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Original Article

Effectiveness as tyrosinase inhibitor from active compounds of *Centella asiatica* (L.) Urb., ethyl ascorbic acid, and coenzyme Q10 as skin whitening by *in silico* evaluation

[Eficacia como inhibidor de la tirosinasa de compuestos activos de *Centella asiatica* (L.) Urb., ácido etilascórbico y coenzima Q10 para el blanqueamiento de la piel mediante la evaluación *in silico*]

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Abstract

Context: Hyperpigmentation and melasma are often treated with hydroquinone-based topical creams. Despite its effectiveness, hydroquinone use is limited by irritation, photosensitivity, and oxidation sensitivity, making long-term application unfavorable.

Aims: To explore *Centella asiatica* phytochemicals as natural alternatives in topical formulations, in combination with oxidative chemical agents such as ethyl ascorbic acid and coenzyme Q10, through preliminary *in silico* evaluation.

Methods: Molecular docking and molecular dynamics simulations were conducted on asiatic acid, madecassic acid, asiaticoside, and madecassoside from *C. asiatica*, along with ethyl ascorbic acid and coenzyme Q10, against the tyrosinase enzyme (PDB: 5I3A). Docking was performed using Molegro Virtual Docker (Molexus v7), and molecular dynamics simulations were carried out in Maestro (Schrödinger) for 100 ns.

Results: Asiatic acid exhibited the most promising activity, with binding affinity comparable to hydroquinone and stable interactions during 100 ns simulations (average RMSD ~3 Å). Glycoside derivatives (asiaticoside and madecassoside) showed weak and unstable binding. Notably, 3-*o*-ethyl ascorbic acid demonstrated stronger binding energy and superior stability (average RMSD 2.971 Å) than hydroquinone, whereas coenzyme Q10 displayed positive binding free energy and poor stability.

Conclusions: The findings suggest that asiatic acid is the most active anti-hyperpigmentation compound in *C. asiatica*, while glycosides lack tyrosinase inhibitory activity. Incorporation of 3-*o*-ethyl ascorbic acid, rather than coenzyme Q10, could enhance the efficacy of *C. asiatica*–based topical formulations for hyperpigmentation management.

Keywords: *Centella asitica;* molecular docking; molecular dynamics; hyperpigmentation; tyrosinase.

Resumen

Contexto: La hiperpigmentación y el melasma a menudo se tratan con cremas tópicas a base de hidroquinona. A pesar de su eficacia, el uso de hidroquinona está limitado por la irritación, la fotosensibilidad y la sensibilidad a la oxidación, lo que hace que la aplicación a largo plazo resulte desfavorable.

Objetivos: Explorar los fitoquímicos de *Centella asiática* como alternativas naturales en formulaciones tópicas, en combinación con agentes químicos oxidativos como el ácido etil ascórbico y la coenzima Q10, mediante evaluación preliminar *in silico*.

Métodos: Se realizaron simulaciones de acoplamiento molecular y dinámica molecular de ácido asiático, ácido madecásico, asiaticósido y madecasósido de *C. asiatica*, junto con ácido etilascórbico y coenzima Q10, contra la enzima tirosinasa (PDB: 5I3A). El acoplamiento se realizó con Molegro Virtual Docker (Molexus v7) y las simulaciones de dinámica molecular se realizaron en Maestro (Schrödinger) durante 100 ns.

Resultados: El ácido asiático exhibió la actividad más prometedora, con una afinidad de unión comparable a la de la hidroquinona y interacciones estables durante simulaciones de 100 ns (RMSD promedio de ~3 Å). Los derivados de glucósidos (asiaticósido y madecasósido) mostraron una unión débil e inestable. En particular, el ácido 3-o-etilascórbico demostró una energía de unión más alta y una estabilidad superior (RMSD promedio de 2,971 Å) que la hidroquinona, mientras que la coenzima Q10 mostró una energía libre de unión positiva y una estabilidad deficiente.

Conclusiones: Los hallazgos sugieren que el ácido asiático es el compuesto antihiperpigmentación más activo en *C. asiatica*, mientras que los glucósidos carecen de actividad inhibidora de la tirosinasa. La incorporación de ácido 3-o-etilascórbico, en lugar de la coenzima Q10, podría mejorar la eficacia de las formulaciones tópicas basadas en *C. asiatica* para el tratamiento de la hiperpigmentación.

Palabras Clave: acoplamiento molecular; *Centella asiática*; dinámica molecular; hiperpigmentación; tirosinasa.

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INTRODUCTION

The skin is the body's outermost organ, serving as a protective barrier against external exposure while also playing an essential role in aesthetics and personal identity. One of the main components that determines skin color is melanin, the most abundant pigment in the epidermis. Melanin serves as the primary defense against ultraviolet (UV) radiation-induced damage (Solano, 2020). However, excessive UV exposure can stimulate increased melanin production, leading to hyperpigmentation. The prevalence of hyperpigmentation varies across populations, with higher rates observed among Malay and Indian populations in Asia compared to fair-skinned Chinese populations. Environmental factors, such as Indonesia's tropical climate, also contribute to the high incidence of hyperpigmentation (Slominski et al., 2022).

Hyperpigmentation can be caused by a variety of internal and external factors, including hormonal changes, dermatitis, drug use, and sun exposure (Suyanto & Saraswati, 2023). One of the key enzymes involved in melanin biosynthesis is tyrosinase, a copper-containing metalloprotein. This enzyme plays a protective role against UV damage, yet it is also the primary target in melanin-inhibition strategies aimed at preventing hyperpigmentation. Therefore, inhibition of tyrosinase activity has become a widely developed approach to reduce melanin accumulation in the skin (Noh et al., 2020).

Several natural compounds have been identified as tyrosinase inhibitors, such as arbutin, azelaic acid, kojic acid, hydroquinone, and other phenolic compounds. Polyphenols and flavonoids found in plants are known to inhibit tyrosinase by blocking the oxidation reactions of L-tyrosine, or L-DOPA, catalysed by the enzyme (Boateng et al., 2023; Harahap et al., 2024).

Centella asiatica (L.) Urb., commonly known as pegagan, is a plant from the *Apiaceae* family that exhibits various pharmacological activities, primarily due to its triterpenoid constituents such as asiaticoside, madecassoside, asiatic acid, and madecassic acid (Fig. 1). Extracts of *C. asiatica* have been used in cosmetic formulations and have demonstrated tyrosinase inhibitory activity of 31.25% at a concentration of 1.67 mg/mL (Fernenda et al., 2023). These triterpenoid compounds are known to promote skin tissue regeneration and reduce melanin content by inhibiting tyrosinase mRNA expression (Chang, 2009; Fernenda et al., 2023).

Ethyl ascorbic acid (EAA) is a stable derivative of vitamin C with superior skin permeability compared to other ascorbic acid derivatives. EAA is widely used in cosmetics as an antioxidant, anti-aging agent, and tyrosinase inhibitor (Iliopoulos et al., 2019). It plays a role in preventing hyperpigmentation primarily through the inhibition of tyrosinase (Chen et al., 2021).

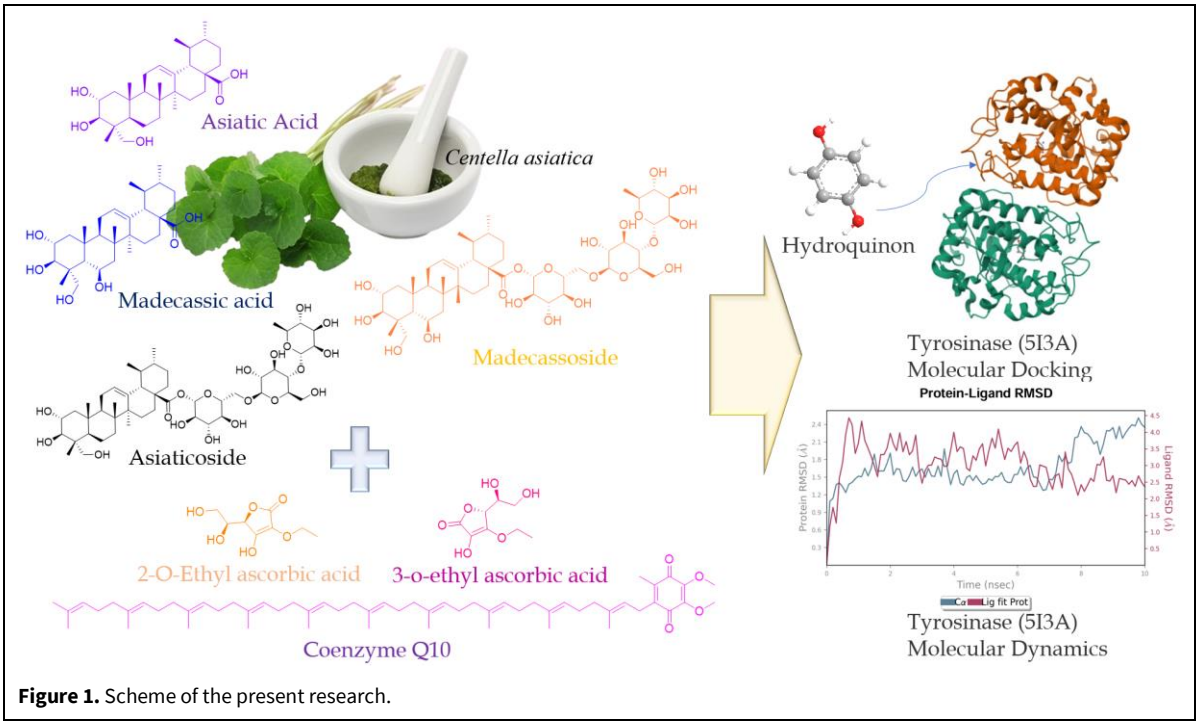


Figure 1. Scheme of the present research.

$$\Delta G_{bind} = E_{\text{complex(minimized)}} - (E_{\text{protein(unbound,minimized)}} + E_{\text{lig(unbound,minimized)}}) \quad [1]$$

Where: ΔGbind denotes the calculated binding free energy; Ecomplex(minimized) corresponds to the minimized MM-GBSA energy of the optimized ligand–protein complex; Eprotein(unbound, minimized) represents the minimized MM-GBSA energy of the protein after separation from its ligand; and Eligand (unbound, minimized) refers to the minimized MM-GBSA energy of the ligand once relaxed and detached from the crystal complex (Ekowati et al., 2023).

Coenzyme Q10 is a component of the mitochondrial electron transport chain and functions as a potent antioxidant. In addition to protecting cells from free radical damage, coenzyme Q10 has been shown to suppress tyrosinase activity by inhibiting cAMP-mediated CREB signaling, thereby reducing melanin synthesis (Atapour-Mashhad et al., 2024; Jiménez-Jiménez et al., 2023).

This study aims to evaluate the tyrosinase inhibitory activity of *C. asiatica* extract, coenzyme Q10, and ethyl ascorbic acid using *in silico* methods. *In silico* evaluations were performed through molecular docking to predict ligand interactions with the tyrosinase enzyme and assess binding affinities, followed by molecular dynamics simulations to examine the stability of the complexes over a 100 ns simulation period. Molecular docking and dynamics analyses were carried out using Molegro Virtual Docker and Desmond (Schrödinger), targeting the tyrosinase enzyme (PDB ID: 5I3A), with hydroquinone, kojic acid, and arbutin as reference ligands to assess the inhibitory potential of the test compounds.

MATERIAL AND METHODS

Molecular docking procedure

Four major phytochemicals from *C. asiatica* (asiatic acid, madecassic acid, asiaticoside, and madecassoside), along with two vitamin C derivatives, namely 2-o-ethyl ascorbic acid and 3-o-ethyl ascorbic acid, and coenzyme Q10, were prepared as ligands. The molecular structures were initially drawn in 2D using ChemBioDraw version 11. These 2D structures were converted to 3D using the Molecular Operating Environment (MOE) software. The 3D ligands were energy-minimized using the MMFF94x force field to obtain the most stable conformations, and the resulting structures were saved in PDB format (Halgren, 1996).

The tyrosinase enzyme was obtained from the Protein Data Bank (PDB ID: 5I3A) and was preprocessed using Molexus version 7 software (Deri et al., 2016). To validate the docking protocol, the enzyme was re-docked with its native ligand (hydroquinone) and with kojic acid and arbutin to ensure the reliability of the docking process for further analysis. Subsequently, the validated docking setup was used to dock the four major phytochemicals from *C. asiatica* along with the three additional compounds.

Tyrosinase is a key enzyme involved in the biosynthesis of skin pigment (melanin), produced by melanocyte cells in the epidermis. During aging, overproduction of melanin can occur, leading to hyperpigmentation via melanogenesis, which is catalyzed by tyrosinase (Deri et al., 2016). Therefore, inhibition of tyrosinase plays a critical role in reducing hyperpigmentation in skin tissue and was selected as the molecular target in this study.

Molecular dynamics procedure

After molecular docking was completed using Molexus, each ligand-tyrosinase complex was saved as a PDB file. These files were then subjected to molecular dynamics (MD) simulations using Desmond (Schrödinger) software. MD simulations were performed on eight compounds: the native ligand (hydroquinone), asiatic acid, madecassic acid, asiaticoside, madecassoside, two vitamin C derivatives (2-*o*-ethyl ascorbic acid and 3-*o*-ethyl ascorbic acid), and coenzyme Q10. The aim of the MD simulation was to evaluate the stability of interactions between each ligand and the tyrosinase enzyme over time.

Simulations were carried out for 100 nanoseconds using the TIP4P water model at normal pressure and temperature (NPT). The simulations were run at 300 K and 1.01325 bar within a cubic water box of dimensions 10 Å × 10 Å × 10 Å. Energy snapshots were recorded every 10 picoseconds. The temperature and pressure were maintained using the Nose–Hoover chain thermostat and the Martyna–Tobias–Klein barostat algorithms, respectively. All minimized and equilibrated systems were simulated under periodic boundary conditions using the OPLS 2005 force field parameters for 10 ns under the NPT ensemble (Kesuma et al., 2025; Prasetiyo et al., 2025; Ruswanto et al., 2022).

Molecular mechanics/generalized Born surface area (MM-GBSA) analysis was carried out using thermal_mmgbsa.py to estimate the binding free energy of ligand–protein complexes. This approach was essential for assessing the interaction strength of potential drug candidates and was defined by the following equation [1].

RESULTS AND DISCUSSION

Molecular docking result

Four major phytochemicals from *C. asiatica*—asiatic acid, madecassic acid, asiaticoside, and madecassoside—along with two vitamin C derivatives (2-*o*-ethyl ascorbic acid and 3-*o*-ethyl ascorbic acid) and coenzyme Q10, were prepared as ligands. The structures were initially drawn in two dimensions using ChemBioDraw version 11, then converted to three dimensions using MOE (Molecular Operating Environment). Each 3D ligand was energy-minimized using the MMFF94x force field to obtain the most stable conformation and saved in PDB format (Halgren, 1996; Putra et al., 2023).

The tyrosinase enzyme structure was retrieved from the Protein Data Bank (PDB ID: 5I3A) and prepared using Molexus version 7 software (Deri et al., 2016). To validate the docking protocol, tyrosinase was redocked with its known ligand, hydroquinone. The validation yielded a root-mean-square deviation (RMSD) of 1.46 Å, confirming that the docking protocol was reliable and could be used for subsequent docking simulations of the selected phytochemicals and additional compounds. In addition to RMSD values, another crucial parameter in the redocking process is the interaction profile between the experimental SC-XRD ligand and the simulated docking ligand. The analysis revealed no significant differences in amino acid interactions, with both ligands showing 100% similarity in their binding residues. Specifically, the ligands consistently interacted with the residues His 20, His 42, His 60, Asn 205, His 208, and Val 218. This high degree of overlap confirms the reliability of the docking protocol and validates the accuracy of the docking simulation in reproducing the experimental binding mode.

The docking grid was defined with coordinates X = 2.74 Å, Y = 99.89 Å, and Z = 25.11 Å, encompassing a binding cavity surrounded by 13 key amino acids: His 42, His 60, His 204, Asn 205, His 208, Met 215, Gly 216, Val 217, Val 218, Ala 221, Phe 227, and His 231. Additionally, two zinc ions were present as cofactors within the binding site. The RMSD value obtained (<2 Å) indicates that the docking method used is valid for predicting the binding affinity and interaction of the test compounds with the tyrosinase enzyme (Sulistyowaty et al., 2016; 2023; Widiyana et al., 2016).

Based on the molecular docking results, a Moldock score was obtained, representing the predicted binding interaction between the ligand and the receptor. A lower Moldock score indicates a higher binding affinity and better compatibility between the ligand and the receptor. The docking results can also be visualized and interpreted to provide a comprehensive overview of the ligand-receptor interactions, including hydrogen bonding, hydrophobic interactions, and electronic interactions. These interactions are summarized in Table 1 and illustrated in Fig. 2.

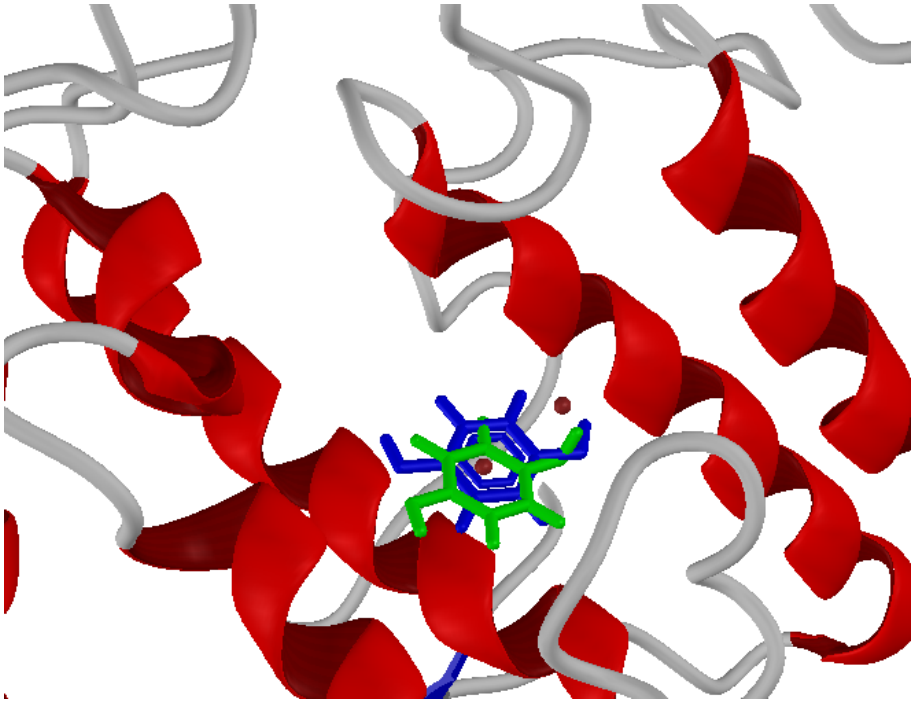


Figure 2. Comparison of the native ligand (dark blue) with the docking result simulation (green) by Molexus Ver.7 with RMSD of 1.46 Å.

Table 1. The molecular docking result of native ligand (hydroquinone) and phytochemicals of *Centella asiatica* into the active site of tyrosinase.

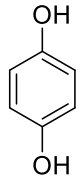
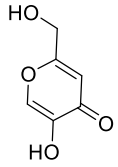
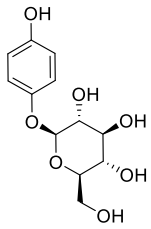
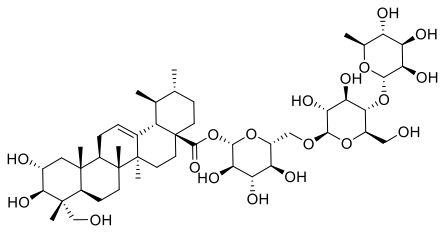
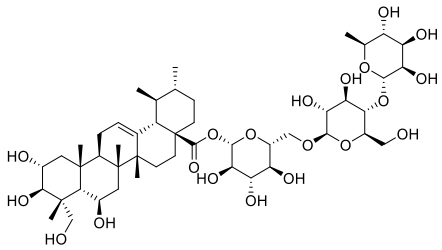
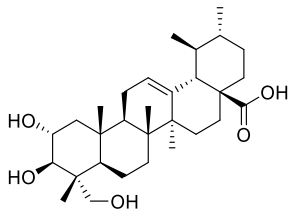
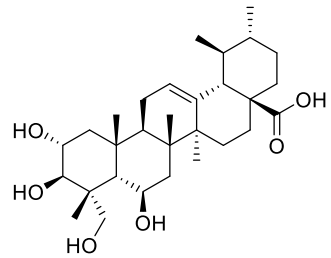
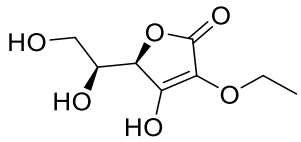
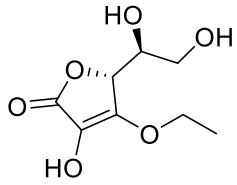
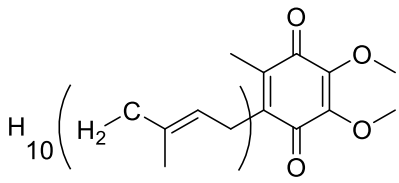
Compound	Moldock score (kcal/mol)	Hydrogen bond	Steric Interaction
 Native ligand (hydroquinone)	-52.64 ± 1.23	His 42 (2.66 Å) Asn 205 (2.51 Å) Val 218 (3.41 Å)	His 20; His 42; His 60; His 208; Val 218
 Kojic acid	-66.54 ± 0.74	Asn 205 (3.29 Å) Met 215 (2.69 Å)	His 204; Asn 205; His 208 Met 215; Val 217; Val 218
 Arbutin	-66.53 ± 0.98	Asn 205 (2.80; 3.10Å) Met 215 (3.53 Å) Gly 216 (2.66 Å)	His 204; Asn 205; His 208; Gly 216; Val 217; Val 218
 Asiaticoside	323.56 ± 1.88	His 42 (1.27; 2.61 Å) Gly 46 (2.73 Å) His 208 (2.56 Å) Arg 209 (2.03 Å) Val 218 (2.56 Å)	His 42; Gly 46; Asn 57; Met 61; Phe 197; Asn 205; His 208; Arg 209; Met 215; Val 217; Val 218; Pro 219; Ala 221; Phe 227
 Madecassoside	145.54 ± 1.98	Asp 55 (2.91 Å) Met 61 (2.46; 3.19 Å) Glu 195 (1.53: 1.82 Å) Asn 205 (2.31 Å)	His 42; Asp 55; Asn 57; His 60; Met 61; Glu 195; Phe 197; His 204; Asn 205; His 208; Arg 209; Met 215; Gly 216; Val 217; Val 218; Pro 219; Ala 221
 Asiatic acid	-45.81 ± 1.68	-	Phe 197; Asn 205; Arg 209; Val 218

Table 1. The molecular docking result of native ligand (hydroquinone) and phytochemicals of *Centella asiatica* into the active site of tyrosinase (continued...)

Compound	Moldock score (kcal/mol)	Hydrogen bond	Steric Interaction
 Madecassic acid	-42.62 ± 1.57	Asn 205 (2.78 Å)	Gly 46; Asn 57; His 60 Met 61; Gly 196; Phe 197 Asn 205; Arg 209
 2-*o*-ethyl ascorbic acid	-64.28 ± 0.43	His 42 (3.23 Å) Asn 205 (3.04 Å)	His 42 Asn 205 Val 218
 3-*o*-ethyl ascorbic acid	-61.47 ± 0.54	Asn 205 (2.93 Å)	Asn 205 His 208 Gly 216
 Coenzyme Q10	725.54 ± 1.97	His 42 (1.83 Å)	His 42; Gly 43; Gly 46; Lys 47; Ala 59; His 60; Met 61; Phe 65; His 69; Glu 195; Asn 205; His 208; Arg 209; Met 215; Gly 216; Val 217; Val 218; Pro 219 Ala 221

Hydroquinone, the native ligand of the tyrosinase enzyme, is widely used clinically to treat hyperpigmentation and melasma (Dipiro et al., 2020; Sweetman, 2009). Hydroquinone exhibits a binding energy (Moldock score) of –52.64 kcal/mol on tyrosinase, forming hydrogen bonds with the amino acid residues His 42 (2.66 Å), Asn 205 (2.51 Å), and Val 218 (3.41 Å), as well as steric (hydrophobic/van der Waals) interactions with His 20, His 42, His 60, His 208, and Val 218 (Figs. 3 and 4). Natural compounds commonly used to inhibit tyrosinase, such as kojic acid and arbutin, were also used as reference drug standards in the molecular docking process of this study. Both kojic acid and arbutin share structural similarity with hydroquinone, which explains their favorable docking scores of –66.54 kcal/mol and –66.53 kcal/mol, respectively. Arbutin, also known as arbutoside, is the glycosylated form of hydroquinone. Upon hydrolysis, arbutin releases the aglycone hydroquinone and a glucose moiety. Kojic acid formed hydrogen bonds with amino acid residues Asn 205 (3.29 Å) and Met 215 (2.69 Å), categorized as weak (>3.2 Å) and moderate (2.5–3.2 Å), respectively (Arunan et al., 2011; Steiner, 2002). In total, kojic acid formed hydrogen bonds with six residues: His 204, Asn 205, His 208, Met 215, Val 217, and Val 218, while also establishing steric interactions with the identical six residues. Meanwhile, arbutin formed three hydrogen bonds with Asn 205 (2.80 and 3.10 Å), Met 215 (3.53 Å), and Gly 216 (2.66 Å). Based on bond distances, arbutin displayed moderate hydrogen bonding (2.2–3.2 Å) with Asn 205 and Gly 216, and a weak hydrogen bond (>3.2 Å) with Met 215. Additionally, arbutin exhibited steric interactions with six residues: His204, Asn 205, His 208, Gly 216, Val 217, and Val 218.

Among the phytochemicals in *C. asiatica*, asiatic acid and madecassic acid demonstrated potential tyrosinase-inhibitory activity, whereas asiaticoside and madecassoside yielded negative results in molecular docking.

Asiatic acid and madecassic acid, which belong to the terpenoid class, exhibited binding energies of –

45.81 kcal/mol and –42.62 kcal/mol, respectively. Although these values are higher (less negative) than those for hydroquinone (–52.64 kcal/mol), they still indicate a relatively strong predicted inhibitory activity against tyrosinase, suggesting that both compounds have promising potential. Asiatic acid showed steric interactions with Phe 197, Asn 205, Arg 209, and Val 218. Madecassic acid formed a hydrogen bond with Asn 205 and steric interactions with Gly 46, Asn 57, His 60, Met 61, Gly 196, Phe 197, Asn 205, and Arg 209, as shown in Table 1 and Figs. 3–4.

Asiaticoside, a glycoside phytochemical in *C. asiatica*, consists of an aglycone (asiatic acid) bound to a trisaccharide chain composed of glucose-glucose-rhamnose (Badal & Delgoda, 2016). Glycosides are typically water-soluble due to their positive Log S values (Badal & Delgoda, 2016); however, their bulky structures often result in poor compatibility with receptor-binding sites. Generally, glycosides must undergo enzymatic hydrolysis in the human body to release their aglycone moieties, which are responsible for the pharmacological activity (Liu et al., 2022; Walle et al., 2005; Yousefi et al., 2015; Zhang et al., 2012). The molecular docking of asiaticoside to tyrosinase produced a Moldock score of +323.56 kcal/mol, indicating an incompatible interaction due to the molecule's large size and poor fit within the small hydroquinone binding cavity, which resulted in significant overlap and red zones in the active site (Figs. 3 and 4).

Similarly, madecassoside—another glycoside in *C. asiatica* composed of madecassic acid as the aglycone and a glucose-glucose-rhamnose trisaccharide chain—also showed poor binding compatibility in molecular docking. The Moldock score of madecassoside was +145.54 kcal/mol, indicating a lack of effective binding to the tyrosinase active site. As with asiaticoside, the molecule's large size causes spatial overlap in the hydroquinone cavity, as visualized by red zones in the active site (Figs. 3 and 4).

Among the three additional compounds evaluated, 2-*o*-ethyl ascorbic acid and 3-*o*-ethyl ascorbic acid demonstrated inhibitory activity against tyrosinase, whereas coenzyme Q10 did not exhibit significant inhibitory potential. Both 2-*o*-ethyl ascorbic acid and 3-*o*-ethyl ascorbic acid are esterified derivatives of ascorbic acid. The ester group in these molecules enhances their lipophilicity, facilitating deeper skin penetration and prolonging their antioxidant effect (Chen et al., 2021). Vitamin C and its derivatives have been clinically validated for the treatment of melasma and other forms of hyperpigmentation. These findings are consistent with the molecular docking results showing that these derivatives can inhibit tyrosinase activity more effectively than the native ligand hydroquinone.

2-*o*-ethyl ascorbic acid exhibited a Moldock score of –64.28 kcal/mol, lower than hydroquinone (–52.64 kcal/mol), suggesting a stronger predicted binding affinity. It formed hydrogen bonds with His 42 and Asn 205, and steric interactions with His 42, Asn 205, and Val 218. 2-*o*-ethyl ascorbic acid demonstrated good compatibility with the active site of tyrosinase due to its molecular volume, which closely resembles that of hydroquinone. As a result, no spatial overlap was observed in the cavity, indicated by the absence of red zones in the cavity area (Figs. 3 and 4).

Similarly, 3-*o*-ethyl ascorbic acid showed a Moldock score of –61.47 kcal/mol, also lower than that of hydroquinone. It formed hydrogen bonds with Asn 205 and steric interactions with His 42, Asn 205, and Val 218. Like 2-*o*-ethyl ascorbic acid, this derivative exhibited structural compatibility with the tyrosinase active site, occupying the cavity without overlap, as evidenced by the lack of red zones (Figs. 3 and 4).

In contrast, coenzyme Q10 had a Moldock score of +725.54 kcal/mol, significantly higher than hydroquinone, indicating poor binding compatibility with tyrosinase. Its large molecular size makes it unsuitable for the relatively small binding cavity of hydroquinone, leading to spatial overlap and the appearance of red zones in the active cavity area (Figs. 3 and 4). Although coenzyme Q10 is known for its antioxidant properties, it does not appear to act via direct tyrosinase inhibition and is therefore less suitable for treating hyperpigmentation or melasma through this mechanism.

Molecular dynamics result

The molecular docking results are supported by molecular dynamics simulations that ran from 0 to 100 ns. The main objective of the molecular dynamics process run for 100 ns is to observe the stability of the bond between the drug and receptor. The bond stability can be assessed from the RMSD profile, where a value of < 2 Å indicates very stable binding, 2-3 Å indicates stable binding, and > 3 Å indicates unstable binding (Henzler-Wildman & Kern, 2007; Kesuma et al., 2025; Putra et al., 2025; Ruswanto et al., 2022).

The molecular dynamics results align with the molecular docking results, showing that the compounds coenzyme Q10, madecassoside, and asiaticoside do not have stable binding with tyrosinase, as indicated by RMSD values > 3 Å. The average RMSD values during the 100 ns run were 10.311 Å for coenzyme Q10, 5.800 Å for madecassoside, and 6.746 Å for asiaticoside. These molecular dynamics results also correspond with the molecular docking results, which indicate very high moldock scores.

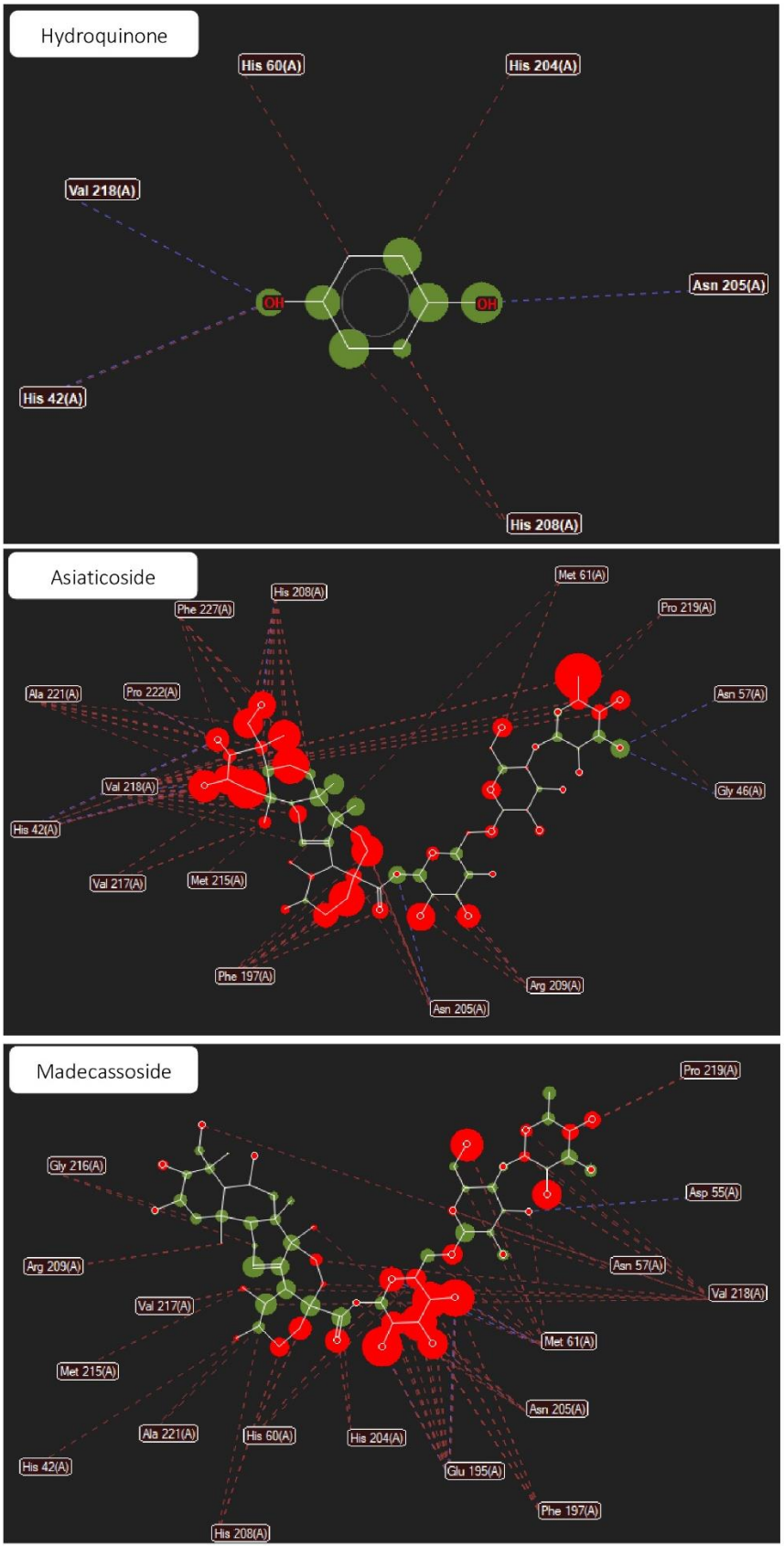


Figure 3. The 2D molecular docking interaction reference standard (native ligand and hydroquinone), four major phytochemicals from *C. asiatica*, vitamin C derivatives, and coenzyme Q10 into tyrosinase.

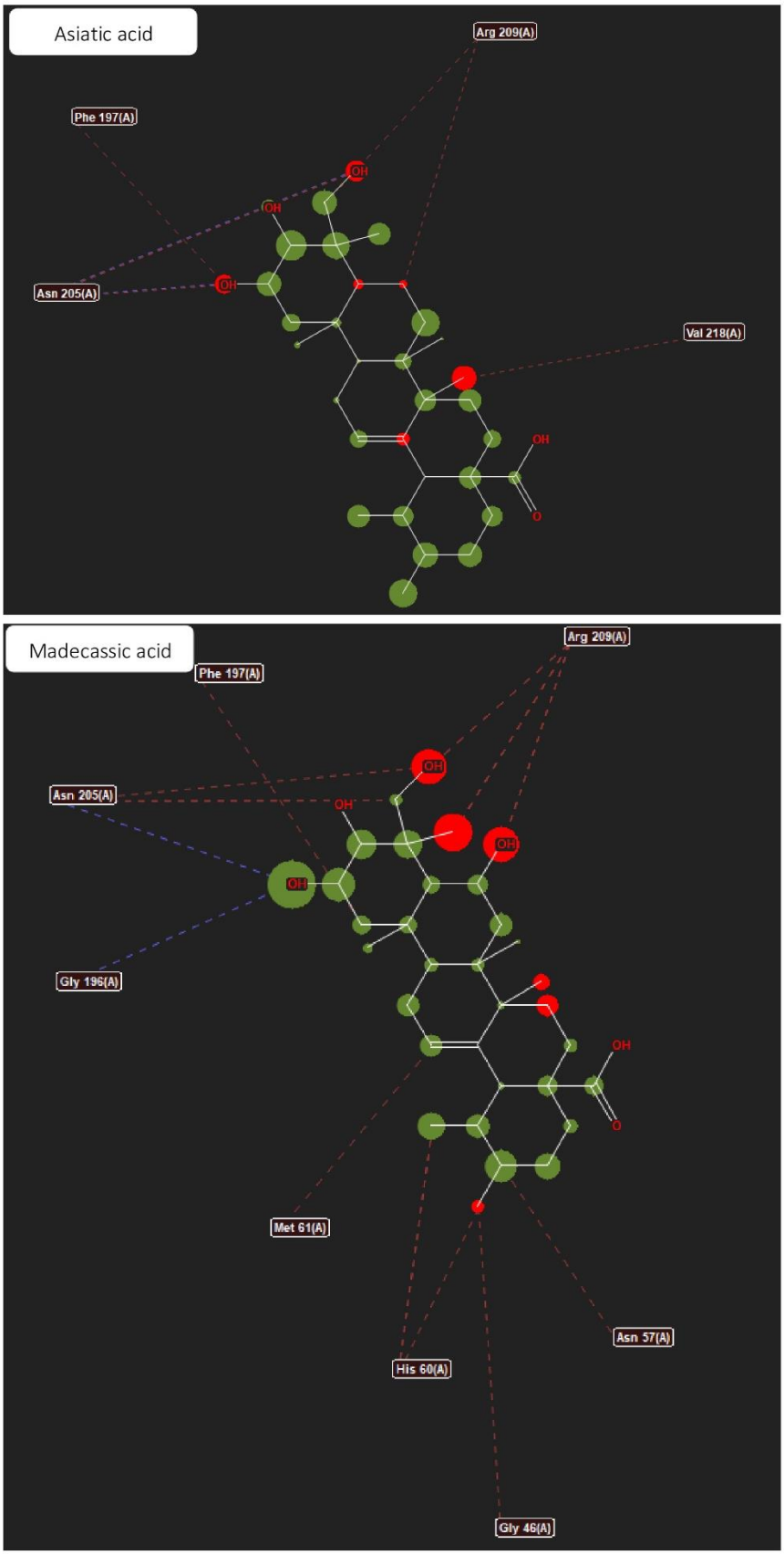


Figure 3. The 2D molecular docking interaction reference standard (native ligand and hydroquinone), four major phytochemicals from *C. asiatica*, vitamin C derivatives, and coenzyme Q10 into tyrosinase (continued…)

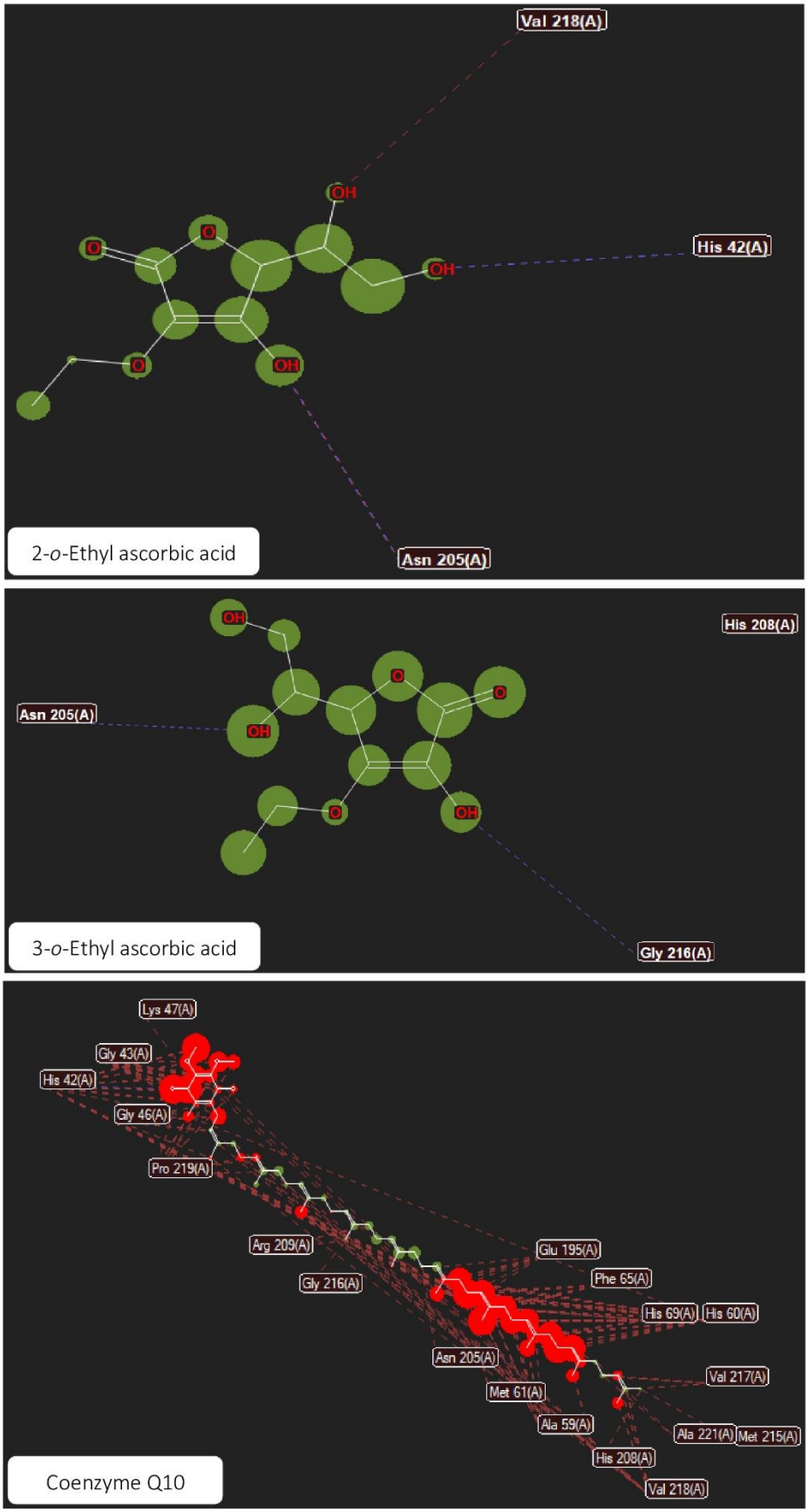


Figure 3. The 2D molecular docking interaction reference standard (native ligand and hydroquinone), four major phytochemicals from *C. asiatica*, vitamin C derivatives, and coenzyme Q10 into tyrosinase (continued…)

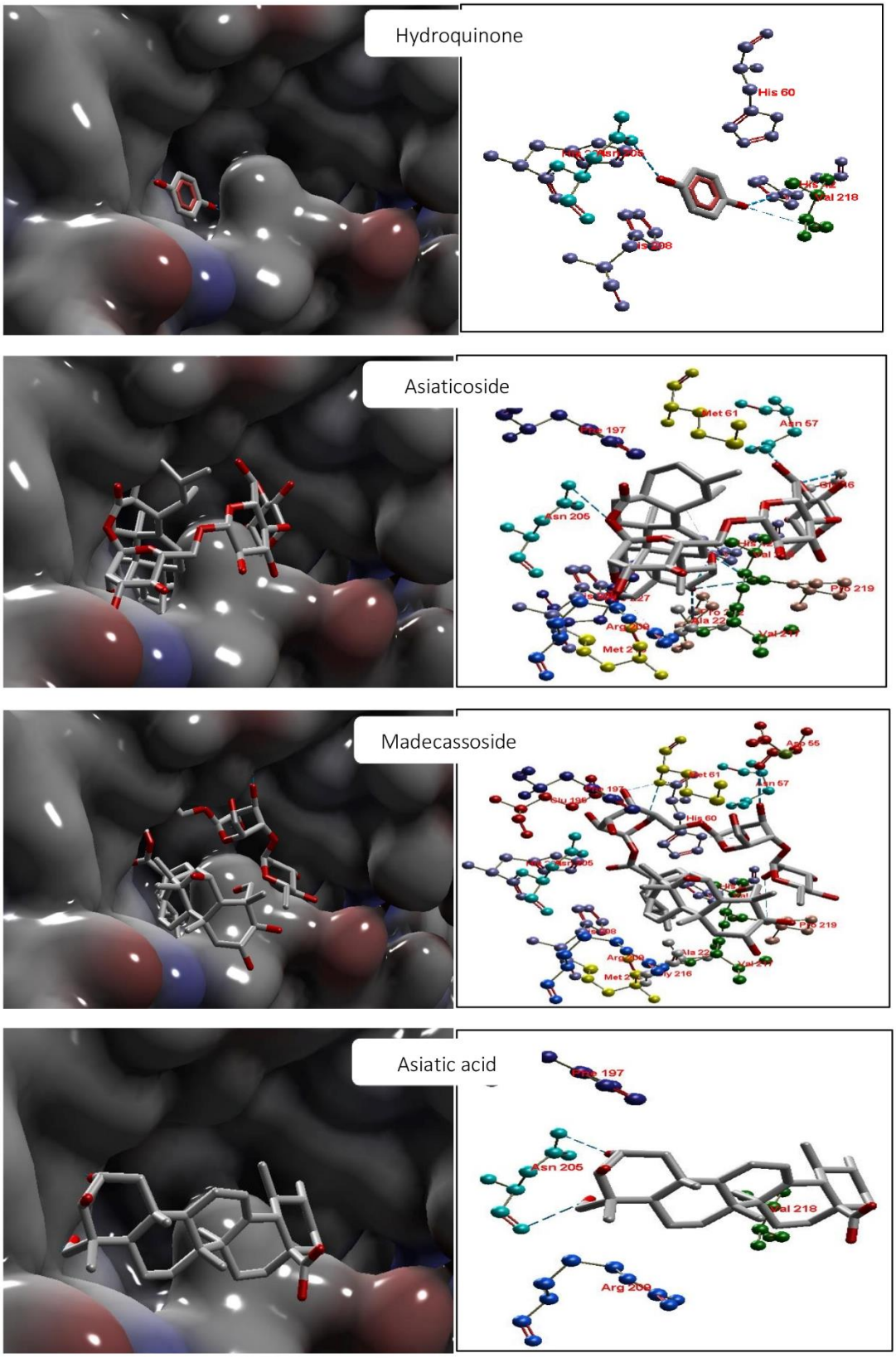


Figure 4. The 3D molecular docking interaction reference standard (native ligand and hydroquinone), four major phytochemicals from *Centella asiatica*, vitamin C derivatives, and coenzyme Q10 into tyrosinase.

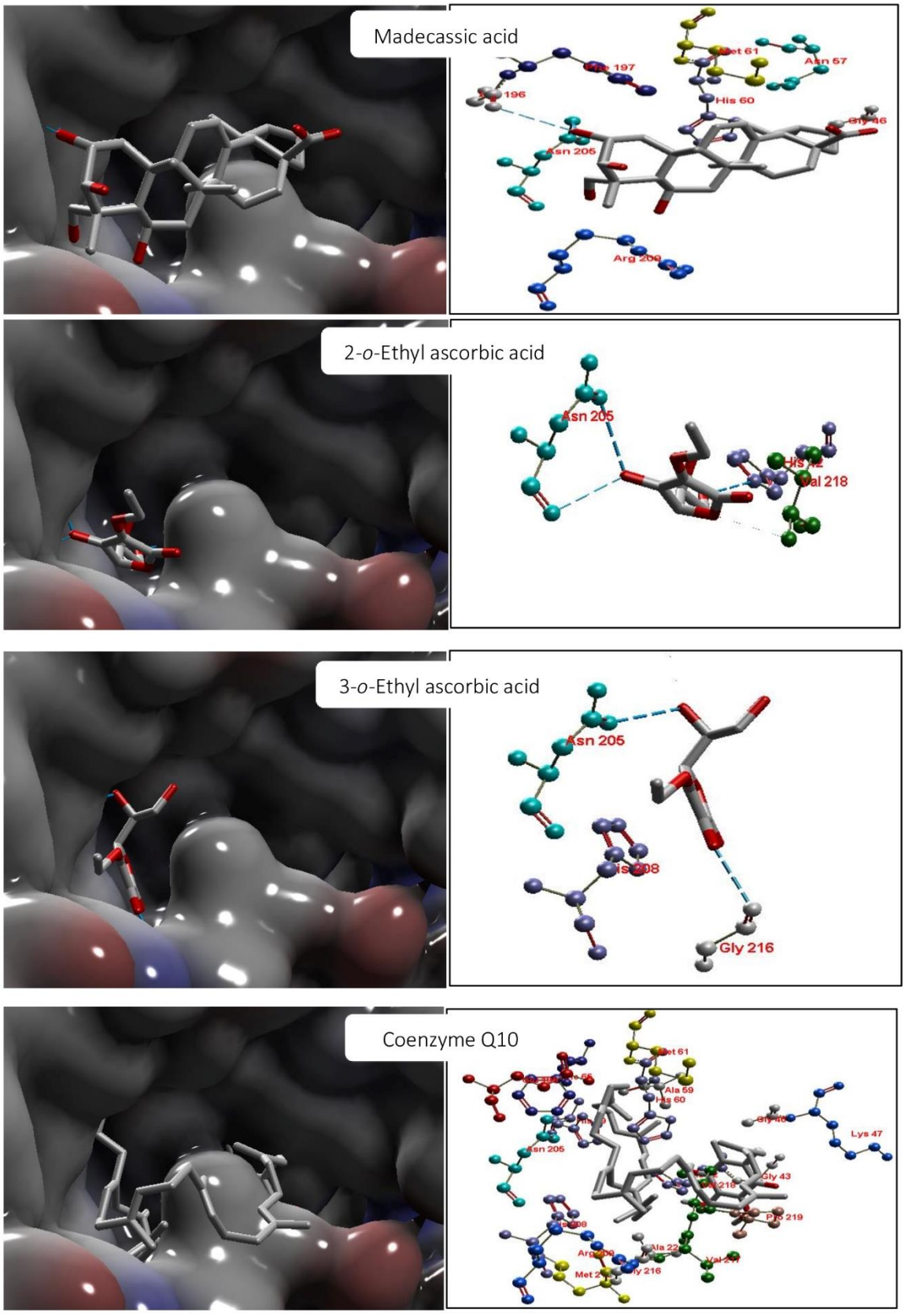


Figure 4. The 2D molecular docking interaction reference standard (native ligand and hydroquinone), four major phytochemicals from *C. asiatica*, vitamin C derivatives, and coenzyme Q10 into tyrosinase (continued…)

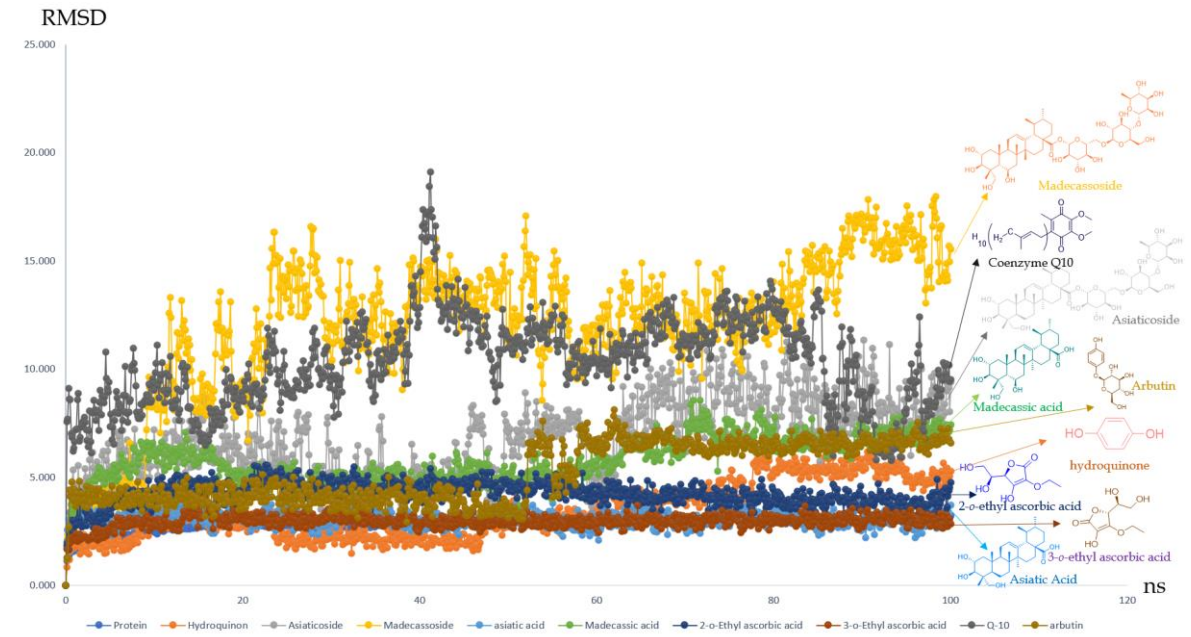


Figure 5. The protein-ligand RMSD of reference drug standard (hydroquinone, arbutin), four major phytochemicals from *Centella asiatica* (asiatic acid, madecassic acid, asiaticoside, madecassoside), ethyl ascorbic acid derivatives (2-*o*-ethyl ascorbic acid and 3-*o*-ethyl ascorbic acid), and coenzyme Q-10 in a 100 ns molecular dynamics simulation.

Table 2. Results of MM-GBSA (ΔG) and RMSD of compounds from a 100 ns molecular dynamics simulation.

Compound	MM-GBSA (ΔG) Kcal/mol	Average RMSD	Min. RMSD	Max. RMSD
Hydroquinone	-79.67	3.456	0.848	6.187
Arbutin	-55.72	5.201	1.261	8.132
Asiaticoside	5.65	6.746	2.013	11.347
Madecassoside	1.23	11.983	1.918	17.973
Asiatic acid	-88.50	3.069	1.997	4.225
Madecassic acid	-44.67	5.800	1.703	8.549
2-*o*-Ethyl ascorbic acid	-85.34	4.234	1.652	5.583
3-*o*-ethyl ascorbic acid	-89.21	2.971	1.679	4.083
Coenzyme Q10	10.27	10.311	5.790	19.110

Asiatic acid and madecassic acid show better RMSD profiles compared to coenzyme Q10, madecassoside, and asiaticoside. The hydrolysis of madecassoside and asiaticoside produces aglycone compounds in the form of madecassic acid and asiatic acid, resulting in smaller and more stable structures that bind more effectively to tyrosinase, with average RMSD values approaching 3 Å.

The compound 3-*o*-ethyl ascorbic acid, a derivative of vitamin C, has the most stable bond and inhibits tyrosinase, with an average RMSD of 2.971 Å, which is much lower than that of the native ligand or the standard reference drug, hydroquinone, which has an average RMSD of 3.456 Å. This result aligns with the molecular docking results, where the compound 3-*o*-ethyl ascorbic acid has a MM-GBSA (ΔG) score of -89.21 kcal/mol, lower than that of hydroquinone (-79.67 kcal/mol; Table 2). Meanwhile, the compound 3-*o*-ethyl ascorbic acid shows poor binding stability, as observed from its molecular dynamics profile (Fig. 5).

The molecular docking results provided an initial estimation of the binding affinity of the tested compounds toward the target protein, as reflected by the Moldock score. However, these results required further validation through molecular dynamics simulations and MM-GBSA calculations, which better represent biological conditions. The docking results, MM-GBSA binding free energy (ΔG), and 100 ns molecular dynamics simulations for each compound are summarized in Table 2. MM-GBSA ΔG, and RMSD were

analysed to evaluate the stability of ligand–receptor complexes (Greenidge et al., 2012; Hou et al., 2011).

As a reference, hydroquinone (synthetic standard) exhibited an MM-GBSA ΔG of –79.67 kcal/mol with an average RMSD of 3.456 Å. In comparison, arbutin (natural standard) showed weaker binding (ΔG –55.72 kcal/mol) and less stability (average RMSD 5.201 Å). Several tested compounds demonstrated superior results to both standards. 3-*o*-ethyl ascorbic acid (ΔG –89.21 kcal/mol, RMSD 2.971 Å) and asiatic acid (ΔG –88.50 kcal/mol, RMSD 3.069 Å) formed more stable interactions than hydroquinone and arbutin. 2-*o*-ethyl ascorbic acid (ΔG –85.34 kcal/mol, RMSD 4.234 Å) also showed stronger binding than hydroquinone, although with slightly higher RMSD. Conversely, asiaticoside, madecassoside, and coenzyme Q10 displayed positive ΔG values and high RMSD, indicating unstable interactions.

Hydroquinone is widely used as the reference drug in hyperpigmentation therapy, while arbutin serves as a safer natural analog, though it is less potent because it must be enzymatically hydrolyzed to release hydroquinone as its aglycone. Therefore, comparison with both standards is important for assessing new candidates. The present findings highlight asiatic acid and 3-o-ethyl ascorbic acid as stronger candidates, supported by lower ΔG values (<-88.50 kcal/mol) and small RMSD (<3.5 Å), suggesting strong and stable ligand–receptor interactions throughout the 100 ns simulation.

Although 2-o-ethyl ascorbic acid exhibited a slightly higher RMSD, its ΔG was lower than that of hydroquinone (–85.34 vs. –79.67 kcal/mol), indicating promising potential that warrants further validation. Compared to arbutin, most candidates (asiatic acid, 2-o-ethyl ascorbic acid, and 3-o-ethyl ascorbic acid) demonstrated significantly lower ΔG and smaller RMSD, confirming arbutin's weaker and less stable binding profile. In contrast, bulky glycosides such as asiaticoside and madecassoside, as well as coenzyme Q10, did not exhibit favorable binding (positive ΔG, RMSD >10 Å), thus excluding them as potential candidates.

In summary, relative to the two standards (hydroquinone and arbutin), asiatic acid, 3-o-ethyl ascorbic acid, and 2-*o*-ethyl ascorbic acid emerged as the strongest candidates, not only more stable than arbutin but also showing superior binding energies compared to hydroquinone.

The total secondary structure content of tyrosinase was 32.51%, consisting of 28.58% α-helices and 3.93% β-sheets (Fig. 6), while the remaining 67.49% comprised primary structural elements. RMSF analysis revealed that the tested compounds interacted with several amino acid residues similar to the native ligand, with RMSF values <1.5 Å (Ekowati et al., 2023; Ghahremanian et al., 2022). Such low RMSF values suggest reduced flexibility, indicating that the compounds bind precisely at the core domain or active-site pocket of tyrosinase, as illustrated in Fig. 6.

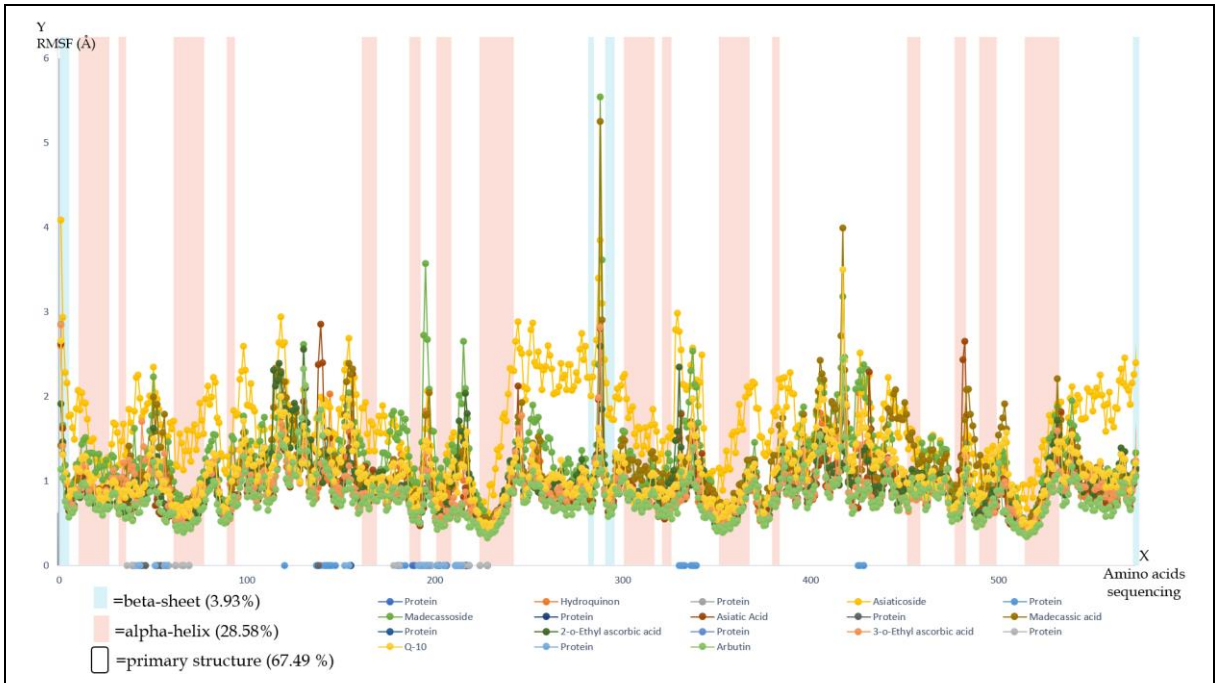


Figure 6. Protein-ligand complex RMSF of native ligand, reference drug standard (hydroquinone, arbutin), four major phytochemicals from *Centella asiatica* (asiatic acid, madecassic acid, asiaticoside, madecassoside), ethyl ascorbic acid derivatives (2-*o*-ethyl ascorbic acid and 3-*o*-ethyl ascorbic acid), and coenzyme Q-10.

Molecular dynamics results of each compound over a 100 ns simulation demonstrated stable interactions with several amino acid residues. Native ligand (hydroquinone): Hydrogen bonds were formed with four amino acid residues: Gly 194 (6.5%); Asn 205 (5.2%); Val 217 (5.6%); Val 218 (33.4%). Ionic/electronic interactions were formed with one amino acid residue: His 60 (100%). Hydrophobic/steric interactions were formed with six amino acid residues: His 60 (5.4%); Met 61 (3.5%); Met 184 (0.1%); Phe 197 (1.6%); His 208 (5.8%); Val 218 (0.6%). Water bridges interactions were formed with 13 amino acid residues: Met 184 (3.3%); Arg 191 (1.4%); Asn 192 (21.0%); Glu 195 (1.7%); Gly 196 (5.1%); Phe 197 (0.5%); Asn 205 (4.2%); Gln 214 (0.3%); Met 215 (8.8%); Gly 216 (5.6%); Val 217 (26.1%); Val 218 (6.6%); Pro (10.5%). Protein-ligand contact results for the native ligand are shown in Fig. 7.

Arbutin: Hydrogen bonds were formed with five amino acid residues: His 60 (3.6%); Glu 158 (61.8%); Asn 205 (5.2%); Arg 209 (3.0%); Val 218 (55.8%). Ionic/electronic interactions were formed with one amino acid residue: Glu 158 (4.9%). Hydrophobic/steric interactions were formed with six amino acid residues: Met 61 (1.0%); Phe 197 (26.6%); Pro 201 (1.2%); Arg 209 (17.9%); Val 217 (3.1%); Val (0.8%). Water bridges interactions were formed with 13 amino acid residues: Gly 46 (0.1%); Lys 47 (0.2%); Asp 55 (0.1%); His 60 (61.6%); Thr 156 (0.1%); Glu 158 (35.7%); Glu 195 (79.9%); Phe 197 (2.2%); Gly 200 (6.0%); Asn 205 (100%); Arg 209 (8.9%); Gly 216 (8.9%); Val 208 (13.2%). Protein-ligand contact results for the native ligand are shown in Fig. 7.

Asiaticoside: Hydrogen bonds were formed with seven amino acid residues: Asp 55 (50.8%); Asn 57 (1.0%); His 60 (74.7 %); Glu 148 (4.5%); Glu 195 (100%); Asn 205 (29.9%); Arg 209 (5.4%).

Ionic/electronic interactions were formed with four amino acid residues: Asn 57 (1.2%); His 204 (100%); His 208 (100%); His 231 (100%). Hydrophobic/steric interactions were formed with five amino acid residues: Met 61 (4.0%); Phe 65 (44.9%); Phe 197 (41.7%); Pro 201 (0.1%); Val 218 (15.5%). Water bridges interactions were formed with 16 amino acid residues: His 42 (0.6%); His 49 (0.1%); Asp 55 (47.9%); Asn 57 (28.0%); Ala 59 (0.1%); His 69 (0.8%); Lys 151 (0.1%); Glu 158 (7.8%); Gly 200 (0.2%); Asn 205 (2.5%); Arg 209 (2.3%); Met 215 (1.5%); Gly 216 (0.5%); Val 217 (0.1%); Val 218 (2.1%); Pro 219(0.4%).

Madecassoside: Hydrogen bond were formed with 16 amino acid residues: Gly 46 (1.5 %); Lys 47 (0.7%); His 49 (4.1%); Asp 140 (1.2%); Glu 141 (100%); Gln 142 (2.6%); Asn 144 (0.7%); Pro 145 (1.2%); Lys (1.0%); Glu 158 (22.3%); Gly (1.2%); Asn 199 (2.3%); Asn 205 (17.3 %); Arg 209 (1.1%); Gly 216 (6.0%); Val 218 (5.0%). Ionic/electronic interactions were formed with four amino acid residues: His 42 (100 %); His 60 (100 %); Asn 199 (2.6%); Gly 200 (1.6 %). Hydrophobic/steric interactions were formed with four amino acid residues: Phe 197 (0.8%); Val 217 (1.6%); Val 218 (3.3%); Pro 219 (3.1%). Water bridges interactions were formed with 19 amino acid residues: Gly 46 (2.1%); Lys 47 (15.0%); Asp 55 (2.1%); Asp 140 (9,7%); Glu 141 (3.6%); Gln 142 (5.4%); Asn 144 (2.5%); Pro 145 (2.4%); Glu 158 (15.9%); Glu 195 (2.4%); Gly 196 (5.4%); Asn 199 (5.4%); Asn 205 (20.2%); Arg 209 (8.7%); Met 215 (4.9%); Gly 216 (6.4%); Val 217 (6.9%); Val 218 (9.6%); Pro 219 (3.9%).

Asiatic acid: Hydrogen bonds were formed with three amino acid residues: Glu 195 (84.1%); Gly 216 (67.3%); Val 217 (37.7%). Ionic/electronic interactions were formed with six amino acid residues: His 42 (100%); His 60 (100%); Glu 195 (100%); His 204 (100 %); His 208 (100%); His 231 (100%). Hydrophobic/steric interactions were formed with one amino acid residue: Val 218 (2.3%). Water bridges interactions were formed with 17 amino acid residues: Glu 158 (13.1%); Glu 195 (0.2%); Gly 196 (0.5%); Phe 197 (0.4%); Ile 198 (1.2%); Asn 199 (0.3%); Gly 200 (57.1%); Pro 201 (0.1%); Asn 205 (2.2%); His 208 (0.2%); Arg 209 (5.5%); Met 215 (4.8%); Gly 216 (5.8%); Val 217 (31.4%); Val 218 (22.7%); Pro 219 (13.9%); Ala 221 (0.9%). Protein-ligand contact results for the native ligand are shown in Fig. 7.

Madecassic acid: Hydrogen bonds were formed with five amino acid residues: His 60 (5.9%); Glu 195 (55.4%); Gly 196 (27.4%); Asn 205 (22.4%); Arg 209 (2.6%). Hydrophobic/steric interactions were formed with six amino acid residues: Met 61 (7.4%); Met 184 (10.5%); Phe (32.2%); Pro 201 (9.4%); Val 218 (13.2%); Pro 219 (0.1%). Water bridges interactions were formed with 15 amino acid residues: Lys 47 (0.1%); His 49 (0.2%); Asp 55 (2,3%); Asn 57 (0.3%); His 60 (0.7%); Glu 141 (0.1%); Glu 158 (1.3%); Met 184 (10.5%); Gly 196 (2.7%); Gly 200 (0.3%); Asn 205 (11.3%); Arg 209 (7.2%); Gly 216 (1.0%); Val 218 (5.0%); Pro 219 (0.1%).

2-*o*-Ethyl ascorbic acid: Hydrogen bonds were formed with three amino acid residues: Arg 209 (19.6%), Met 215 (0.1%), and Val 217 (14.8%). Ionic/electronic interactions were formed with six amino acid residues: His 42 (100%); His 60 (100%); Glu 195 (100%); His 204 (100 %); His 208 (100%); His 231 (100%). Hydrophobic/steric interactions were formed with one amino acid residue: Val 218 (3.5%). Water bridges interactions were formed with eight amino acid residues: Glu 158 (0.1 %); Asn 205 (19.3%); Arg 209 (6.9%); Met 215 (10.6%); Gly 216 (28.4%); Val 217 (2.9%); Val 218 (0.5%); Pro 219 (0.1%). Protein-ligand contact results for the native ligand are shown in Fig. 7.

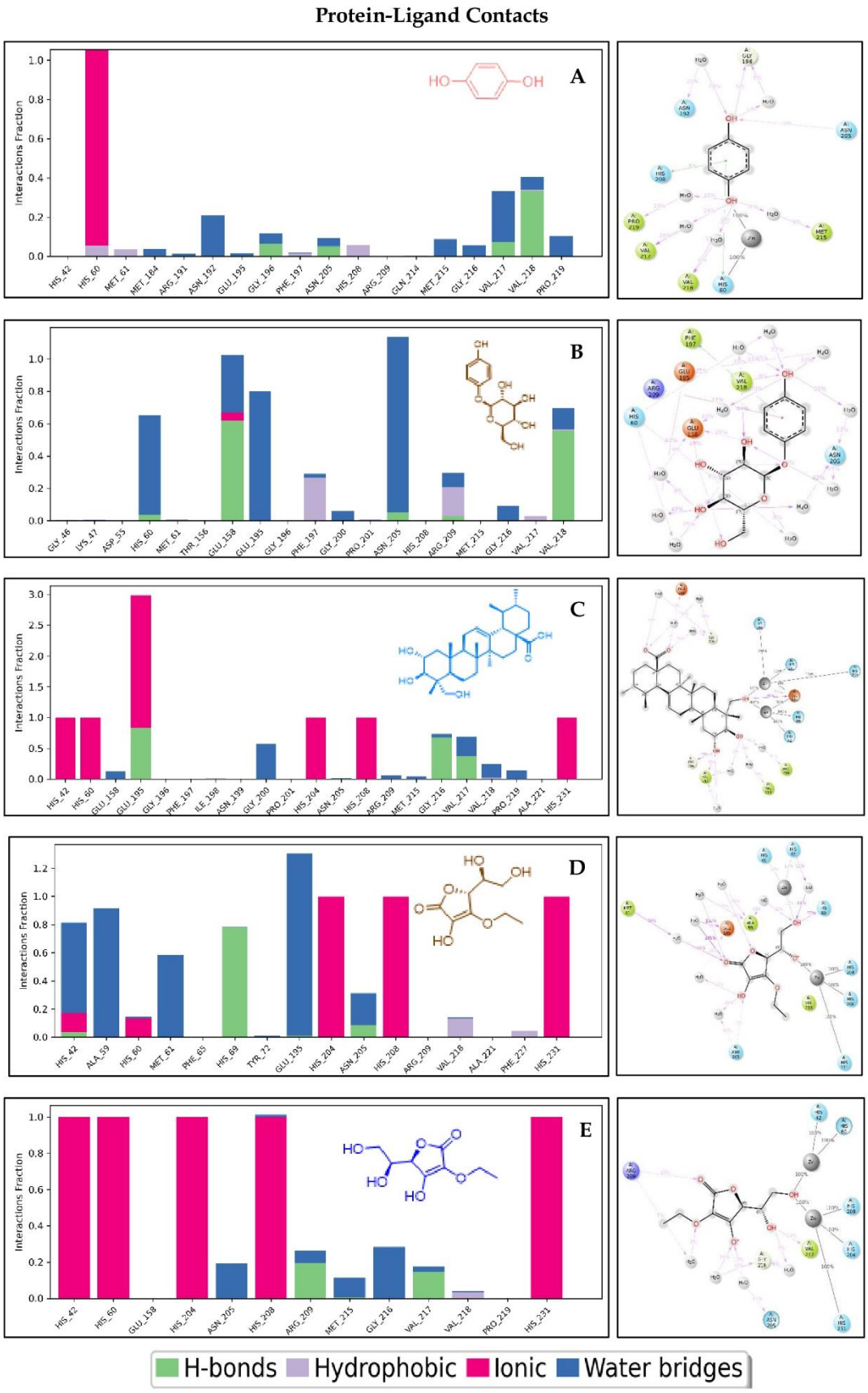


Figure 7. The protein-ligand interaction contacts with tyrosinase **(A)** native ligand (hydroquinone), **(B)** arbutin, **(C)** asiatic acid, **(D)** 3-*o*-ethyl ascorbic acid, and **(E)** 2-o-ethyl ascorbic acid in a 100 ns molecular dynamics simulation.

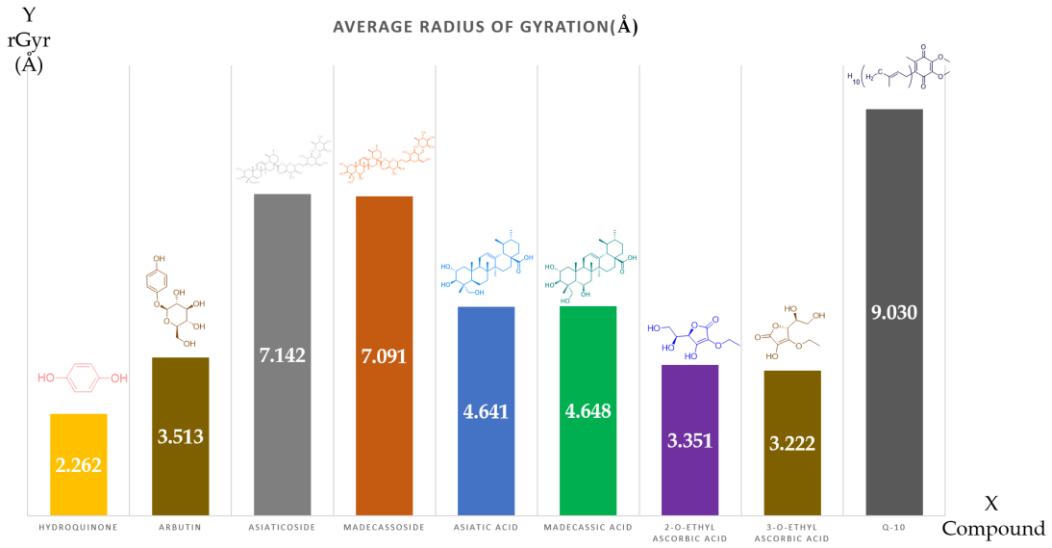


Figure 8. Average of radius of gyration (rRyr) of native (hydroquinone, arbutin), four major phytochemicals from *Centella asiatica* (asiatic acid, madecassic acid, asiaticoside, madecassoside), ethyl ascorbic acid derivatives (2-*o*-ethyl ascorbic acid and 3-*o*-ethyl ascorbic acid), and coenzyme Q-10.

3-*o*-Ethyl ascorbic acid: Hydrogen bonds were formed with four amino acid residues: His 42 (3.8%); His 69 (77.8%); Glu 195 (1.0%); Asn 205 (8.6%0. Ionic/electronic interactions were formed with seven amino acid residues: His 42 (13.5%); Ala 59 (0.1%); His 60 (13.5%); Met 61 (0.1%); His 204 (100%); His 208 (100%); His 231 (100%). Hydrophobic/steric interactions were formed with three amino acid residues: Val 218 (13.3%), Ala 221 (0.4%), and Phe 227 (4.5%). Water bridges interactions were formed with 12 amino acid residues: His 42 (64.2%); Ala 59 (91.0%); His 60 (0.1%); Met 61 (58.2 %); Phe 65 (0.1%); His 69 (0.3%); Tyr 72 (1.1%); Glu 195 (100%); Asn 205 (22.7%); Arg 209 (0.1%); Val 218 (0.1%); Ala 221 (0.1%). Protein-ligand contact results for the native ligand are shown in Fig. 7.

Coenzyme Q10: Hydrogen bonds were formed with two amino acid residues: His 42 (0.1%); His 69 (10.7%). Ionic/electronic interactions were formed with three amino acid residues: His 204 (100 %), His 208 (100%), and His 231 (100%). Hydrophobic/steric interactions were formed with 14 amino acid residues: His 42 (0.1%); Ala 59 (0.2%); Met 61 (9.0%); Phe 65 (32.2%); Trp 68 (24.3%); Trp 72 (22.0%); Pro 181 (0.1%); Met 184 (17.0%); Phe 197 (46.1%); Ile 198 (8.5%); Val 217 (0.1%); Val 218 (27.3%); Ala 221 (11.8%); Phe 227 (67.7%). Water bridges interactions were formed with six amino acid residues: Ile 39 (0.1%); Ala 59 (4.1 %); His 69 (7.5%); Tyr 72 (0.3%); Glu 195 (0.7%); Gly 216 (0.1%).

Radius of gyration (Rg) analysis was performed to evaluate the degree of compaction and structural stability of the ligand–protein complexes during the 100 ns molecular dynamics simulation (Lobanov et al., 2008). The average Rg values of each compound are presented in Fig. 8 and analyzed in conjunction with Table 2, alongside binding free energy (MM-GBSA) and RMSD values.

Hydroquinone, as the synthetic reference standard, exhibited a low Rg value (2.262 Å), indicating a relatively compact complex, with an MM-GBSA ΔG of –79.67 kcal/mol. In contrast, arbutin showed a higher Rg (3.513 Å) and weaker binding energy (–55.72 kcal/mol). Asiatic acid (Rg 4.641 Å; ΔG –88.50 kcal/mol) and 3-*o*-ethyl ascorbic acid (Rg 3.222 Å; ΔG –89.21 kcal/mol) demonstrated the lowest ΔG values with moderate Rg, suggesting stable interactions with a reasonably compact structural conformation. Similarly, 2-o-ethyl ascorbic acid (Rg 3.351 Å; ΔG –85.34 kcal/mol) displayed favorable results. In contrast, larger molecules such as asiaticoside (Rg 7.142 Å), madecassoside (Rg 7.091 Å), and coenzyme Q10 (Rg 9.030 Å) exhibited substantially higher Rg values, with positive or only slightly negative ΔG and elevated RMSD values. These findings indicate unstable complexes with looser structural conformations throughout the simulation.

Rg reflects the degree of compaction of a ligand–protein complex. A lower Rg value generally indicates a more compact and stable complex, whereas a higher Rg value suggests excessive flexibility or unstable binding. In this study, hydroquinone exhibited the lowest Rg (2.262 Å), consistent with its small molecular size, which allows tight interaction within the protein's active pocket. Interestingly, several test candidates showed higher binding energies than hydroquinone, despite slightly higher Rg values.

Among these, 3-*o*-ethyl ascorbic acid and asiatic acid emerged as the most promising candidates. Both compounds showed the lowest ΔG values (–89.21 and –88.50 kcal/mol, respectively) and moderate Rg values (3.222–4.641 Å), which remain within a stable range. This indicates that although their complexes are slightly more flexible than hydroquinone, the binding energies achieved are significantly stronger and more stable. Conversely, arbutin, the natural reference standard, exhibited a weaker binding energy (–55.72 kcal/mol) and a higher Rg than hydroquinone, consistent with previous reports that arbutin is less potent than hydroquinone. Larger molecules, such as asiaticoside and madecassoside, displayed Rg values >7 nm, positive ΔG, and very high RMSD (>10 Å), indicating unstable complexes prone to dissociation during the simulation. Similarly, coenzyme Q10 showed the highest Rg (9.030 nm) with a positive ΔG (10.27 kcal/mol), suggesting an inability to form favorable thermodynamic interactions.

Overall, the combined analysis of Rg, MM-GBSA, RMSD, and RMSF demonstrated that 3-*o*-ethyl ascorbic acid and asiatic acid are the best candidates, as they maintained structural stability (relatively low Rg, RMSD <3.5 Å, RMSF <3 Å) while exhibiting stronger binding energies than both hydroquinone and arbutin.

Based on molecular docking and molecular dynamics studies, it can be concluded that the phytochemicals from *C. asiatica* responsible for the pharmacological effect as an anti-hyperpigmentation agent are asiatic acid, whereas its glycoside forms are inactive in inhibiting tyrosinase, according to *in silico* studies. The addition of 3-*o*-ethyl ascorbic acid to the antimelasma cream formulation is more likely to enhance the anti-hyperpigmentation activity, as this compound has been shown *in silico* to be more potent at inhibiting tyrosinase than the clinically used standard reference drug, hydroquinone.

CONCLUSION

Based on molecular docking and molecular dynamics studies, it can be concluded that the phytochemicals from *C. asiatica* responsible for the pharmacological effect as an anti-hyperpigmentation agent are asiatic acid, while its glycoside forms are inactive in inhibiting tyrosinase according to *in silico* studies. The addition of 3-*o*-ethyl ascorbic acid to the antimelasma cream formulation is more likely to enhance anti-hyperpigmentation activity than coenzyme Q10.

CONFLICT OF INTEREST

The research was conducted entirely free from any involvement in commercial, financial, or personal matters that might be perceived as a possible conflict of interest or that could have influenced the outcomes or interpretation of the study.

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GENERATIVE ARTIFICIAL INTELLIGENCE (AI)

The authors used Grammarly Inc. to improve the language and readability of the manuscript. The authors reviewed and edited the content and take full responsibility for its accuracy. No images were generated or manipulated using AI tools.

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AUTHOR CONTRIBUTION:

Contribution	Aryani NLD	Kesuma D	Yasinta AD	Andreyana E
Concepts or ideas	x	x		
Design	x	x		
Definition of intellectual content	x	x		
Literature search	x	x	x	x
Experimental studies	x	x		
Data acquisition	x	x	x	x
Data analysis		x	x	x
Statistical analysis		x		x
Manuscript preparation				x
Manuscript editing	x	x	x	x
Manuscript review	x	x	x	x

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1.- Original Article

Tukiran T. Tukiran, Syahrul L. Hendrawan, Andika P. Wardana (2026) **Inhibitory activity o the ethyl acetate extract of *Desmanthus virgatus* (L.) Willd. leaves against a glucosidase enzyme: *In silico* and *in vitro* studies.** | [Actividad inhibitoria del extracto d acetato de etilo de hojas de *Desmanthus virgatus* contra la enzima α-glucosidasa Estudios *in silico* e *in vitro*]. J Pharm Pharmacogn Res 14(1): 241 https://doi.org/10.56499/jppres_14.1.2419 FREE PDF [3.02 Mb] [ABSTRACT]

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Na'ilah I. Alifiyah, Wirdatun Nafisah, Rizki, Arie Aryanto, Hikmah Zikriyani (2026) **GC-M profiling and *in silico* multi-target docking of carvone, p-cymene, and linalool fron *Cuminum cyminum* seeds extract against breast cancer proteins.** | [Perfiles GC-MS acoplamiento multiobjetivo *in silico* de carvona, p-cimeno y linalol del extracto d semillas de *Cuminum cyminum* contra proteínas de cáncer de mama]. J Pharm Pharmacogn Res 14(1): 2394. https://doi.org/10.56499/jppres_14.1.2394 FREE PDF [5.29 Mb [ABSTRACT]

3.- Review

Rosemary Estremor-Rodríguez, Adriana Redondo-Barrera, Santiago Gil-Cure, Jua Garcés-Barraza, Neyder Contreras-Puentes (2026) **Use of curcumin as a potentic therapeutic agent in Alzheimer's disease: A systematic review.** | [Uso de la curcumin como posible agente terapéutico en la enfermedad de Alzheimer: una revisió sistemática]. J Pharm Pharmacogn Res 14(1): 227 https://doi.org/10.56499/jppres_14.1.2274 [784 Kb] [ABSTRACT]

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Munira Munira, Nurdin Saidi, Binawati Ginting, Suhartono Suhartono (2026) **GC-M analysis of active compounds from ethanolic extract of *Jatropha gossypiifolia* L. an antibacterial activity against *Pseudomonas aeruginosa*.** | [Análisis GC-MS d compuestos activos del extracto etanólico de *Jatropha gossypiifolia* L. y activida antibacteriana frente a *Pseudomonas aeruginosa*]. J Pharm Pharmacogn Res 14(1): 235 https://doi.org/10.56499/jppres_14.1.2353 [866 Kb] [ABSTRACT]

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Binawati Ginting, Nadia Isnaini, Khairan Khairan, Nurdin Saidi, Murniana Murniana Muhammad Bahi, Mustanir Yahya, T. Zaid Thariq Gunana, Sitti Saleha, Cantika Dw Riski (2026) **Antibacterial and anti-tyrosinase activity of eucalyptus leaf [*Melaleuc leucadendra* (L.) L.] acne spot emulgel: Formulation and evaluation.** | [Activida antibacteriana y antitirosinasa del emulgel para el acné de hoja de eucalipto [*Melaleuc leucadendra* (L.) L.]: formulación y evaluación]. J Pharm Pharmacogn Res 14(1): 229 https://doi.org/10.56499/jppres_14.1.2299 [478 Kb] [ABSTRACT]

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Herni Kusriani, Yani Mulyani, Rahmat Santoso, Garnadi Jafar, Fatiya Z. Ishmah, Nadhira A Zahra (2026) **Pharmacological assessment of standardized *Curcuma longa* L. an *Centella asiatica* (L.) Urban extracts for diabetes management.** | [Evaluació farmacológica de extractos estandarizados de *Curcuma longa* y *Centella asiática* par el manejo de la diabetes]. J Pharm Pharmacogn Res 14(1): 229 https://doi.org/10.56499/jppres_14.1.2290 [881 Kb] [ABSTRACT]

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Muhammad Maskur, Asep A. Prihanto, Muhamad Firdaus, Rahmi Nurdiani (2026) **Potentic of seaweed bioactives for pharmaceutical applications.** | [Potencial de los bioactivos d las algas marinas para aplicaciones farmacéuticas]. J Pharm Pharmacogn Res 14(1) 2477. https://doi.org/10.56499/jppres_14.1.2477 FREE PDF [648 Kb] [ABSTRACT]

8.- Original Article

Cyntiya Rahmawati, Heru Sasongko, Baiq Lenysia Puspita Anjani, Safwan Safwan (2026 **Cost-effectiveness analysis of AC vs. TAC chemotherapy in West Nusa Tenggar breast cancer patients.** | [Análisis de costo-efectividad de la quimioterapia AC vs. TA en pacientes con cáncer de mama en Nusa Tenggara Occidental]. J Pharm Pharmacog Res 14(1): 2278. https://doi.org/10.56499/jppres_14.1.2278 FREE PDF [376 Kb] [ABSTRACT]

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Ambrocio T. Esteves Pairazaman, Jesús D. Collanque Pinto, Veronica L. Esteves Cárdenas Elmer Oyarce Alvarado, Jose Rincon Chavez, Carmela G. Barboza Justiniano, Nelcy C Quintana Marquez, Daniel R. Reyes Villalobos (2026) **Validación microbiológica de u desinfectante de superficies de amonio cuaternario al 0,25% mediante el método d dilución-neutralización.** | [Microbiological validation of a 0.25% quaternary ammoniur surface disinfectant using the dilution-neutralisation method]. J Pharm Pharmacogn Re 14(1): 2205. https://doi.org/10.56499/jppres_14.1.2205 FREE PDF [1.02 Mb] [ABSTRACT]

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12.- Review

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Indira Prakoso, Yustinus Maladan, Fachrur Rizal Mahendra, Mochamad Nurcholis, Aniss Nofita Sari (2026) **Immunoinformatics design of a multi-epitope vaccine for *Chlamydi pneumoniae* targeting the Indonesian population.** | [Diseño inmunoinformático de un vacuna multiepítopa contra *Chlamydia pneumoniae* dirigida a la población indonesa]. Pharm Pharmacogn Res 14(1): 2264. https://doi.org/10.56499/jppres_14.1.2264 FREE PDF [2.6 Mb] [ABSTRACT]

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16.- Original Article

Oktavia Rahayu Adianingsih, Wibi Riawan, Aina Angelina, Fifi Farida Fajrin, Violita Ay Puspita, Surya Saputri, Genera Dinan Adlina, Akbar Saitama, Eko Widaryanto (2026 **Effects of *Kaempferia galanga* L. extract on monosodium iodoacetate-induce osteoarthritis in rats.** | [Efectos del extracto de *Kaempferia galanga* L. sobre l osteoartritis inducida por yodoacetato monosódico en ratas]. J Pharm Pharmacogn Re 14(1): 2468. https://doi.org/10.56499/jppres_14.1.2468 FREE PDF [984 Kb] [ABSTRACT]

17.- Original Article

Van Anh T. Pham, Hanh M. Hoang, Trung H. Le, Phong X. Pham, Hung D. Tran, Thanh C Doan, Su Q. Pham, Hong L. To, Hung T. Bui, Loan T. T. Nguyen, Duong T. Dau (2026) **Bacteric cellulose wound dressing immersed in electrolyzed water: A promising treatment fo burn injuries.** | [Apósito de celulosa bacteriana sumergido en agua electrolizada: u tratamiento prometedor para las quemaduras]. J Pharm Pharmacogn Res 14(1): 246 https://doi.org/10.56499/jppres_14.1.2466 FREE PDF [1.61 Mb] [ABSTRACT]

18.- Original Article

Fitmawati, Asih Rahayu Ajeng Agesti, Hestia Hairima, Khairunnisa, Nur Anisa, Titrawan Vita Sindiya (2026) **Identification of *Mangifera laurina* Blume potential as anticance An *in silico* study.** | [Identificación del potencial de *Mangifera laurina* Blume com anticancerígeno: estudio *in silico*]. J Pharm Pharmacogn Res 14(1): 240 https://doi.org/10.56499/jppres_14.1.2401 FREE PDF [1.24 Mb] [ABSTRACT]

19.- Original Article

Mochamad Fathurohman, Tursino, Muhammad Azhari, Anjali Patel, Elin Julianti (2026 **Isolation and characterization of *Bacillus subtilis* BPP16: A marine-derived α-amylas producer.** | [Aislamiento y caracterización de *Bacillus subtilis* BPP16: un productor de a amilasa de origen marino]. J Pharm Pharmacogn Res 14(1): 234 https://doi.org/10.56499/jppres_14.1.2340 FREE PDF [871 Kb] [ABSTRACT]

20.- Original Article

Ni L. D. Aryani, Dini Kesuma, Armiza D. Yasinta, Elya Andreyana (2026) **Effectiveness a tyrosinase inhibitor from active compounds of *Centella asiatica* (L.) Urb., ethy ascorbic acid, and coenzyme Q10 as skin whitening by *in silico* evaluation.** | [Eficaci como inhibidor de la tirosinasa de compuestos activos de *Centella asiatica* (L.) Urb ácido etilascórbico y coenzima Q10 para el blanqueamiento de la piel mediante l evaluación *in silico*]. J Pharm Pharmacogn Res 14(1): 247 https://doi.org/10.56499/jppres_14.1.2475 FREE PDF [2.03 Mb] [ABSTRACT]

21.- Original Article

Khalish Arsy Al Khairy Siregar, Fachrur Rizal Mahendra, Alfa Marzelino, Dwi Wahyu Indrian Joko Pebrianto Trinugroho, Febby Nurdiya Ningsih, Annisa Krama, Wirdatun Nafisah, Indir Putri Negari, Anissa Nofita Sari (2026) **Elucidation of therapeutic targets an mechanisms of *Clitoria ternatea* L. in colorectal cancer inhibition using networ pharmacology and bioinformatics approaches.** | [Elucidación de dianas terapéuticas mecanismos de *Clitoria ternatea* L. en la inhibición del cáncer colorrectal mediant enfoques de farmacología de redes y bioinformática]. J Pharm Pharmacogn Res 14(1 2399. https://doi.org/10.56499/jppres_14.1.2399 FREE PDF [2.49 Mb] [ABSTRACT]

22.- Original Article

Kasta Gurning, Yehezkiel S. Kurniawan, Friska S. Silitonga, Muslih Anwar, Charlie E. d Fretes, Mario R. Sohilait, Endang Astuti, Sunarta, Winarto Haryadi (2026) **Phytochemica profiling, antimicrobial and antioxidant activities of *Coleus amboinicus* Lour. leaves: *I vitro*, network pharmacology, and molecular docking analyses.** | [Perfil fitoquímica actividades antimicrobianas y antioxidantes de las hojas de *Coleus amboinicus* Lour análisis *in vitro*, farmacología de redes y acoplamiento molecular]. J Pharm Pharmacog Res 14(1): 2440. https://doi.org/10.56499/jppres_14.1.2440 FREE PDF [1.74 Mb] [ABSTRACT]

23.- Review

Christopher D. Tristan, Risalina Myrtha, Nanang Wiyono, Irnizarifka Irnizarifka (2026 **Current landscape and future potential of sodium-glucose cotransporter 2 inhibitors i heart failure: A systematic review and bibliometric analysis.** | [Panorama actual potencial futuro de los inhibidores del cotransportador de sodio y glucosa tipo 2 en l insuficiencia cardíaca: una revisión sistemática y análisis bibliométrico]. J Pharn Pharmacogn Res 14(1): 2253. https://doi.org/10.56499/jppres_14.1.2253 FREE PDF [2.79 Mb [ABSTRACT]

24.- Original Article

Karnelasatri, Candra Yulius Tahya, Shellina, Sri Wahyu Ningsih Munthe, Riskianto Andriyani, Marcelia Sugata (2026) **LC-MS/MS profiling, total phenolic and flavonoi contents, and antibacterial activity of *Allium cepa* L. peel extract agains *Staphylococcus epidermidis*.** | [Perfil LC-MS/MS, contenido total de fenólicos flavonoides y actividad antibacteriana del extracto de cáscara de *Allium cepa* L. contr *Staphylococcus epidermidis*]. J Pharm Pharmacogn Res 14(1): 227 https://doi.org/10.56499/jppres_14.1.2279 FREE PDF [887 Kb] [ABSTRACT]

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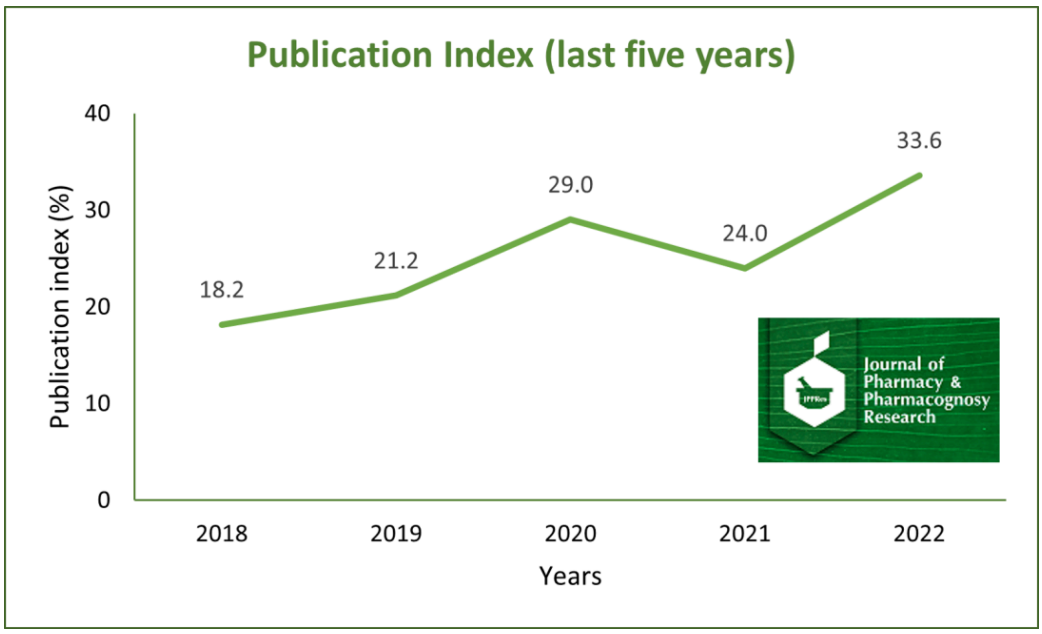
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