

Anti-Aging Activity of Ethanol Extract of the Oil Palm Mesocarp (*Elaeis guineensis* Jacq.): *In Vitro* and *In Silico* Studies

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*Anti-Aging Activity of Ethanol Extract of the Oil Palm Mesocarp (*Elaeis guineensis* Jacq.): In Vitro and In Silico Studies*

*Etanol Ekstresi Palm Yağı Mezokarpının (*Elaeis guineensis* Jacq.) Yaşlanma Karşıtı Etkisi: In Vitro ve In Silico Çalışmaları*

SUMMARY

Aging constitutes a natural biological process and represents a major global health concern. In tropical regions such as Indonesia, elevated ultraviolet (UV) exposure accelerates cutaneous aging through mechanisms involving DNA damage and mitochondrial dysfunction. Although numerous chemical-based anti-aging products are commercially available, their frequent adverse effects, including irritation and itching, necessitate the exploration of safer alternatives. Natural ingredients are therefore of increasing interest, with palm oil (*Elaeis guineensis* Jacq.) recognized as a potential candidate due to its empirical use in wound healing and tissue regeneration. The present study investigated the anti-aging potential of secondary metabolites from the ethanol extract of oil palm mesocarp (EEOPM) through *in vitro* enzymatic assays and *in silico* molecular docking. *In vitro* evaluation was conducted against mushroom tyrosinase and collagenase from *Clostridium histolyticum*. Molecular docking simulations were performed to analyze binding interactions with tyrosinase (PDB: 5M8P) and collagenase (PDB: 2D1N). The enzymatic assays demonstrated dose-dependent inhibitory activity, with IC_{50} values of 218.42 $\mu\text{g/mL}$ for tyrosinase and 22.44 $\mu\text{g/mL}$ for collagenase. These inhibitory effects were lower in potency compared with standard agents, kojic acid ($IC_{50} = 46.42 \mu\text{g/mL}$) and ascorbic acid ($IC_{50} = 5.58 \mu\text{g/mL}$). Docking analysis further revealed that α -tocotrienol exhibited the strongest affinity toward tyrosinase (-7.33 kcal/mol), while β -carotene displayed the highest affinity toward collagenase (-12.71 kcal/mol). Collectively, these findings suggest that EEOPM contains bioactive secondary metabolites capable of inhibiting tyrosinase and collagenase, thereby demonstrating anti-aging potential. Although its activity is lower than that of standard inhibitors, this study provides the first combined *in vitro* and *in silico* evidence supporting EEOPM as a prospective natural alternative for the development of safer anti-aging agents.

Keywords: Anti-aging, *Elaeis guineensis* Jacq., human & health, *in vitro*, *in silico*.

ÖZ

Yaşlanma doğal bir biyolojik süreçtir ve küresel çapta önemli bir sağlık sorunu teşkil eder. Endonezya gibi tropikal bölgelerde, yüksek ultraviyole (UV) maruziyeti, DNA hasarı ve mitokondriyal işlev bozukluğunu içeren mekanizmalar aracılığıyla cilt yaşlanmasını hızlandırır. Çok sayıda kimyasal bazlı yaşlanma karşıtı ürün ticari olarak mevcut olsa da, tahriş ve kaşıntı gibi sık görülen yan etkileri, daha güvenli alternatiflerin araştırılmasını gerektirmektedir. Bu nedenle doğal içeriklere olan ilgi giderek artmaktadır ve yara iyileşmesi ve doku rejenerasyonundaki deneysel kullanımı nedeniyle palmye yağı (*Elaeis guineensis* Jacq.) potansiyel bir aday olarak kabul edilmektedir. Bu çalışmada, *in vitro* enzimatik deneyler ve *in silico* moleküler yerleştirme yoluyla yağ palmyesi mezokarpının etanol özütü (YPMEO) elde edilen sekonder metabolitlerin yaşlanma karşıtı potansiyeli araştırılmıştır. *In vitro* değerlendirme, *Clostridium histolyticum*'dan elde edilen mantar tirozinaz ve kolajenaz enzimlerine karşı gerçekleştirilmiştir. Bağlanma etkileşimlerini tirozinaz (PDB: 5M8P) ve kolajenaz (PDB: 2D1N) ile analiz etmek için moleküler yerleştirme simülasyonları gerçekleştirildi. Enzimatik analizler, tirozinaz için 218,42 $\mu\text{g/mL}$ ve kolajenaz için 22,44 $\mu\text{g/mL}$ IC_{50} değerleriyle doza bağlı inhibitör aktivite gösterdi. Bu inhibitör etkileri, standart ajanlar olan kojik asit ($IC_{50} = 46,42 \mu\text{g/mL}$) ve askorbik asit ($IC_{50} = 5,58 \mu\text{g/mL}$) ile karşılaştırıldığında daha düşük etkiliydi. Yerleştirme analizi ayrıca, α -tocotrienol'ün tirozinaza karşı en güçlü afinitiyi (-7,33 kcal/mol) gösterdiğini, β -karotenin ise kolajenaza karşı en yüksek afinitiyi (-12,71 kcal/mol) gösterdiğini ortaya koydu. Bu bulgular topluca değerlendirildiğinde, YPMEO'un tirozinaz ve kolajenazı inhibe edebilen biyoaktif sekonder metabolitler içerdiği ve dolayısıyla yaşlanma karşıtı potansiyele sahip olduğu ortaya çıkmaktadır. Etkinliği standart inhibitörlerden daha düşük olsa da, bu çalışma, YPMEO'un daha güvenli yaşlanma karşıtı ajanların geliştirilmesinde potansiyel bir doğal alternatif olduğunu destekleyen ilk birleşik *in vitro* ve *in silico* kanıtı sunmaktadır.

Anahtar Kelimeler: Yaşlanma karşıtı, *Elaeis guineensis* Jacq., insan ve sağlık, *in vitro*, *in silico*.

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INTRODUCTION

Aging is a natural biological process and has become a significant concern in the global population. In tropical countries like Indonesia, where exposure to ultraviolet (UV) radiation is high, the issue of skin aging is growing rapidly each year. According to the Badan Pusat Statistik (2023), the elderly population reached 11.75% and is projected to increase to 15.77% by 2035. Skin aging is characterized by reduced skin function, resulting in sagging skin, wrinkles, dark spots, and dryness, which ultimately reduce skin elasticity and collagen synthesis, accelerating skin tissue degradation (Brzezinski et al., 2017).

Skin aging is closely linked to DNA damage and mitochondrial dysfunction. In addition to extrinsic factors such as pollution, oxidative stress, and UV exposure, this process is impacted by internal factors, including age, hormonal changes, and heredity (Anwar et al., 2022). Both intrinsic and extrinsic factors contribute to macromolecular damage and the overall decline of skin structure and function. As awareness of skin health increases, the global demand for anti-aging products continues to grow, with a compound annual growth rate (CAGR) of 8.61% predicted between 2022 and 2030 (Facts & Factors, 2023).

However, many synthetic anti-aging products, such as isotretinoin and retinoids, often cause side effects including dryness, redness, irritation, and other skin complications (Brzezinski et al., 2017). This emphasizes the need for anti-aging medications that are safer and more efficient, especially those that address oxidative stress and inhibit the degradation of the extracellular matrix through antioxidant, collagenase, and tyrosinase inhibition mechanisms.

The development of natural-based cosmetics is becoming increasingly popular due to their perceived safety, environmental friendliness, and minimal side effects. One promising natural source is the oil palm (*Elaeis guineensis* Jacq.), a member of the Arecaceae family widely cultivated in Asia and predicted to reach

a global demand of 240 million tons by 2050. Traditionally, palm oil has been used to promote wound healing and enhance tissue regeneration (Wondi et al., 2024). Palm mesocarp oil accounts for approximately 45–55% of the total oil yield and contains key bioactive compounds such as unsaturated fatty acids, vitamin E (tocopherols and tocotrienols), carotenoids, phytosterols, and coenzyme Q10, which are known for their strong antioxidant properties (Okpe, 2022).

Previous research has shown that tocopherols and tocotrienols from palm oil possess antioxidant properties with low toxicity, making them promising candidates for anti-aging applications. However, further studies are needed to investigate the potential of palm oil extracts as inhibitors of the enzymes tyrosinase and collagenase, which are involved in the skin aging process.

The use of 96% ethanol for extraction is considered effective for isolating bioactive compounds such as vitamin E and β -carotene without altering their chemical structures (Lee et al., 2024). Bioactive compounds were identified using LC-MS, which offers high precision in molecular detection and structural analysis (Alanazi, 2025). In addition, *in silico* studies such as molecular docking are valuable tools for predicting compound interactions with target proteins related to aging (Forli et al., 2016). The results are further validated through *in vitro* assays, including tyrosinase and collagenase inhibition tests. Therefore, this study aims to analyze potential anti-aging compounds from the mesocarp extract of oil palm using *in silico* methods and to evaluate their enzyme inhibition activity through *in vitro* experiments.

MATERIALS AND METHODS

Plant material

The plant material used in this study was palm oil from plantations of *Elaeis guineensis* Jacq. located in Bukit Makmur Village, Mentohi Raya District, Lamandau Regency, Central Kalimantan in February 2025. Then, plant determination was carried out at

the UPT Laboratorium Herbal Materia Medica Batu, Malang.

Extraction materials

The materials used were mesocarp oil palm simplicia and 96% technical ethanol. The instruments used were maceration equipment, oven, microwave, glassware, grinder (Fomag FCT-Z200), vacuum pump, rotary evaporator (Buchi Heating Bath B-490 and Buchi Rotavapor R-200), and analytical balance (OHAUSS PX224/E).

***In vitro* assay materials**

Mushroom Tyrosinase 250 U/mL, 0.1 M PBS pH 6.8 dan 5 mM DOPA (3,4-dihydroxy-L-phenylalanine) were used. BODIPY and Gelatin (Type B) served as fluorogenic substrates. Collagenase Assay Buffer XXXVIII, active collagenase, and the inhibitor (1,10)-phenanthroline (400 mM) were employed, along with distilled water and ethanol. 3T3 fibroblast cells were obtained from National Chiayi University, Taiwan, and cultured in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum (FBS). Additional reagents included 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide (MTT; Sigma Aldrich, USA), trypsin-EDTA, trypan blue (Sigma), bidistilled water and 70% alcohol. The MTT stock solution (5mg/mL PBS; 50 mg MTT dissolved in 10 mL PBS, pH 7.4) was prepared fresh. Stopper reagents consisted of 10% (w/v) sodium dodecyl sulphate (SDS; Merck-Schuchardt, Germany) in 0.01 N HCl (Merck, Darmstadt, Germany) protected from light with aluminum foil.

Equipment and consumables included an ELISA reader (Biochrom EZ Read 2000), Collagenase Inhibitor Screening Kit (Fluorometric; ab211108), tyrosinase kit, biological safety cabinet (BSC; EXCO SC2-4S1), reservoirs, 96-well plates (Biologix), CO₂ incubator (New Brunswick Galaxy 170R), beakers, vortex mixer (Thermo Scientific), centrifuge, analytical balance (Shimadzu), autoclave (Hiryama), hemocytometer (Neubauer), hand tally counter, invert-

ed microscope (Zeiss MC 80), tissue culture dishes (IWAKI), conical tube (IWAKI), micropipette (2-20 µL; 20-200 µL; 100-1000 µL), disposable plastic gel casting cassettes, sterile yellow and blue pipette tips, (Eppendorf), OPF pen marker, label stickers, shelf, aluminum foil, and a camera (Oppo Reno 5F).

***In silico* materials**

Secondary metabolite compounds identified through LC-MS in the ethanol extracts of oil palm mesocarp were used in this investigation. Fatty acids, β-carotene, and vitamin E were the primary substances under study. The chemical structure of these compounds was obtained from the PubChem database (<https://pubchem.ncbi.nlm.nih.gov/>). Crystal structure of human tyrosinase-related protein 1 complexed with tyrosine (PDB ID: 5M8P) was shown in (Figure 1.), and Collagenase-3 (MMP-13) complexed with a hydroxamic acid inhibitor (PDB ID: 2D1N) was shown in (Figure 2.) were retrieved from the Protein Data Bank (<https://www.rcsb.org/>), both with their ligands bound. The resolutions of proteins 5M8P and 2D1N are 2.80 Å and 2.37 Å, respectively. Kojic acid and ascorbic acid, obtained from PubChem, were used as comparator compounds for molecular docking with tyrosinase and collagenase, respectively.

AutoDockTools are used for molecular docking simulation, which facilitates the preparation of macromolecules and the execution of tethering protocols. Grid creation and binding operations used autogrid4.exe and autodock4.exe. To minimize ligand energy before binding, Avogadro software was used. Visualization and analysis of ligand-receptor interactions used BIOVIA Discovery Studio Visualizer 2024 v.24.1.0.23298. All computational work was performed on the ASUS VivoBook laptop with 4.00 GB of RAM, running Windows 11 on an x64-based processor.

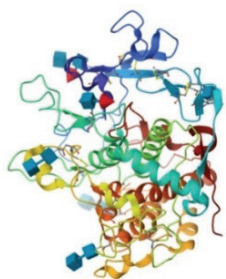


Figure 1. Tyrosinase (PDB ID: 5M8P)

Research method

This study is an experimental laboratory study with a post-test only control group design. Data collection for this study was carried out through experimental studies. Laboratory studies for in vitro work were carried out using tyrosinase inhibitor activity tests and collagenase inhibitor assays to analyze their IC_{50} values. The data collection method involved using a molecular database for in silico with protein preparation, ligand preparation, method validation, and molecular docking, followed by analysis of binding free energy, inhibition constants of binding interactions, and amino acid residues.

Procedures

Simplicia processing and extraction method

The samples were cleaned of dirt and then wet-sorted, washed under running water, the mesocarp was separated, and weighed to determine wet weight, reduced in size, air-dried without exposure to direct sunlight, dry-sorted, and finally weighed. Furthermore, the simplicia was ground using a grinder. Extraction was carried out on the mesocarp of oil palm with the MAE method using 96% ethanol solvent (1:10) at a frequency of 2450 MHz and a maximum power of 1000 W. Approximately 800 grams of mesocarp sample was reduced in size using a grinder, then extracted in a microwave using 96% ethanol 8000 mL for 3 minutes in stages. The mixture was filtered using a Buchner funnel, and the filtrate was evaporated with a rotating evaporator to produce a viscous extract

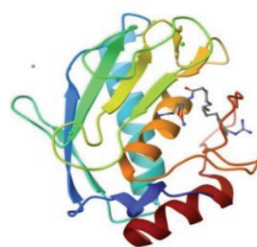


Figure 2. Collagenase (PDB ID: 2D1N)

from the oil palm mesocarp. After that, the filtrate was evaporated in an oven at 45°C for 24 hours to a constant weight, yielding the extract (Furi et al., 2022).

The extract yield was calculated using the following equation: $\% \text{ yield} = \frac{\text{weight of extract}}{\text{weight of simplicia}} \times 100$ (1)

In vitro assay

Tyrosinase inhibitor test

Tyrosinase inhibitory activity was measured using mushroom tyrosinase as an enzyme, L-DOPA as a substrate, phosphate buffer as a color control, DMSO solution as a blank, and kojic acid as a positive control (Widyowati et al., 2016). Mushroom tyrosinase reagent (250 U/mL) was prepared in cold conditions and protected from light. PBS pH 6.9 reagent (A) was made up in 50 mL of water. Then, 1 M phosphate dibasic (B) was prepared in 50 mL of water. Solution A, 4.97 mL, and solution B, 5.03 mL were mixed, and 100 mL of water was added. Reagent L-DOPA (5 mM) was made up in 50 mL of water. A standard kojic acid solution of 1000 mg/mL was prepared, and a standard kojic acid series solution was made into a 1.5 mL microtube, dilution series was carried out using 0.1 M PBS pH 6.8. The sample stock solution was prepared at a concentration of 100,000 mg/mL using 1 mL of DMSO, and homogenized. A series of six different sample concentrations was prepared in 1.5-mL microtubes, then 0.1 M PBS pH 6.8 was added according to the calculated volume, and homogenized. The first working step was to add 40 μ L of L-DOPA solution to

a 96-well plate that had been made into a map plate, then add 40 μL of EEOPM sample solution, then add 160 μL of PBS 0.1 M pH 6.8 to the sample, and finally add 40 μL of mushroom tyrosinase 250 Units/mL. The second step was to cover the well-plate with aluminum foil and incubate for 15 minutes at 37°C. The results could be seen in the color change to brown or black due to oxidation to dopamine or melanin,

$$\%Inhibition = \left(\frac{\text{enzyme control absorbance} - (\text{sample absorbance} - \text{buffer absorbance})}{\text{enzyme control absorbance}} \right) \times 100 \quad (2)$$

Collagenase inhibitor test

Collagenase inhibition test using active collagenase enzyme from *Clostridium histolyticum*, with gelatin substrate solution (BODIPY) and ascorbic acid as a positive control. A stock sample concentration of 10 mg/mL was prepared by weighing 10 mg of dry extract, then placing it in a microtube, and then adding 1 mL of DMSO, vortexing vigorously until homogeneous. 1 μL of the dissolved sample extract was added to a 96-well plate, then 5 $\mu\text{g}/\text{mL}$ collagenase enzyme and 44 μL buffer XXXVIII were added to the 96-well

and the amount of dopachrome was determined by measuring the absorbance at 475 nm with an ELISA Reader. Analysis of IC_{50} values was performed (Nur-rochmad et al., 2018).

The data obtained was in the form of absorbance, and then the inhibition percentage was calculated using the following equation:

microplate, and then preincubated for 15 minutes at 37°C. Then, a substrate solution (10 μM concentration) was added to initiate the reaction. Fluorescence results were measured at 490/520 nm on excitation and emission after 0 and 30 minutes of incubation, using a fluorescence plate reader. The results were in the form of fluorescence values, and IC_{50} values were analyzed (Widyowati et al., 2016). The data obtained is in the form of absorbance, and then the inhibition percentage is calculated using the equation:

$$\%Inhibition = \left(\frac{\text{enzyme control absorbance} - (\text{sample absorbance} - \text{buffer absorbance})}{\text{enzyme control absorbance}} \right) \times 100 \quad (3)$$

In silico test (Molecular docking)

Proteins preparation

AutoDockTools was used to prepare the collagenase and tyrosinase protein structures for the ensuing molecular docking simulations. Tyrosinase-related protein 1 (TYRP1), complexed with chain A of 5,6-dihydroxyindole-2-carboxylic acid oxidase, was solved at an atomic resolution of 2.80 Å for the tyrosinase preparation. Meanwhile, collagenase with a protein resolution of 2.37 Å was prepared using chain A of collagenase-3 (MMP-13) complexed with a hydroxamic acid inhibitor. Before docking, all water molecules and nonstandard residues were meticulously eliminated from protein structures. In addition, hydrogen atoms and Kollman charges were added to guarantee accurate chemical representation. The processed protein structures were then saved in the.pdbqt format for use in molecular docking.

Ligand preparation

In a different examination in our study, certain chemicals from EEOPM were discovered using prior LC-MS/MS-QToF profiles. These identified compounds include α -tocotrienol, β -sitosterol, 3-(1,3-Benzodioxol-5-yl)-3-(((2-methyl-2propanyl)oxy)carbonyl)amino)propanoic acid, tocopherol, squalene, apigenin 6,8-diglucoside, β -carotene, Coenzym Q10, oleic acid, myristic acid and palmitic acid. For molecular docking simulations, the 3D structures of these chemicals were obtained in *.sdf format from PubChem. The "Optimize Geometry" feature in Avogadro software was used to minimize the energy of each compound in order to guarantee the most stable conformation for docking. The *.pdb format was used to store the optimized structures. AutoDockTools was used to continue the docking preparation.

Method validation

The technique validation approach guarantees the precision and dependability of molecular docking simulations. In this procedure, the native ligand was re-docked to the active site of each target protein. A grid box, usually 40 x 40 x 40 points, was defined using AutoDockTools and was centered on the native ligand's known location inside the protein's binding pocket. For the 5M8P protein, re-docking was carried out using a grid box centered at coordinates x: 30.088, y: 136.057, and z: 216.68 with a grid spacing of 0.142 Å. The grid box for the 2D1N protein had a grid spacing of 0.375 Å and was centered at x: -44.048, y: 25.846, and z: -19.485. The RMSD value is a crucial measure for successful validation. The ability of the docking method to precisely reproduce the ideal ligand binding position is confirmed when the re-docked ligand posture is sufficiently near to the native conformation as determined by experiment, as indicated by an RMSD value of less than 2.0 Å. Tyrosinase (tyrosine) and collagenase (hydroxamic acid), the native ligands of each protein, were re-docked to verify this accuracy. Their corresponding RMSD values were confirmed to be below the 2.0 Å threshold.

Molecular docking

Using AutoDockTools, molecular docking simulations were conducted to assess the molecular interactions and binding affinity of mesocarp oil palm mesocarp molecules with 5M8P and 2D1N receptors. The

binding energies were given in kcal/mol. To guarantee the accuracy and consistency of the docking data, the grid box size and coordinates for every receptor were kept constant throughout the validation procedure.

Data analysis

Every experiment was conducted three times, and the mean ($n=3$) \pm SD was used to assess the results. The data obtained from the tests were analyzed statistically using parametric methods in IBM SPSS Statistics 27 software, so that the significance of the previously quantified data could be concluded. Normally distributed and homogeneous data were subjected to parametric analysis using the 95% confidence level with a one-way Analysis of Variance (ANOVA) test. Tyrosinase and collagenase assay concentration variations were ascertained using the one-way ANOVA approach against each test, as seen in the significance number. If the assumptions were met, the Post Hoc test was continued using the Tukey HSD test to evaluate significant differences in data between treatment groups using a confidence level of $p < 0.05$.

RESULTS AND DISCUSSION

Plant identification

Plant identification results indicated that the palm oil (*Elaeis guineensis* Jacq.) is a species from the Araceae (areca nut) family.

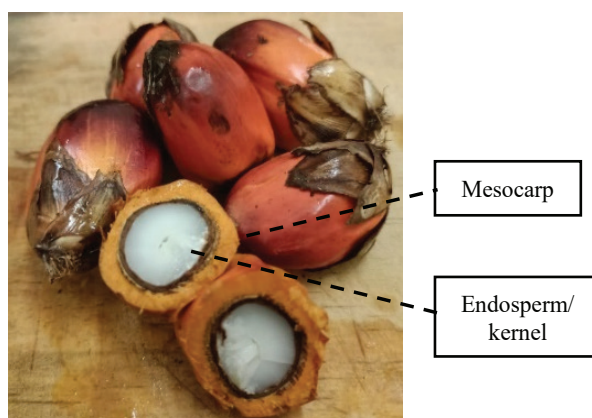


Figure 3. Samples of palm oil fruit after harvesting

Preparation and extraction of simplicia



Figure 4. Simplicia of oil palm mesocarp



Figure 5. Ethanol extract of oil palm mesocarp

The yield results from the extraction and organoleptic observation were listed in (Tables 1 and 2.).

Table 1. Yield of 96% ethanol extract of oil palm mesocarp

Simplicia	Simplicia weight (g)	Ethanol 96% volume (ml)	Extract weight (g)	Yield (%)	MC (%)
Mesocarp	800	8000	575	71.8	9.0

Table 2. Organoleptic observation of ethanol extract of oil palm mesocarp

Organoleptic observation	Result
Form	Condensed extract
Color	Brownish orange
Odor	Typical sweet caramel palm

The drying process for the mesocarp of oil palm was carried out using the air-drying method at room temperature, avoiding exposure to sunlight. The drying time was approximately 7 days. Careful monitoring of the drying process was crucial to ensure the preservation of desired secondary metabolites and the quality of the dried oil palm mesocarp. In this study, the extraction method used was MAE with 96% ethanol, a polar solvent that can dissolve a variety of substances, such as polar, semipolar, and nonpolar active ingredients. Its low boiling point and inert nature make it suitable for extraction and evaporation without the need for high temperatures. The 71.8% yield in this study is thought to be due to the effect of the

extraction time, which was 30 seconds in increments with six repetitions, maximizing the extraction process. The yield percentage is a measure of the efficiency of the extraction process and indicates the amount of active compounds contained in the extract. A higher yield percentage indicates that more active compounds are extracted from oil palm mesocarp, which are useful for various applications, such as pharmaceuticals and cosmetics, where these compounds are used for various health benefits. The results of the moisture content test (MC) for the EEOPM were 9.0%. This result is in accordance with the standard extract water content of <10% (BPOM, 2017). This means that the EEOPM in this study meets the stan-

dard. Too high water content can become a medium for the growth of fungi and bacteria and can cause a decrease in the stability of the active compounds in the extract (Krismayadi et al., 2024). The purpose of conducting an organoleptic test of extracts (Table 2.) is to introduce a simple start as objectively as possible (BPOM RI, 2017). The results of the EEOPM organoleptic test showed a thick liquid form because the use of 96% ethanol as a solvent accelerated the evaporation process during the evaporation stage, resulting in a concentrated extract. The extract had a brownish orange color, attributed to the reddish orange pulp used, which is rich in carotene compounds that are easily dissolved and will be carried into the extract (Riansyah et al., 2021). It had a distinctive odor, resembling

the typical sweet smell of palm caramel.

In vitro assay using enzymatic test

Tyrosinase inhibition test

The enzyme mushroom tyrosinase, the substrate l-1,4-dihydroxyphenylalanine (L-dopa), the positive control kojic acid, and the color control phosphate buffer were used to assess the tyrosinase inhibitory activity (Widyowati et al., 2016). Moreover, various concentrations of sample extracts were dissolved in DMSO, yielding concentrations of 6,250; 12,500; 25,000; 50,000, and 100,000 ppm. And the concentration for kojic acid was 2.34; 4.69; 9.38; 18.75; 37.50; 75.00; 150.00 ppm. Tyrosinase inhibitor activity with IC₅₀ values for kojic acid and extract of mesocarp oil palm is shown in Table 3.

Table 3. IC₅₀ value of the tyrosinase inhibitory properties of oil palm mesocarp extract and kojic acid

Sample	Concentration (µg/mL)	Inhibition(%)±SD	IC ₅₀ Value (µg/mL)	Category
Kojic acid (Control +)	2.34	8.36±0.66	46.42	Strong
	4.69	13.12±0.23		
	9.38	14.73±1.72		
	18.75	26.11±0.47		
	37.50	43.98±1.05		
	75.00	63.47±1.58		
	150.00	76.95±0.32		
Ethanol extract of Mesocarp	6.250	18.31±0.62	nd	nd
	12.500	21.24±0.46		
	25.000	26.61±0.67		
	50.000	32.32±1.44		
	100.000	42.81±0.21		

Fit (Sigmoidal, 4 parameters logistic, X is Concentration); nd (not defined)

The percentage of tyrosinase enzyme inhibition increased dose-dependently across all concentrations, within the activity test range of 6.25-100 µg/mL, with inhibition percentages ranging from 18-42% (Table 3.). From these results, the IC₅₀ value was calculated based on the percentage of tyrosinase inhibition against the concentration of oil palm mesocarp extract using a non-linear regression model (curve fit) (Figure 6B.). The analysis yielded an IC₅₀ value of

218.42 µg/mL for the oil palm mesocarp extract with an R-squared of 0.978. This IC₅₀ value is an extrapolated estimate and does not define within the test concentration range. The extract showed no inhibitory activity against tyrosinase at the test concentration under these test conditions.

The anti-tyrosinase activity test against the reference compound kojic acid showed a profile similar to that of the oil palm mesocarp extract, with increased activity at low doses and stable activity at high doses (Figure 6A.). The percentage of kojic acid inhibition

in the concentration range of 1-20 µg/mL increased from 8% to 76% (Table 3.), indicating that increasing kojic acid concentration is directly proportional to the increase in inhibitory activity. From these results, the IC₅₀ value of kojic acid was obtained, namely 46.42 µg/mL with an R-squared of 0.990. These results indicate that kojic acid has higher tyrosinase inhibitory activity than oil palm mesocarp extract.

The higher IC₅₀ value observed in this study compared to previous reports, such as those Suzana et al. (2009), may be due to differences in extraction methods, phytochemical composition, and testing conditions. In that study, a tocotrienol-rich fraction

(TRF) was used as a melanin synthesis inhibitor by inhibiting tyrosinase activity and reducing TYRP2 gene expression. Ethanol extracts of oil palm mesocarp are predominantly rich in lipophilic compounds, which are known to exhibit weaker tyrosinase inhibition than phenolic compounds, which are typically enriched in polar extracts. Furthermore, variations in enzyme source, substrate type, and assay parameters can substantially affect IC₅₀ values.

The graph showing the relationship between concentration and percentage of inhibition of tyrosinase enzyme by kojic acid and oil palm mesocarp is shown in Figure 6.

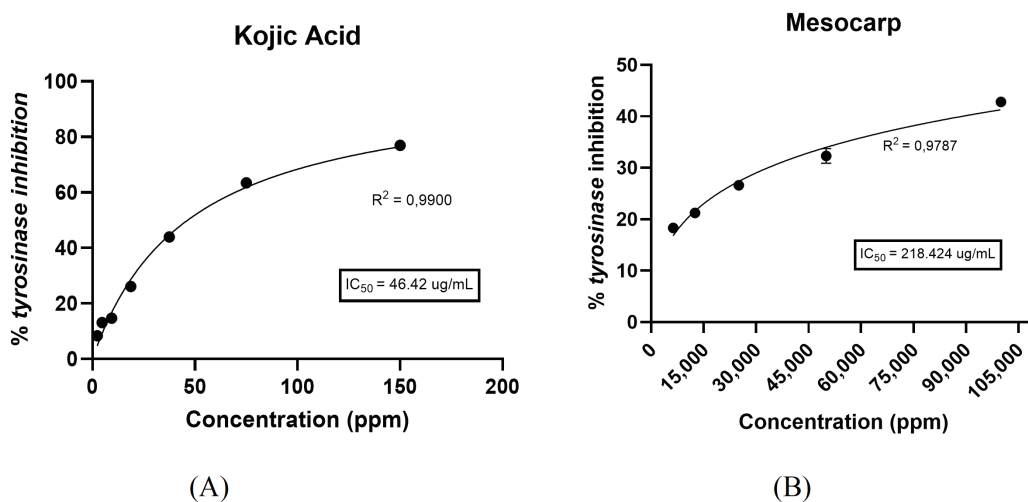


Figure 6. Regression graph of the relationship between concentration and percentage inhibition of (A) kojic acid and (B) oil palm mesocarp.

Based on the extrapolation results using Graph-Pad, the IC₅₀ value was obtained at 218.42 µg/ml, where the results of the EOPM reaction test on tyrosinase inhibition showed moderate activity potential based on the enzymatic inhibition test parameters. This means that a dose of 218 µg/ml can inhibit 50% of tyrosinase activity in the melanogenesis reaction. When compared with other plants, namely *Magnolia officinalis* essential oil, which was reported to have a tyrosinase IC₅₀ test result of 61.9 µg/ml and is classified as a strong tyrosinase inhibitor (IC₅₀ 50 - 200 µg/

ml); moderate activity (IC₅₀ 201-500 µg/ml) (You et al., 2022). The findings of a study conducted by Plyduang et al. (2022), palm oil contains several fatty acids, including palmitic acid (44%), oleic acid (39%), and lauric acid (48%), which have antioxidant properties and protect the skin from water loss. The anti-tyrosinase potential of a single composite isolate showed superior inhibitory potential. A study by Yusof et al. (2016) evaluated the potential application of oil palm (*elaeis guineensis*) leaf extract (ople) as a skin lightening agent and topical sunscreen. Ople also inhibited

fungus tyrosinase with an IC₅₀ of 254.88 µg ml⁻¹, significantly different from kojic acid, a more potent inhibitor with the lowest IC₅₀ of 4.46 µg/ml. GTE (green tea extract) showed a comparable IC₅₀ value to ople, namely 240.50 µg ml⁻¹. The catechin group, which prevents melanin synthesis in B16 melanoma cells, is likely responsible for the tyrosinase-inhibiting effect on ople and GTE. The gallic acid content in ople likely adds anti-tyrosinase properties in addition to the catechin group. Tyrosinase activity and melanin formation are significantly inhibited by gallic acid (Yusof et al., 2016). These results indicate that the fatty acid and vitamin E compounds from EEPOM have tyrosinase-inhibiting potential.

Collagenase inhibition test

In vitro collagenase inhibition was determined using the Collagenase Assay Kit (Abcam). Collagenase activity testing aims to determine the ability of a material to inhibit collagenase, an enzyme involved in the skin aging process. Collagenase inhibitory activity was measured using active collagenase from *Clostridium histolyticum* as the enzyme and BODIPY-Gelatin as the substrate, which fluoresces when the gelatin breaks into fragments, and BODIPY is released. Collagenase and gelatin substrate were prepared by adding assay buffer at a ratio consistent with the Kit

Protocol. Ascorbic acid served as a positive control, phosphate buffer saline XXXVIII as a color control, and various concentrations of sample extracts were dissolved separately in DMSO. The test was conducted by reacting the extract sample (80 mL) at concentrations of 10, 25, 50, 100, and 200 µg/mL with buffer and active collagenase (100 mL) in a 96-well plate, then incubated for 15 minutes, protected from light and at room temperature, and added with gelatin substrate solution (20 mL). The results were read using a fluorescence microplate reader (Spectramax M5, Molecular Devices, Sunnyvale, CA) with an excitation/emission wavelength of 490/520 nm. The ability to inhibit gelatinase/collagenase was calculated as follows:

$$\%inhibition = \left(\frac{A_{enzymecontrol} - (A_{sampel} - A_{buffer})}{A_{enzymecontrol}} \right) \times 100 \tag{4}$$

The results of collagenase inhibition are shown in (Table 4). The test extracts inhibited collagenase in a dose-dependent manner. The test extracts showed a very strong collagenase inhibitory effect, although still below the positive control, namely ascorbic acid. Regarding the anti-collagenase activity of mesocarp and ascorbic acid, they had comparable effects with IC₅₀ values of 22.44 µg/mL and 5.58 µg/mL, respectively.

Table 4. IC₅₀ value of collagenase inhibitor activity of ascorbic acid and mesocarp extract of oil palm

Sample	Concentration (µg/mL)	Inhibition(%)±SD	IC ₅₀ value (µg/mL)	Category
Ascorbic acid (Control +)	1	19.31±1.00	5.58	Very strong
	2.5	31.16±2.13		
	5	46.59±5.12		
	10	65.21±4.12		
	20	74.62±4.44		
Ethanol extract of Mesocarp	10	43.59±6.15	22.44	Very strong
	25	50.63±0.46		
	50	56.04±3.28		
	100	62.43±1.49		
	200	77.24±1.02		

The results of the collagenase activity test demonstrated a dose-dependent rise in enzyme inhibition percentage across the concentration range of 10-50

µg/mL, with an inhibition percentage of 43-56% (Table 4.). Collagenase inhibition activity showed no increase at concentrations of 100 µg/mL and 200 µg/mL.

At doubled and quadrupled concentrations, enzyme inhibition did not increase linearly with increasing dose, but only by 62-77%. From these results, the IC_{50} value was calculated based on the percentage of collagenase activity inhibition against the log concentration of oil palm mesocarp extract using a non-linear regression model (curve fit) (Figure 7B). The analysis yielded an IC_{50} value of 22.44 $\mu\text{g}/\text{mL}$ for oil palm mesocarp extract with an R-square of 0.925, which is considered very strong.

The anti-collagenase activity test against the ascorbic acid reference compound showed a similar profile to that of oil palm mesocarp extract, namely increased activity at low doses and stable activity at

high doses (Figure 7A.). The percentage of ascorbic acid inhibition in the concentration range of 1 - 20 $\mu\text{g}/\text{mL}$ increased from 19% to 74% (Table 4.), indicating that the increase in ascorbic acid concentration was proportional to the increase in inhibitory activity. From these results, the IC_{50} value of ascorbic acid was also obtained, which was 5.58 $\mu\text{g}/\text{mL}$ with an R squared of 0.993. These results indicate that the collagenase inhibition activity of ascorbic acid was higher than that of oil palm mesocarp extract.

The graph of the relationship between the concentration and percentage of inhibition of ascorbic acid and mesocarp oil palm against the collagenase enzyme is shown in Figure 7.

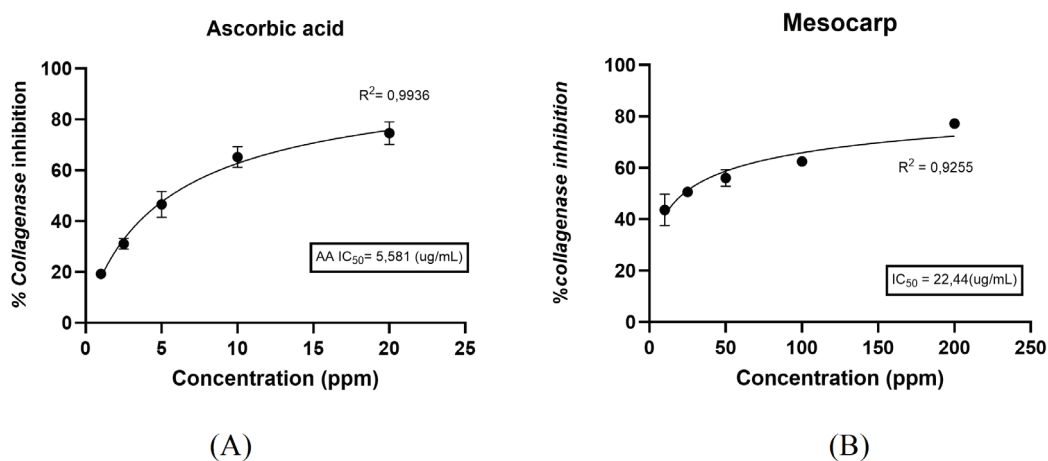


Figure 7. Regression graph of the relationship between concentration and percentage of inhibition of (A) ascorbic acid and (B) mesocarp oil palm

With an IC_{50} value of 22.44 $\mu\text{g}/\text{mL}$, the collagenase inhibition activity test findings demonstrated that the potential of EEOPM was active. Similar to the tyrosinase test, the phytochemical profile of the EEOPM sample was associated with the amount of vitamin E and fatty acid molecules in the collagenase test. A prior study by Aldrin et al. (2016) supported the findings of this investigation. Chemical testing of the extract revealed that it contained tocopherol ($5.34 \pm 3.22 \text{ g}/100 \text{ g}$) and tocotrienol ($4.23 \pm 0.15 \text{ g}/100 \text{ g}$) determined using HPLC-PDA and β -carotene ($21.89 \pm 0.23 \text{ g}/100 \text{ g}$) determined using HPLC-UV, various types of fatty acids, such as caprylic acid ($2.18 \pm 0.12 \text{ g}/100 \text{ g}$), capric acid (0.45 ± 0.01

$\text{g}/100 \text{ g}$), lauric acid ($8.65 \pm 0.14 \text{ g}/100 \text{ g}$), myristic acid ($3.33 \pm 0.21 \text{ g}/100 \text{ g}$), palmitic acid ($74.53 \pm 0.68 \text{ g}/100 \text{ g}$), and stearic acid ($6.48 \pm 0.76 \text{ g}/100 \text{ g}$) determined using gas chromatography (GC) analysis revealed that oil palm mesocarp extract accumulates significant vitamin E content, with 1300 $\mu\text{g}/\text{g}$ total tocopherols, with γ -tocotrienol as the primary tocopherol, followed by α -tocopherol, α -tocotrienol, and α -tocomonoenol (Su et al., 2013). No results have been found to investigate anti-collagenase activity in oil palm mesocarp extract. However, similar results were demonstrated in a study of the anti-tyrosinase, anti-collagenase, anti-elastase, and anti-hyaluronidase activities of a *Stenocarpus sin-*

uatus leaf extract (Younis et al., 2022). In this study, the volatile components of the hexane-soluble fraction of the methanolic extract of *Stenocarpus sinuatus* (Proteaceae) leaves (SSHF) were identified. An amount of 52.59% of the extract was made up of vitamin E (α -tocopherol), which was followed by γ -sitosterol (8.65%), neophytadiene (8.19%), and β -tocopherol (6.07%). With IC_{50} values of 60.03, 177.5, 67.5, and 38.8 μ g/mL, respectively, in vitro enzymatic assays demonstrated significant inhibition of collagenase, elastase, tyrosinase, and hyaluronidase by SSHF. These values were comparable to the positive controls, kojic acid (for tyrosinase) and epigallocatechin gallate (for collagenase, elastase, and hyaluronidase). Thus, in addition to the combined effects of other volatile ingredients, the high

vitamin E content of SSHF may be responsible for its anti-aging properties. In vitro enzymatic testing results indicate that EEOPM can inhibit the activity of tyrosinase and collagenase enzymes, thus supporting the potential of EEOPM as an inhibitor of enzymes involved in premature skin aging.

In silico test using molecular docking

The RMSD (Root Mean Square Deviation) value was less than 2Å, indicating that the docking process is valid. The position of the cocrystal ligand as the binding site determines how the grid box coordinates are arranged. Table 5 displays the validation results of the docking method. The validation results obtained an RMSD value of 1.004 for the tyrosinase receptor and 1.375 for the collagenase receptor.

Table 5. Validation results and RMSD values

Target Receptor	PDB ID	Grid Center			Docking area (x;y;z)	ΔG (Kcal/mol)	RMSD (Å)
		X	Y	Z			
Tyrosinase	5M8P	30.088	136.057	216.68	40 x 40 x 40	-5.81	1.004
Collagenase	2D1N	-44.048	25.846	-19.485	40 x 40 x 40	-7.87	1.375

The results of molecular docking of 12 compounds obtained from LC-MS/MS-QToF of EEOPM against 5M8P and 2D1N can be observed in Table 5.

Table 6. Molecular docking results of EEOPM compounds identified by LC-MS/MS-QToF against 5M8P and 2D1N (Mean \pm SD)

Ligands	5M8P		2D1N	
	Docking score (ΔG ; kcal/mol)	Inhibition constant (Ki; μ M)	Docking score (ΔG ; kcal/mol)	Inhibition constant (Ki; μ M)
α -Tocotrienol	-7.33 \pm 0.24	4.56 \pm 1.87	-10.11 \pm 0.38	0.04 \pm 27.07
β -sitosterol	-7.20 \pm 0.02	5.28 \pm 0.89	-11.49 \pm 0.09	3.79 \pm 12.09
3-(1,3-Benzodioxol-5-yl)-3-(((2-methyl-2-propenyl)oxy)carbonyl)amino)propanoic acid	-7.12 \pm 1.11	28.79 \pm 2.21	-8.80 \pm 0.38	428.02 \pm 7.21
Tocopherol	-6.36 \pm 0.29	24.58 \pm 12.76	-10.03 \pm 0.29	0.05 \pm 26.09
Squalene	-6.25 \pm 0.29	29.88 \pm 16.09	-8.66 \pm 0.08	0.45 \pm 58.62
Apigenin 6,8-diglucoside	-6.19 \pm 0.00	28.68 \pm 6.15	-9.21 \pm 0.00	0.87 \pm 5.76
β -carotene	-5.65 \pm 0.01	372.30 \pm 50.42	-12.71 \pm 0.24	0.00 \pm 21.29
Coenzym Q10	-5.23 \pm 0.19	154.29 \pm 48.48	-6.95 \pm 0.02	8.01 \pm 0.36
Oleic acid	-4.52 \pm 0.33	571.29 \pm 33.26	-6.18 \pm 0.34	33.79 \pm 15.97
Myristic acid	-4.37 \pm 0.05	620.64 \pm 48.33	-5.26 \pm 0.18	143.56 \pm 38.05
Palmitic acid	-4.23 \pm 0.21	959.30 \pm 39.11	-5.58 \pm 0.08	81.21 \pm 11.15
Kojic acid (+ control)	-4.60 \pm 0.00	424.47 \pm 8.71	-	-
Ascorbic acid (+ control)	-	-	-4.36 \pm 0.17	669.84 \pm 20.62

Based on the molecular docking data shown in Table 6 with the target 5M8P, the test compound with the lowest binding free energy (ΔG) value, namely α -tocotrienol (-7.33 kcal/mol), β -sitosterol (-7.20 kcal/mol), 3-(1,3-benzodioxol-5-yl)-3-(((2-methyl-2propanyl)oxy)carbonyl) amino)propanoic acid (-7.12 kcal/mol), tocopherol (-6.36 kcal/mol), squalene (-6.25 kcal/mol), and Apigenin 6,8-diglucoside (-6.19 kcal/mol). Meanwhile, the native ligand compound 5M8P that has a binding free energy value of -5.81 kcal/mol can be seen in Table 5. On the other hand,

the molecular docking data shown in Table 6 with the 2D1N target shows that the test compounds with the lowest binding free energy (ΔG) values are β -carotene (-12.71 kcal/mol), β -sitosterol (-11.49 kcal/mol), α -tocotrienol (-10.11 kcal/mol), tocopherol (-10.03 kcal/mol), Apigenin 6,8-diglucoside (-9.21 kcal/mol), and 3-(1,3-benzodioxol-5-yl)-3-(((2-methyl-2propanyl)oxy)carbonyl) amino)propanoic acid (-8.80 kcal/mol). Meanwhile, the native ligand compound 2D1N that has a free binding energy value of -7.87 kcal/mol can be seen in Table 6.

Table 7. Interaction of amino acid compounds from EEOPM with tyrosinase receptor (5M8P)

Parameter	Native ligand (TYR)	α -tocotrienol	β -sitosterol	Propanoic acid	Tocopherol	Squalene	Apigenin 6,8-diglucoside
Chromophore group							
Amino acid residue	Asn378A ^a Ser394A ^a Arg374A ^a His192A ^a Thr391A ^c Tyr513A ^c His381A ^c Arg321A ^f	- - - - - His381A ^c - Asp212A ^a His377A ^c His215A ^c	- - - - - - - - His215A ^c His377A ^a Leu382A ^c Glu360A ^a	- - - His192A ^a Thr391A ^a - His381A ^c - His377A ^c His215A ^c His192A ^b	- - - His192A ^a - - His381A ^d - His377A ^a His224A ^a His404A ^a His215A ^a Tyr362A ^a His392A ^c Val196A ^c	- - - His192A ^d - - His381A ^d - Lys198A ^c His392A ^c His215A ^c	Asn378A ^a - Arg374A ^a His192A ^a - - His381A ^c Arg321A ^a Leu382A ^d
Resemblance of amino acid with native ligand (%)		12.50	00.00	37.50	25.00	25.00	62.50
Resemblance of interaction with the native ligand (%)		00.00	00.00	25.00	12.50	00.00	50.00
Resemblance in ligand-receptor interaction (%)*		12.50	00.00	31.25	18.75	12.50	56.25
Interaction :		^a Hydrogen bond/Conventional hydrogen bond ^b Van der Waals ^c Alkyl/pi-alkyl ^d Pi-sigma ^e Pi-cation ^f Attractive Charge ^g Amide-Pi Stacked					

Further analysis of the interaction of the lowest binding free energy (ΔG) value with 5M8P (Table 7.) shows a high amino acid similarity score in the Apigenin 6,8-diglucoside compound is 62.50% with Asn378A, His192A, Arg374A, Arg321, and His381A. This indicates the presence of the same binding residues as the original ligand, the similarity score of the interaction between Apigenin 6,8-diglucoside and the original ligand is 50.00%. The high amino acid similarity score in propanoic acid compound is 37.50% with His192A, Thr391A, and His381A. This signals the presence of the same critical binding residues as

the original ligand, the similarity score of the interaction between propanoic acid and the original ligand is 25.00%. Interestingly, Apigenin 6,8-diglucoside forms more hydrogen bonds at the 4 sites (Asn378A, His192A, Arg374A, Arg321) of the 5M8P binding site than at the other ligands tested. However, the higher docking score results were between α -tocotrienol and β -sitosterol. Fig.8 illustrates the complex relationship between the tyrosinase receptor and the highest docking score results of α -tocotrienol, β -sitosterol and 3-(1,3-benzodioxol-5-yl)-3-(((2-methyl-2propanyl)oxy]carbonyl} amino)propanoic acid.

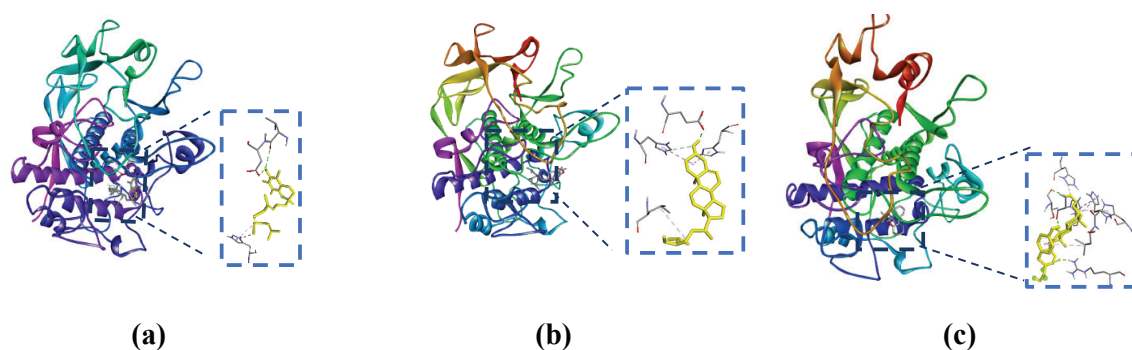


Figure 8. Compounds with the highest docking scores interacting with the 5M8P receptor: (a) α -tocotrienol; (b) β -sitosterol and (c) 3-(1,3-benzodioxol-5-yl)-3-(((2-methyl-2propanyl)oxy]carbonyl} amino)propanoic acid

In the collagenase receptor (2D1N), such as Apigenin 6,8-diglucoside in 5M8P, propanoic acid has a binding site with an amino acid similarity score of 72.72% with the native ligand 2D1N, namely Val219A, His222A, His226, His232, Glu223, Pro242, Ile243 and Ala186A (Table 8.). The interaction profile of propanoic acid shows a similarity of 27.27%, which results in hydrogen bonds at His222A, His232A, Glu223A, Pro242A, Ile234A, and Ala186A with the native ligand

at the 2D1N binding site, thus forming the highest hydrogen bond among all ligands tested. The superior docking score of propanoic acid is weakened by this large hydrogen bond network, which is comparable to that shown in Figure 8, while the highest docking score values interacting with the collagenase receptor are β -carotene, β -sitosterol and α -tocotrienol presented visually in Figure 9.

Table 8. Interaction of amino acid compounds from EEOPM with collagenase receptor (2D1N)

Parameter	Native ligand (FA4)	β -carotene	β -sitosterol	α -tocotrienol	Tocopherol	Apigenin 6,8-diglucoside	Propanoic acid
Chromophore group							
Amino acid residue	Ala188A ^a His187A ^a Val219A ^a His222A ^a His226A ^a His232A ^a Glu223A ^a Leu184A ^c Pro242A ^c Ile243A ^g Ala186A ^h	- Val219A ^c His222A ^c His226A ^c His232A ^c - - Pro242A ^c - - - Leu218A ^c Leu259A ^c	- Val219A ^c His222A ^d - - - Leu184A ^c - - - - Leu185A ^c Tyr244A ^c Leu218A ^c Leu239A ^c	- - Val219A ^c His222A ^c - His232A ^c - - Pro242A ^a Ile243A ^b - - Leu185A ^c Tyr244A ^c Pro236A ^a Leu239A ^c	- - Val219A ^c His222A ^c - - - - - - - - Leu185A ^c Leu239A ^c Tyr244A ^c	- - - His222A ^e - - - - - - - Ala186A ^a Leu185A ^a Ala238A ^a Thr245A ^a Val219A ^c Leu239A ^c	- - Val219A ^d His222A ^a His226A ^c His232A ^a Glu223A ^a - Pro242A ^a Ile243A ^a Ala186A ^a Thr245A ^a Asp231A ^a Leu185A ^c
Resemblance of amino acid with native ligand (%)		45.45	27.27	45.45	27.27	18.18	72.72
Resemblance of interaction with the native ligand (%)		9.09	9.09	00.00	00.00	00.00	27.27
Resemblance in ligand-receptor interaction (%)*		27.27	18.18	22.73	13.64	9.09	49.99
Interaction:	^a Hydrogen bond/Conventional hydrogen bond ^b Van der Waal ^c Alkyl/pi-alkyl ^d Pi-sigma ^e Pi-cation ^f Attractive Charge ^g Amide-Pi Stack ^h Unfavorable Positive-Positive ⁱ pi-lonepair						

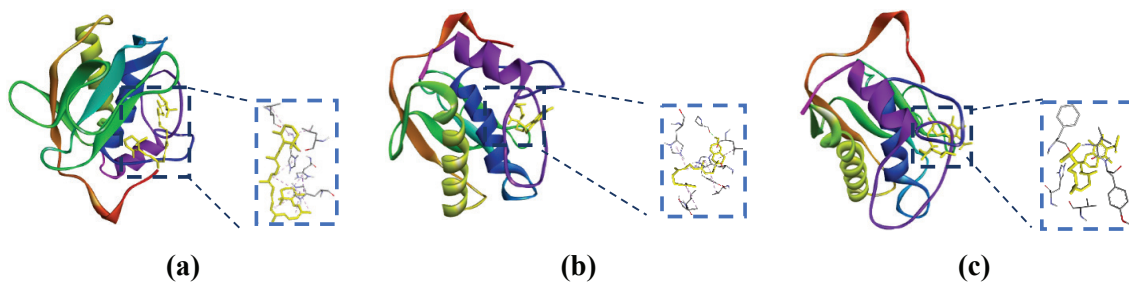


Figure 9. Compounds with the highest docking scores interacting with the 2D1N receptor: (a) β -carotene, (b) β -sitosterol and (c) α -tocotrienol

Not every molecule in plant extracts contributes equally to pharmacological activity because they are complex combinations of metabolites. Nonetheless, a

large number are categorized as bioactive substances that can have antagonistic, additive, or synergistic effects. The intricate makeup of extracts, which usually

include hundreds of metabolites, makes it difficult to identify specific activities for each compound, thus classifying plant extracts as multitarget interacting agents (Vaou et al., 2022). Tyrosinase and collagenase activity can be markedly increased by elevated quantities of free radicals, which come from both internal metabolic processes and external environmental influences. Consequently, the extracellular matrix, which is mainly made up of essential structural proteins as collagen, elastin, and hyaluronic acid, degrades (Abdelfattah et al. 2022). β -carotene, tocotrienols, and tocopherols are prominent compounds identified in ethanolic extracts of oil palm mesocarp, widely recognized as the main active components of the oil palm plant, contributing to its proven antioxidant properties. The anti-aging effects of β -carotene, tocotrienol, and tocopherol have been attributed to their capacity to reduce oxidative stress and wound healing. In several animal models, it has been demonstrated that β -carotene, tocotrienol, and tocopherol raise glutathione (GSH) levels and the activity of key antioxidant enzymes such as glutathione peroxidase (GPX), catalase (CAT), and superoxide dismutase (SOD) (Ayustaningwarno et al., 2024). Both mmp-13 and mmp-12 are significant macromolecular targets belonging to the mmp family. These enzymes are essential for the breakdown of the collagen matrix, which has a direct impact on the strength, flexibility, and suppleness of the skin. In particular, different forms of collagen (i, ii, iii, and iv) and elastin are broken down by MMP-13 and MMP-12, respectively (Alipour et al., 2016). Numerous studies have shown that β -carotene, tocotrienol, and tocopherol have anti-collagenase and anti-tyrosinase properties. In a human fibroblast cell culture, for instance, it has been demonstrated that oil palm, which is high in β -carotene and vitamin E, inhibits the activity of several MMPs, such as MMP-1, MMP-3, and MMP-13 (Hwang et al., 2017). Given that MMPs play a crucial role in aging-related tissue degradation, one important tactic for reducing the effects of systemic aging and for the creation of cosmetic goods is their inhibition.

CONCLUSION

The 96% ethanol extract of oil palm mesocarp (*Elaeis guineensis* Jacq.) showed a dose-dependent inhibition of the tyrosinase enzyme with a moderate IC_{50} value under the positive control of kojic acid and a dose-dependent inhibition of the collagenase enzyme with a very strong IC_{50} value but still below the positive control of ascorbic acid. Confirmed in an in silico study, α -tocotrienol compounds showed the strongest binding affinity to tyrosinase, and β -carotene compounds showed the highest affinity to collagenase. Thus, it can be concluded that secondary metabolites in EEOPM have potential as anti-aging agents by inhibiting aging-causing enzymes, namely tyrosinase and collagenase.

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AUTHOR CONTRIBUTION STATEMENT

Study concept and design, control of research activities, critical revision of the manuscript for important intellectual content, contribution to manuscript completion, obtaining funding, study supervision (RW), Literature search, data collection, raw material preparation, data extraction, analysis, and interpretation, manuscript preparation, statistical analysis, contribution to manuscript completion, molecular docking assay for protein docking, and enzymatic reaction assays of tyrosinase and collagenase (AYP), Contributed to the molecular docking assay for protein docking, critical revision of the manuscript, technical and administrative support and contributed to the completion of the manuscript (S), Technical and material support, study supervision, contributed to manuscript completion (IS), Technical and material support and study supervision (RH), Technical and material support and study supervision (KM), Technical and material support and study supervision (HC).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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