The mixture was then sequentially partitioned with *n*-hexane, a mixture of *n*-hexane and ethyl acetate (1:1), and ethyl acetate. This extraction process resulted in three fractions: H (70.0 g), HE (255.0 g), and EA (217.0 g). The HE extract (255.0 g) underwent silica gel column chromatography, eluted with the gradient solvent system of *n*-hexane:EtOAc (from 10:1 to 1:1), to afford six fractions (HE1–HE6). Fraction HE2 (14.2 g) was further fractionated through silica gel column chromatography, using a solvent mixture of *n*-hexane:CH_2Cl_2:acetone (5:1:0.5), resulting in five subfractions (HE2.1–HE2.5). Subfraction HE2.2 (8.9 g) was subsequently fractionated by a Sephadex LH-20 gel column with a solvent mixture of CH_2Cl_2 and MeOH (1:1), yielding three subfractions (HE2.2.1–HE2.2.3). Compounds **1** (7.0 mg), **2** (6.0 mg), **3** (14.0 mg), and **7** (7.5 mg) were isolated from HE2.2.2 (1.2 g) by employing silica gel chromatography with *n*-hexane:CH_2Cl_2:acetone (2:1:0.2). Subfraction HE3 (3.7 g) yielded compounds **4** (4.5 mg), **5** (10.5 mg), **6** (2.0 mg), and **8** (9.0 mg) *via* successive silica gel separations using *n*-hexane:EtOAc (4:1) and *n*-hexane:CH_2Cl_2:acetone (2:1:0.5). From HE5 (4.1 g), compounds **9** (2.0 mg), **10** (10.0 mg), and **11** (6.5 mg) were obtained using CH_2Cl_2:MeOH (4:0.1), followed by RP-C18 CC (MeOH:H_2O 1:1, 2:1 and 4:1).

The cytotoxic properties of the isolated compounds were assessed against MCF-7 and HeLa cancer cell lines utilizing the sulforhodamine B (SRB) assay (Monks et al. 1991) by established protocols (Tran et al. 2021). The DPPH radical scavenging activity was evaluated to identify antioxidants among the isolated compounds, in alignment with the methodology presented by Kim et al. (Kim, Son, and Lee 2017). The inhibitory effect of the isolated compounds on *α*-glucosidase activity was assessed following the procedure outlined by Duong et al. (Duong et al. 2024). The inhibition of tyrosinase activity was conducted according to the method of Chatatikun et al. (Chatatikun et al. 2023), using kojic acid as the positive control.

Molecular Docking

Molecular docking was utilized to assess protein-ligand binding affinities and determine ligand-binding sites (Nguyen et al. 2019; Trott and Olson 2010), which provided an enhanced understanding of biological characteristics. The docking simulations were conducted using AutoDock Vina (Trott and Olson 2010). Since the crystallographic structure of *α*-glucosidase of *Saccharomyces cerevisiae* was unavailable, the 3D model designated AF-P38158-F1 (MAL32), was retrieved from AlphaFold Protein Structure Database (https://alphafold.ebi.ac.uk/entry/P38158). This model was validated as the best representation of *S. cerevisiae*-derived *α*-glucosidase prior to the availability of its crystal structure (Tian

et al. 2023). Crystal structures of other target proteins were retrieved from the RCSB Protein Data Bank (https://www.rcsb.org/pdb/). For cytotoxicity assessments, isolated compounds were evaluated against multiple cancer cell lines with associated protein structures: A549 (PDB ID: 4ZXT) (Shin et al. 2016) and MCF-7 (PDB ID: 1H7K) (Andreoletti et al. 2001). The crystal structure of *Klebsiella pneumoniae* R204Q HpxO complexed with FAD (PDB ID: 3RP8) (Hicks et al. 2013) and mushroom tyrosinase structure (PDB ID: 2Y9X) (Ismaya et al. 2011) were also selected. Prior to molecular docking, each protein crystal structure was refined by removing water molecules, heteroatoms, and cofactors. The docking grid box was set to 23 Å × 23 Å × 23 Å for PDB IDs 2Y9X and 3RP8, and 26 Å × 26 Å × 26 Å for PDB IDs 1H7K, 4ZXT, and MAL32 (AlphaFold ID: AF-P38158-F1). The molecular docking outcomes were visualized using Biovia Discovery Studio Visualizer 2021 (Systèmes 2021).

Results and Discussion

The chemical examination of the methanol extract from *E. cochinchinensis* led to the isolation of eleven compounds. Their structures were established through NMR analysis and comparing with previous references, identified as cycloart-25-ene-3 β,24-diol (**1**) (Paula et al. 2002), euphorfistrine A (**2**) (Wei et al. 2021), lupeol (**3**) (Shwe et al. 2019), baccatin (**4**) (Wang, Zhang, and Pan 2003), ergosterol peroxide (**5**) (Nowak et al. 2016), 7 β-hydroxysitosterol (**6**) (Li, Wang, and Li 2005), 7 α-hydroxysitosterol (**7**) (Li, Wang, and Li 2005), 7-oxo- β-sitosterol (**8**) (Pettit et al. 2000), gallic acid (**9**) (Hernández-García et al. 2019), emodin (**10**) (Chu, Sun, and Liu 2005), and aurantiamide acetate (**11**) (Zhou et al. 2017), as shown in Fig. 1. Notably, all compounds, except for **3**, **4**, and **9**, were isolated from *E. cochinchinensis* for the first time.

Among these isolated compounds, **1**–**8**, and **10–11**, including triterpenoids (**1–4**), steroids (**5–8**), anthraquinone (**10**), and dipeptide (**11**) were selected for biological activity investigation on cytotoxicity against human cancer cell lines MCF-7, A549, and HeLa, antioxidant, and enzyme inhibition against α-glucosidase and tyrosinase which were presented in Table 1.

Table 1
The cytotoxicity against MCF-7, A549, and HeLa cancer cell lines, antioxidant, and enzyme inhibition against α-glucosidase and tyrosinase of the tested compounds.

Compounds	IC_{50} (μM)					
	Cancer cell lines			Antioxidant	Enzyme inhibition	
	MCF-7	A549	Hela	DPPH	α-glucosidase	Tyrosinase
1	> 100	95.39 ± 3.06	61.08 ± 3.31	69.34	> 200	182.26
2	67.72 ± 3.28	59.80 ± 3.34	41.29 ± 1.26	> 200	> 200	> 300
3	92.01 ± 4.35	89.31 ± 3.68	67.32 ± 1.76	> 200	> 200	> 300
4	31.88 ± 2.68	45.17 ± 3.05	60.68 ± 3.73	163.66	155.08	> 300
5	> 100	> 100	54.50 ± 2.89	> 200	> 200	> 300
6	> 100	> 100	> 100	> 200	> 200	293.18
7	> 100	> 100	> 100	> 200	194.65	> 300
8	> 100	> 100	> 100	178.63	> 200	> 300
10	> 100	> 100	> 100	> 200	> 200	> 300
11	> 100	> 100	> 100	> 200	> 200	195.75
Ellipticine	0.33 ± 0.02	0.37 ± 0.03	0.30 ± 0.03			
Ascorbic acid				82.33		
Acarbose					168.0	
Kojic acid						251.28

The cytotoxicity was evaluated using the sulforhodamine B assay, with ellipticine as the positive control. Compounds **1**–**5** displayed moderate cytotoxic activity against these cell lines. Notably, compound **4** exhibited the strongest cytotoxicity against the MCF-7 and A549 cell lines, with IC_{50} values of 31.88 ± 2.68 μM and 45.17 ± 3.05 μM, respectively, followed by compounds **2** and **3**. Compound **2** showed the most significant effect for the HeLa cell line, with an IC_{50} value of 41.29 ± 1.26 μM. In contrast, compounds **6**–**8**, **10**, and **11** showed no inhibitory effects on all cancer cell lines. Regarding the antioxidants, compounds **1, 4**, and **8** displayed effectiveness in the DPPH assay with IC_{50} values in the range of 69–179 μM. Among them, **1** revealed the most potent activity with an IC_{50} value of 69.34 μM in

comparison with the positive control (ascorbic acid, IC_{50} 82.33 μM). Moreover, in the enzyme inhibition, compounds **4** and **7** (IC_{50} value of 155.08 and 194.65 μM, respectively) showed good *α*-glucosidase inhibition, while **1** and **11** (IC_{50} value of 182.26 and 195.75 μM, respectively) revealed good tyrosinase inhibitory activity, in comparison with those of acarbose (IC_{50} value of 168.0 μM) and kojic acid (IC_{50} value of 251.28 μM), respectively. Furthermore, the above results also indicated that the triterpenoids (**1**–**4**) displayed the most potent activities compared to those of steroids (**5–8**) and anthraquinone (**10**). Among the isolated triterpenoids, the cycloartane-type triterpenoid (**1**) showed more potential activity in the DPPH and tyrosinase assay, while nor-triterpene peroxide (**4**) revealed more potential activity in the cytotoxicity against MCF-7 and A549 cancer cell lines and *α*-glucosidase inhibition.

To further understand the conformation of the most active compound for each bioassay in the target binding site of their proteins, the binding interactions of **1** with the tyrosinase (2Y9X) and DPPH (3RP8) proteins and of **4** with MCF-7 (1H7K), A549 (4ZXT), and *α*-glucosidase (MAL32) proteins were studied using molecular docking simulation *via* vina-docking.

In the tyrosinase inhibition and antioxidant activities, compound **1** exhibited one H-bonding to each protein as an H-donor from 3-OH to 2Y9X (with Asn B:81, 2.9 Å) and 3RP8 proteins (with Ser A:156, 2.2 Å) (Fig. 2, Table S1), indicating the importance of the 3-OH moiety in the cycloartane triterpenoids to the respective activities. Moreover, the presence of carbon-carbon double bond moiety at C-25-C-26 led to the formation of H-*α* (H-24 and H_3-27), due to the hyper-conjugation effect, which can form the carbon-hydrogen bond (H-24 with Asn 260 of 2Y9X and with Tyr 216 of 3RP8) or pi-sigma bond (H_3-27-His 263) and pi-alkyl bonds (H_3-27-His 259 and H_3-27-Val 283) of tyrosinase protein (2Y9X). Therefore, the presence of the C-25–C-26 double bond in the cycloartane structure may significantly contribute to its tyrosinase inhibitory and antioxidant activities compared to those of a related 3-hydroxycycloartane (**2**), lacking this feature.

As to the cytotoxicity, compound **4** interacted with the active site of the MCF-7 (1H7K) and A549 (4ZXT) proteins with affinity values of − 9.0 kcal/mol for each protein (Table S1), explaining why this compound was the most active on the cytotoxicity against these cancer cell lines. The data was further supported by the formation of two hydrogen bonds of **4** with Asp 339 (2.4 Å) and Ser 336 (3.1 Å), for 1H7K, and two with Ser 153 (2.5 Å) and Lys 114 (2.7 Å), for 4ZXT (Fig. 3). In two hydrogen bonds of **4** with 1H7K or 4ZXT, one of these is H-donor (**4**-Asp 339 or **4**-Ser 153, respectively), and another is H-acceptor (**4**-Ser 336 or **4**-Lys 114, respectively), indicating that the highly oxygenated function could display more potential activity on the cytotoxicity. In addition, compound **4** formed one hydrogen bond (with Phe 157, 2.7 Å) with MAL32 as an H-donor, indicating the significant role of the hydroxyl moiety on the A-ring of nor-triterpene peroxide in inhibiting the enzyme *α*-glucosidase activity.

Conclusion

The phytochemical analysis of the aerial parts of *E. cochinchinensis* resulted in the isolation and identification of eleven compounds comprising triterpenoids, sterols, phenolic compounds, and a

dipeptide. Notably, eight of these compounds were reported for the first time in this species. Their structures were determined through extensive spectroscopic analysis. Biological evaluations showed that the triterpenoids (compounds **1**–**4**) exhibited moderate cytotoxicity against MCF-7 and HeLa cancer cell lines, with compound **4** presenting the most potent cytotoxic activity. Additionally, compound **1** displayed significant antioxidant and tyrosinase inhibitory activities, surpassing standard controls. Compounds **4** and **7** also illustrated considerable *α*-glucosidase inhibition. Molecular docking studies confirmed these findings by highlighting the important interactions that contribute to the observed bioactivities.

Declarations

Supplementary Information

The online version contains supplementary material available at

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Author Contributions

Isolation and purification: NVK, PDSN, VHGL; Biological tests: PTTM, BXH; Structure identification: NVK, LTTH, THNK; Molecular docking: HLTTT, TTN; Writing, review, and editing: NVK, PHVT, LLTH. All authors read and approved the manuscript.

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Data Availability

All data generated or analyzed during this study are included in this published article.

Ethics approval

Not applicable.

Competing interests

The authors declare no competing interests.

References

1. Andreoletti P, Gambarelli S, Sainz G, Stojanoff V, White C, Desfonds G, Gagnon J, Gaillard J, Jouve HM (2001) Formation of a tyrosyl radical intermediate in *Proteus mirabilis* catalase by directed mutagenesis and consequences for nucleotide reactivity. Biochemistry 40:13734–13743. https://doi.org/10.1021/bi010687f
2. Chatatikun M, Tedasen A, Pattaranggoon NC, Palachum W, Chuaijit S, Mudpan A, Pruksaphanrat S, Sohbenalee S, Yamasaki K, Klangbud WK (2023) Antioxidant activity, anti-tyrosinase activity, molecular docking studies, and molecular dynamic simulation of active compounds found in nipa palm vinegar. PeerJ 11:e16494. https://doi.org/10.7717/peerj.16494
3. Chen B, Wang X (2015) Studies on chemical constituents of *Excoecaria cochinchinensis*. J Pharm Res 34:147–149.
4. Chu X, Sun A, Liu R (2005) Preparative isolation and purification of five compounds from the Chinese medicinal herb *Polygonum cuspidatum* Sieb. et Zucc by high-speed counter-current chromatography. J Chromatogr A 1097:33–39. https://doi.org/10.1016/j.chroma.2005.08.008
5. Duong TKY, Nguyen VK, Dao NVT, Bui XH, Thao VTM, Nguyen MK, Dong PSN, Phan HVT, Tran TN, Ngo HNT (2024) Annoglabrin A-C, three new ent-kaurane diterpenoids from the *Annona glabra* fruit pulp. Nat Prod Res 1–9. https://doi.org/10.1080/14786419.2024.2414397
6. Giang PM, Son PT, Matsunami K, Otsuka H (2005) New megastigmane glucosides from *Excoecaria cochinchinensis* Lour. var. *cochinchinensis*. Chem Pharm Bull 53:1600–1603. https://doi.org/10.1248/cpb.53.1600
7. Hernández-García E, García A, Avalos-Alanís FG, Rivas-Galindo VM, Delgadillo-Puga C, Camacho-Corona MR (2019) Nuclear magnetic resonance spectroscopy data of isolated compounds from *Acacia farnesiana* (L) Willd fruits and two esterified derivatives. Data Brief 22:255–268. https://doi.org/10.1016/j.dib.2018.12.008
8. Hicks KA, O'Leary SnE, Begley TP, Ealick SE (2013) Structural and mechanistic studies of HpxO, a novel flavinadenine dinucleotide-dependent urate oxidase from *Klebsiella pneumoniae*. Biochemistry 52:477–487. https://doi.org/10.1021/bi301262p
9. Hieu LH, Thao NP, Hanh TTH, Cong ND, Cuong NT, Van Thanh N, Cuong NX, Nam NH, Dai Quang N, Van Minh C (2020) Metabolites from *Excoecaria cochinchinensis* Lour. Phytochem Lett 37:116–120. https://doi.org/10.1016/j.phytol.2019.08.003
10. Hung NP (2021) The ethanol extract of *Excoecaria cochinchinensis* Lour. leaves inhibits cell migration and arrests cell cycle in gastric cancer cell MKN45. Viet J Biotechnol 19:147–154. https://doi.org/ 10.15625/1811-4989/15291
11. Ismaya WT, Rozeboom HJ, Weijn A, Mes JJ, Fusetti F, Wichers HJ, Dijkstra BW (2011) Crystal structure of *Agaricus bisporus* mushroom tyrosinase: identity of the tetramer subunits and interaction with tropolone. Biochemistry 50:5477–5486. https://doi.org/10.1021/bi200395t
12. Jiangcun W, Silu H, Haisheng Z, Huang D, Chengtong L, Qiji Z, Boughan Q (2020) Preliminary experimental study on anti-inflammatory effect of extract from *Excoecaria cochinchinensis* Lour. as a national medicine. Med Plant 11. https://doi.org/10.19600/j.cnki.issn2152-3924.2020.01.007

13. Karamsetty HJ, Aluri JSR (2018) Ambophily in the dioecious weedy mangrove associate, *Excoecaria agallocha* (Euphorbiaceae). Transylv Rev Syst Ecol Res 20:15–28. https://doi.org/10.2478/trser-2018-0009
14. Kim YK, Son HK, Lee JJ (2017) Nutritional components and antioxidant activities of various *Stachys sieboldii* Miq parts. Korean J Community Living Sci 28:203–215. https://doi.org/10.7856/kjcls.2017.28.2.203
15. Le HTT, Dong PSN, Hoang LTTTT, Nguyen-Si HV, Phan HVT, Vo TMT, Tran TTL, Le TT, Nguyen VK (2025) Excochinlignan: A new coumarino lignan from *Excoecaria cochinchinensis* Lour. Med Chem Res 1–10. https://doi.org/10.1007/s00044-025-03447-9
16. Li GY, Wang JH, Li X (2005) Note: Sterols from the pericarp of *Sphaerophysa salsula* DC. J Asian Nat Prod Res 7:165–169. https://doi.org/10.1080/1028602031000161719
17. Li ZY, Jinghua, Wang Y, Huang R, Li L (2006) Chemical constituents of *Excoecaria cochinchinensis*. Zhongcaoyao 37:826–829.
18. Manjia JN, Njoya EM, Harishchander A, Munvera AM, Ogundolie FA, Mkounga P, Mcgaw LJ, Njayou FN, Moundipa PF (2024) Anti-elastase, anti-tyrosinase, and anti-inflammatory activities of three compounds isolated from *Psorospermum aurantiacum*: in silico and in vitro assays. Rev Bras Farmacogn 34:1116–1128. https://doi.org/10.1007/s43450-024-00558-z
19. Monks A, Scudiero D, Skehan P, Shoemaker R, Paull K, Vistica D, Hose C, Langley J, Cronise P, Vaigro-Wolff A (1991) Feasibility of a high-flux anticancer drug screen using a diverse panel of cultured human tumor cell lines. J Natl Cancer Inst 83:757–766. https://doi.org/10.1093/jnci/83.11.757
20. Nguyen NT, Nguyen TH, Pham TNH, Huy NT, Bay MV, Pham MQ, Nam PC, Vu VV, Ngo ST (2019) AutoDock Vina adopts more accurate binding poses but AutoDock4 forms better binding affinity. J Chem Inf Model 60:204–211. https://doi.org/10.1021/acs.jcim.9b00778
21. Nowak R, Drozd M, Mendyk E, Lemieszek M, Krakowiak O, Kisiel W, Rzeski W, Szewczyk K (2016) A new method for the isolation of ergosterol and peroxyergosterol as active compounds of *Hygrophoropsis aurantiaca* and in vitro antiproliferative activity of isolated ergosterol peroxide. Molecules 21:946. https://doi.org/10.3390/molecules21070946
22. Nurhasana D, Febriansyah R, Avidlyandi A, Banon C, Oktiarni D, Adfa M (2023) In-vitro antibacterial activity of *Excoecaria cochinchinensis* Lour's methanol extract and its combination with commercial drugs. J Ilmu Kefarm Indones 21:179–185. https://doi.org/10.35814/jifi.v21i2.1383
23. Paula VF, Barbosa LC, Errington W, Howarth OW, Cruz MP (2002) Chemical constituents from *Bombacopsis glabra* (Pasq.) A. Robyns: complete ^{1}H and ^{13}C NMR assignments and X-ray structure of 5-hydroxy-3,6,7,8,4'-pentamethoxyflavone. J Braz Chem Soc 13:276–280. https://doi.org/10.1590/S0103-50532002000200022
24. Pettit GR, Numata A, Cragg GM, Herald DL, Takada T, Iwamoto C, Riesen R, Schmidt JM, Doubek DL, Goswami A (2000) Isolation and structures of schleicherastatins 1–7 and schleicheols 1 and 2 from the teak forest medicinal tree *Schleichera oleosa*. J Nat Prod 63:72–78. https://doi.org/10.1021/np990346r

25. Rojas-Castano BA, Hernández-Rojas AC, Pereda-Miranda R, Fragoso-Serrano M (2024) Cytotoxicity of salvigenin from *Asterohyptis stellulata* in combination with clinical drugs against colorectal cancer. Rev Bras Farmacogn 34:1172–1176. https://doi.org/10.1007/s43450-024-00549-0
26. Shin SH, Lee MH, Malakhova M, Kurinov I, Wu Q, Xu J, Jiang Y, Dong Z, Liu K, Lee KY (2016) A natural small molecule, catechol, induces c-Myc degradation by directly targeting ERK2 in lung cancer. Oncotarget 7:35001. https://doi.org/10.18632/oncotarget.9223
27. Shwe HH, Win KK, Moe TT, Myint AA, Win T (2019) Isolation and structural characterization of lupeol from the stem bark of *Diospyros ehretioides* Wall. IEEE-SEM 7:140–144.
28. Systèmes D (2021) Discovery Studio Visualizer. *v16.1*:15350.
29. Tian JL, Zhao M, Xu JY, Lv TM, Liu XC, Sun S, Guan Q, Zhou ZC, Wu J, Zhao MY (2023) Inhibitory mechanism of prenylated flavonoids isolated from mulberry leaves on α-glucosidase by multi-spectroscopy and molecular dynamics simulation. J Agric Food Chem 71:9135–9147. https://doi.org/10.1021/acs.jafc.3c00776
30. Tran TH, Le HT, Nguyen HM, Tran TH, Do Thi T, Nguyen XC, Ha MT (2021) Garcinoxanthones S–V, new xanthone derivatives from the pericarps of *Garcinia mangostana* together with their cytotoxic and antioxidant activities. Fitoterapia 151:104880. https://doi.org/10.1016/j.fitote.2021.104880
31. Trott O, Olson AJ (2010) AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. J Comput Chem 31:455–461. https://doi.org/10.1002/jcc.21334
32. Vasas A, Hohmann J (2014) *Euphorbia* diterpenes: isolation, structure, biological activity, and synthesis (2008–2012). Chem Rev 114:8579–8612. https://doi.org/ 10.1021/cr400541j.
33. Wang H, Zhang XF, Pan L (2003) Chemical constituents from *Euphorbia wallichii*. Nat Prod Res Dev 15:483–486.
34. Wang Y, Huang R, Zhang H, Li L, Yang J (2009) Studies on chemical constituents of *Excoecaria cochinchinensis* Lour. J Trop Subtrop Bot 17:156–159.
35. Wei JC, Huang HH, Zhong NF, Gao YN, Liu XL, Long GQ, Hu GS, Wang AH, Jia JM (2021) Euphorfistrines A–G, cytotoxic and AChE inhibiting triterpenoids from the roots of *Euphorbia fischeriana*. Bioorg Chem 116:105395. https://doi.org/10.1016/j.bioorg.2021.105395
36. Yang JH, Luo SD, Zhao JF, Wang YS, Huang R, Zhang HB, Li L (2005) Three new highly oxygenated diterpenoids from *Excoecaria cochinchinensis* Lour. Helv Chim Acta 88:968–973. https://doi.org/10.1002/hlca.200590090
37. Zhou B, Yang Z, Feng Q, Liang X, Li J, Zanin M, Jiang Z, Zhong N (2017) Aurantiamide acetate from *Baphicacanthus cusia* root exhibits anti-inflammatory and anti-viral effects via inhibition of the NF-κB signaling pathway in Influenza A virus-infected cells. J Ethnopharmacol 199:60–67. https://doi.org/10.1016/j.jep.2017.01.038

Figures

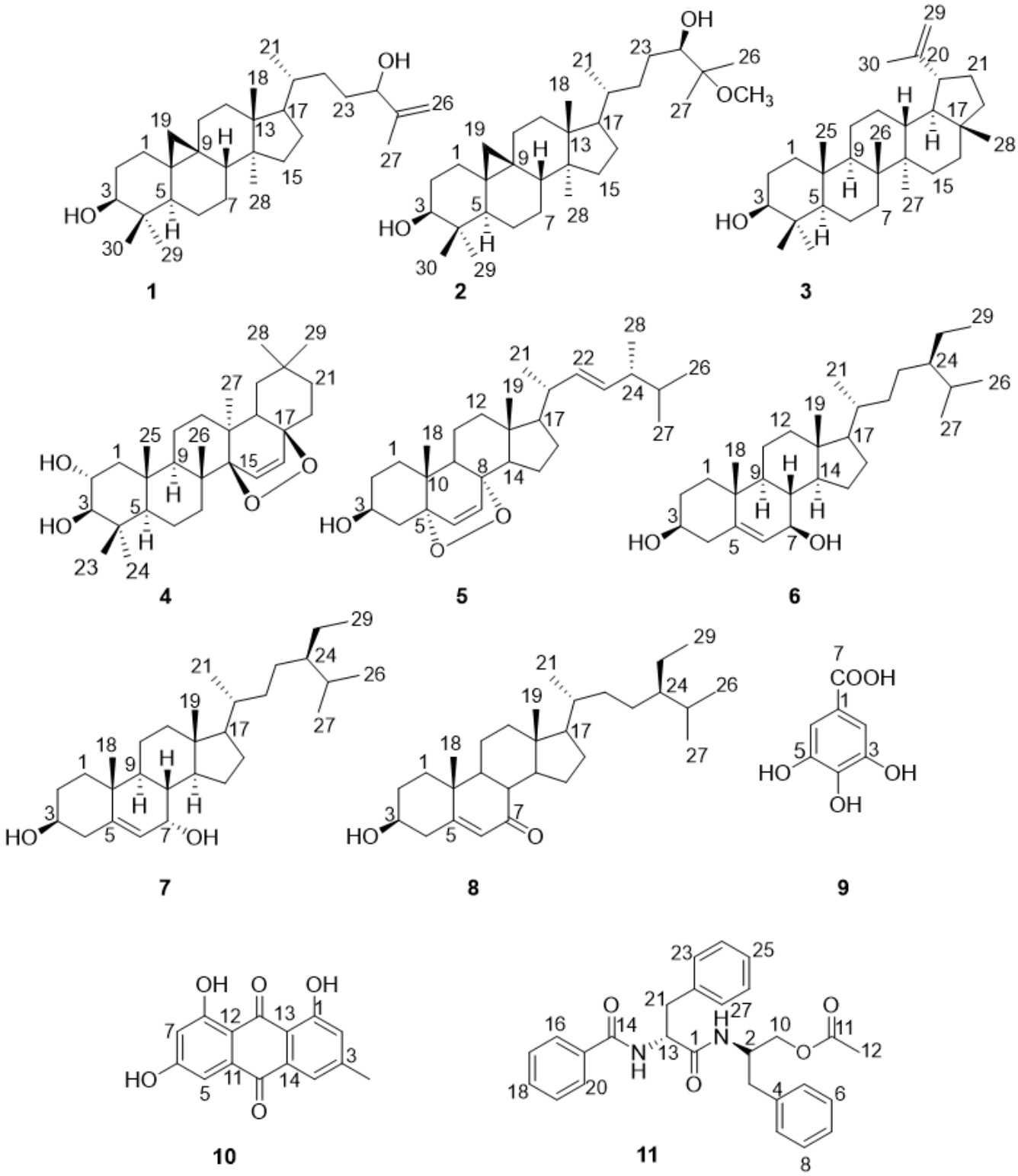

Figure 1

Structures of isolated compounds **1**–**11** from *E. cochinchinensis*

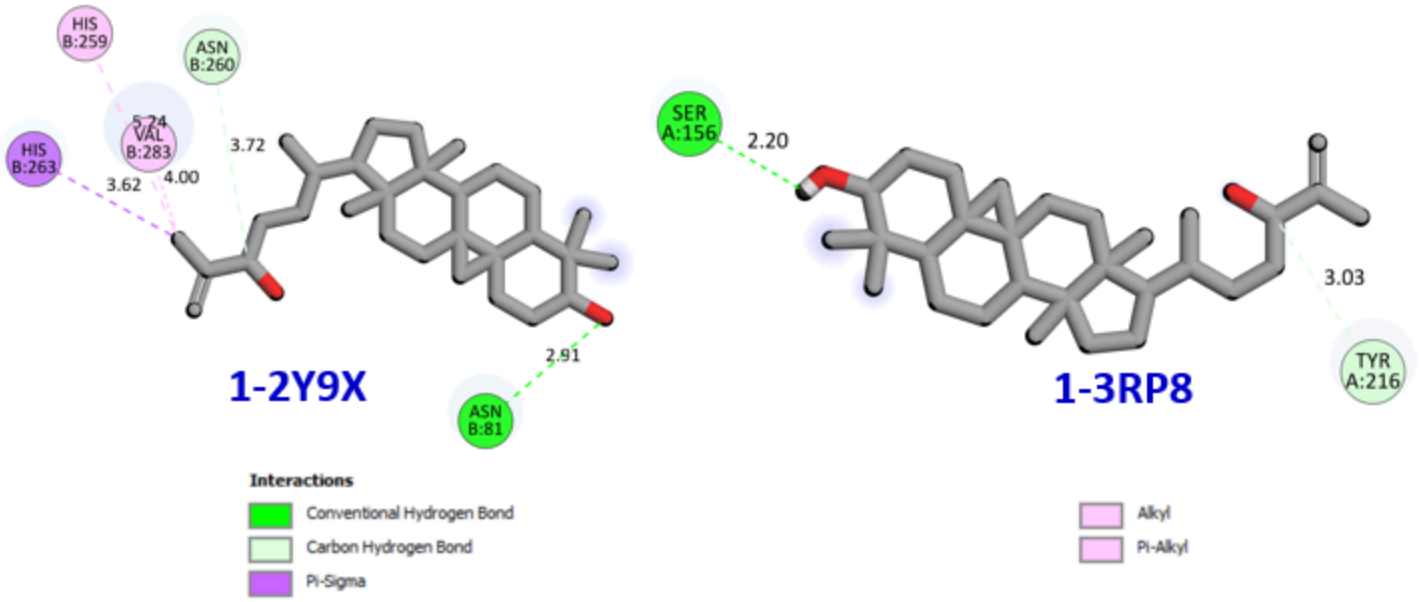

Figure 2

Corresponding amino acid residues of tyrosinase (2Y9X) and DPPH (3RP8) proteins interacted with **1**.

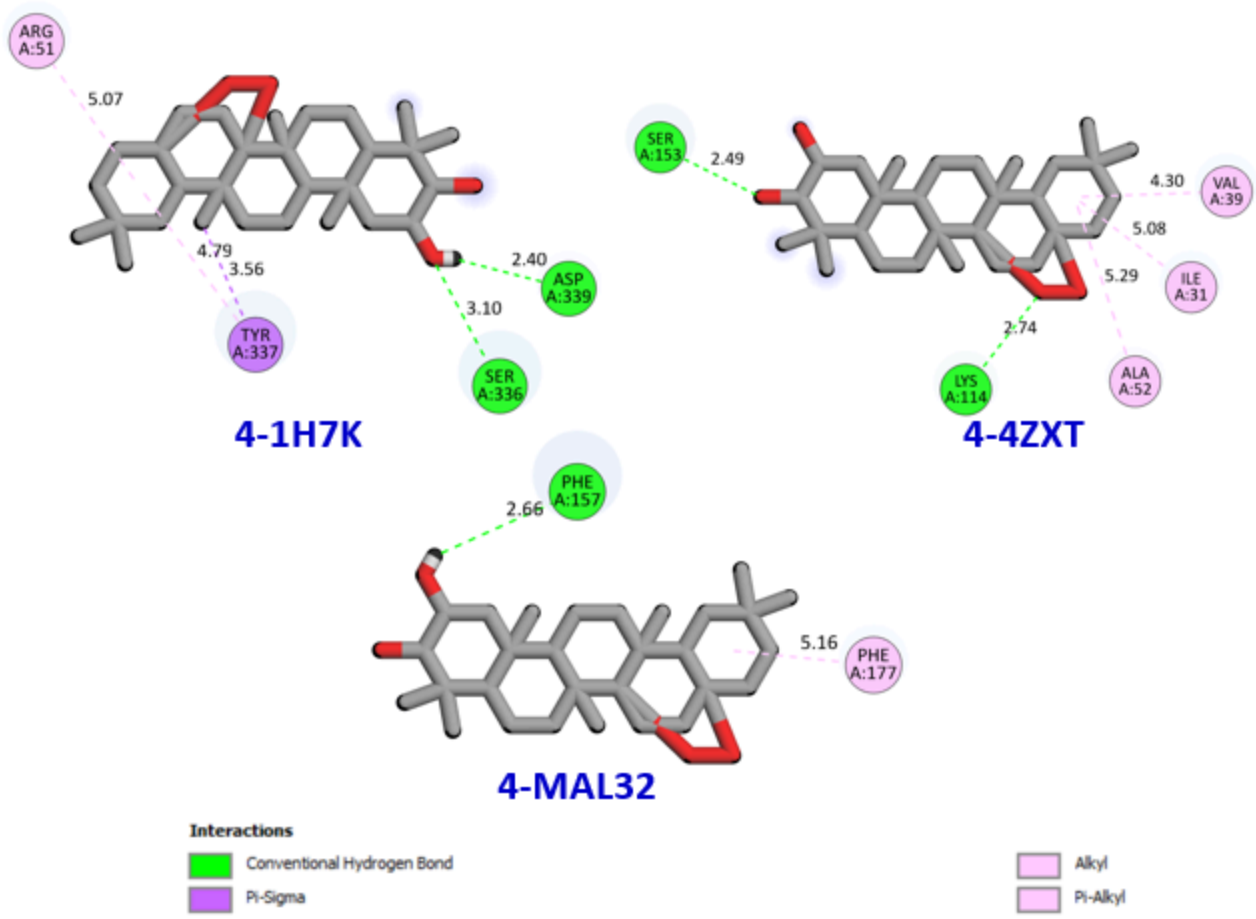

Figure 3

Corresponding amino acid residues of MCF-7 (1H7K), A549 (4ZXT), and α-glucosidase (MAL 32) proteins interacted with **4**.

Supplementary Files

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- Graphicalabstract.png
- SupportingInformation.pdf