



Strawberry (*Fragaria ananassa* L.) Fruit Extract as an Antioxidant and Extracellular Matrix Protector for Anti-Photoaging

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Abstract

Skin aging, exacerbated by oxidative stress and environmental factors including UV radiation, has led to increased demand for effective anti-aging solutions. Strawberry extract, rich in antioxidants including catechins and flavonoids, has garnered attention for its potential in combating skin aging through its antioxidant and anti-inflammatory properties. This study investigates the anti-aging effects of strawberry (*Fragaria ananassa* L.) extract, focusing on its antioxidant capacity, inhibition of collagenase and elastase, and its impact on key aging biomarkers. Antioxidant activity was assessed using DPPH and H₂O₂ scavenging assays. The inhibition of collagenase and elastase was evaluated through enzyme activity assays. Molecular docking simulations assessed interactions between bioactive compounds in strawberry extract and anti-aging target proteins, including KEAP1, MMP1, and elastase. Strawberry extract demonstrated marked antioxidant capacity, as reflected by its IC₅₀ values of 229.91 ± 4.42 µg/mL (DPPH) and 234.08 ± 4.20 µg/mL (H₂O₂). It also showed enzyme inhibitory effects, with IC₅₀ values of 112.81 ± 1.96 µg/mL for collagenase and 28.03 ± 0.68 µg/mL for elastase. Cyanidin-3-glucoside showed binding interactions with KEAP1 and elastase (ΔG values of -9.6 and -6.4 kcal/mol), while cyanidanol interacted with MMP1 (ΔG = -9.8 kcal/mol). Strawberry extract demonstrated significant anti-aging and antioxidant effects, both *in vitro* and through molecular docking simulations, highlighting its potential as a potential anti-aging agent. These results highlight the potential application of strawberry extract in topical skincare products or as a dietary supplement.

Keywords: Anti-aging, antioxidant, collagenase, elastase, strawberry

1. Introduction

Photoaging, or premature skin aging due to chronic UV exposure, represents a significant dermatological challenge [1]. Modern lifestyles, including outdoor activities and increased pollution, further exacerbate UV-related skin damage [2]. Unlike intrinsic aging, photoaging is driven by external factors, mainly UV radiation, which degrades collagen and elastin, causing wrinkles and loss of elasticity [3]. Chronic UV exposure has been reported to account for 80% of visible skin aging changes, positioning photoaging as the dominant driver of premature skin aging and a major dermatological challenge requiring effective preventive strategies [1-3]. These changes not only affect appearance but also psychological well-being. While existing treatments are available, their limitations underscore the need for safer, sustainable alternatives [4].

UV-induced oxidative stress plays a central role in skin aging by generating reactive oxygen species (ROS), which damage proteins, lipids, and DNA, thereby accelerating extracellular matrix (ECM) degradation. ROS also activates matrix metalloproteinases (MMPs), including MMP9 and MMP1, which degrade elastin and collagen [5]. Plant-derived antioxidants are promising candidates to counteract these effects by scavenging ROS, reducing inflammation, and inhibiting MMP activity [6].

A key regulator in this defense mechanism is the KEAP1–NRF2 pathway, which controls antioxidant responses. Oxidative stress triggers the disengagement of NRF2 from KEAP1, enabling its nuclear translocation and subsequent activation of cytoprotective gene expression, such as HO-1, NQO1, and GCLC [7]. However, aging reduces the efficiency of this pathway, increasing susceptibility to oxidative damage [8-9]. Thus, modulating KEAP1–NRF2 signalling could be an effective strategy for photoaging prevention. Previous studies have demonstrated that anthocyanins from strawberries, particularly cyanidin-3-glucoside, play a critical role in activating the KEAP1–NRF2 signaling pathway. Cyanidin-3-glucoside has been reported to disrupt the KEAP1–NRF2 complex, facilitating NRF2 nuclear translocation and subsequent upregulation of antioxidant defense enzymes [9].

Despite research on synthetic antioxidants, plant-based sources like strawberries remain underexplored [10]. Strawberries (*Fragaria ananassa* L.) are enriched with bioactive compounds, including ellagic acid, cyanidanol, and cyanidin-3-glucoside, which exhibit antioxidant, anti-inflammatory, and anti-aging activities [11–12]. However, the synergistic effects of bioactive compounds in whole strawberry extract on photoaging-related pathways have not been fully elucidated. Although individual strawberry-derived compounds have demonstrated antioxidant and anti-aging properties, studies integrating enzyme inhibition assays with molecular docking analyses in the context of photoaging remain scarce.

This study evaluates the anti-aging potential of strawberry extract through both *in vitro* and *in silico* approaches. The antioxidant capacity was examined through H₂O₂ and DPPH scavenging assays, alongside its inhibitory effects on elastase and collagenase, key enzymes in ECM degradation. *In silico* molecular docking was carried out to assess the interaction of strawberry bioactive compounds with KEAP1, MMP1, and elastase. By integrating experimental and computational methods, this research seeks to elucidate the mechanisms through which strawberry extract may counteract UV-induced oxidative stress and ECM breakdown, highlighting its potential as a natural alternative in skin care.

2. Material and Methods

2.1 Strawberry extract preparation

The strawberry fruit extract (SFE) was processed at the FAST Laboratory (Depok, West Java, Indonesia) and accompanied by a Certificate of Analysis (Batch No. 0010424084). Extraction was performed using 70% ethanol under GMP standards. The obtained extract was subsequently blended with lactose as a carrier at a ratio of 1:10 (w/w) to improve stability and handling properties. Concentrated stock solution (10,000 µg/mL) was obtained by dissolving 10 mg of the powdered extract in 1 mL of 100% DMSO (Merck, Germany). In addition, serial dilutions were made by using 10% DMSO, in which all working solutions were sterilized using a 0.22 µm syringe filter (Merck Millipore, SLGV033RB) before use [13]. The final concentration of DMSO in all assays did not exceed 1% (v/v) to avoid solvent-induced interference.

2.2 Antioxidant capacity assay (DPPH and H₂O₂ assay)

The antioxidant activity of SFE was evaluated using DPPH and H₂O₂ scavenging assays. For the DPPH assay, 50 µL of SFE at seven concentrations (3.125–200 µg/mL) was mixed with 200 µL of 0.077 mM DPPH in DMSO (Sigma-Aldrich, D9132) in a 96-well plate, incubated for 30 minutes in the dark, and measured at 517 nm using the Multiskan™ GO spectrophotometer from Thermo Scientific (51119200). DPPH solution served as the negative control; methanol was used as the blank. For H₂O₂ scavenging, 12 µL of ferrous ammonium sulfate 1 mM from Sigma, 60 µL of SFE (3.125–500 µg/mL), and 3 µL of 5 mM H₂O₂ (Merck) were incubated in the dark for 5 minutes, followed by the administration of 75 µL of 1 mM 1,10-phenanthroline (Sigma). Absorbance was recorded at 510 nm after an additional 10-minute incubation [14].

2.3 Collagenase activity assay

In this method, the reaction mixture consisted of 30 µL of the sample at varying concentrations (3.9–250 µg/mL), 10 µL of collagenase from *Clostridium histolyticum* (0.1 mg/mL; Sigma, C8051), and 60 µL of tricine buffer (50 mM tricine, 10 mM CaCl₂, 400 mM NaCl, pH 7.5), then the mixture was incubated for 20 minutes at 37°C. Control and blank solutions were also prepared in which the control contained 10 µL of enzyme and 90 µL of phosphate buffer, while the blank included 10 µL of enzyme, 80 µL of phosphate buffer, and 30 µL of sample. After incubation, 20 µL of N-[3-(2-Furyl)acryloyl]-Leu-Gly-Pro-Ala or FALGPA substrate 1 mM from Sigma (F5135) was administered to all mixtures, except for the blank. FALGPA was used as a specific synthetic substrate due to its high sensitivity and reproducibility in collagenase inhibition assays. Then, absorbance measurements were taken at 335 nm using a microplate reader to assess the enzyme activity [15].

2.4 Elastase activity assay

The assay solution was prepared by combining 10 μL of samples (ranging from 1.5 to 66.7 $\mu\text{g/mL}$), 5 μL of elastase enzyme from porcine pancreas 0.01 mg/mL from Sigma (45124), and 125 μL of tris buffer (pH 8, 100 mM). This mixture was incubated for 15 minutes at 25°C. A control solution was also prepared, consisting of 5 μL of enzyme and 135 μL of tris buffer, while the blank contained 130 μL of tris buffer and 10 μL of sample. Following the incubation, 10 μL of N-Succinyl-Ala-Ala-Ala-p-nitroanilide (SucAla-3-pNA) substrate was added, and the mixture was incubated again at 25°C for another 15 minutes. SucAla-3-pNA was employed because it allows quantitative assessment of elastase activity through the release of p-nitroaniline, which can be accurately monitored spectrophotometrically. Absorbance was then measured at a wavelength of 410 nm [15].

2.5 Molecular docking

In silico molecular docking was employed to predict the interactions between active compounds from strawberry including ellagic acid (CID: 5281855), cyanidanol (CID: 9064), flavan-3-ols (CID: 3707243), and cyanidin-3-glucoside (CID: 441667) and target proteins, including KEAP1 (PDB ID: 4L7B), MMP1 (PDB ID: 966C), and elastase (PDB ID: 6E69). These target proteins were selected due to their established roles in oxidative stress regulation (KEAP1) and extracellular matrix degradation associated with photoaging (MMP1 and elastase). The three-dimensional structures of the ligands and proteins were prepared and docked using AutoDock Vina software [16]. Molecular docking simulations were conducted using AutoDock Vina with an exhaustiveness value of 16. Grid boxes were centered on the active site region of each protein based on the reported binding pockets and adjusted individually according to protein size and active site geometry. The grid box dimensions were set to 16 $\times$ 16 $\times$ 16 Å for KEAP1, 30 $\times$ 30 $\times$ 30 Å for MMP1, and 18 $\times$ 18 $\times$ 18 Å for elastase. Default settings were applied to all other docking parameters. Subsequently, the docking poses were evaluated and ranked according to their predicted binding affinities. The interaction patterns and binding modes were visualized and further examined using the Biovia Discovery Studio to identify key molecular interactions, providing insights into potential therapeutic mechanisms [17].

2.6 Statistical analysis

All experiments were carried out in quadruplicate ($n = 4$), and data are expressed as mean $\pm$ SD. One-way ANOVA with Tukey's post-hoc test was used for parametric data, while Kruskal–Wallis followed by Mann–Whitney tests were applied for non-parametric data. Statistical analyses were conducted using SPSS (IBM®, v20.0), with $p < 0.05$ identified as significant.

3. Results

3.1 Antioxidant capacity assay (DPPH and H_2O_2 assay)

The DPPH scavenging activity of strawberry fruit extract was evaluated across a concentration range of 3.125 to 200 $\mu\text{g/mL}$. As shown in Figure 1A, a concentration-dependent increase in scavenging activity was observed, with the highest activity observed at 200 $\mu\text{g/mL}$ (45.25% $\pm$ 0.61) and the lowest at 3.125 $\mu\text{g/mL}$ (13.70% $\pm$ 0.62). One-way ANOVA revealed significant differences among most concentrations ($p < 0.05$), with no significant difference between 12.5 and 6.25 $\mu\text{g/mL}$, indicating a plateau. The IC_{50} value was 229.91 $\pm$ 4.42 $\mu\text{g/mL}$, with the regression equation $y = 0.2078x + 20.567$ and $R^2 = 0.9786$, indicating moderate antioxidant capacity in a dose-dependent manner (Table 1). Similarly, the inhibitory activity of the strawberry extract on H_2O_2 was assessed across different concentrations, and the results are summarized in Figure 1B. The H_2O_2 scavenging activity was evaluated from 3.125 to 500 $\mu\text{g/mL}$. The highest inhibition (93.96% $\pm$ 1.25) was observed at 500 $\mu\text{g/mL}$, while the lowest (6.90% $\pm$ 0.79) was at 3.125 $\mu\text{g/mL}$. Significant differences were found between 500 $\mu\text{g/mL}$ and all lower concentrations ($p < 0.05$), with no significant difference between 15.625 and 3.125 $\mu\text{g/mL}$. The IC_{50} value was 234.08 $\pm$ 4.20 $\mu\text{g/mL}$, with a strong correlation ($R^2 = 0.9900$) from the equation $y = 0.1694x + 10.355$, confirming the extract's dose-dependent inhibition of H_2O_2 (Table 1).

Table 1 IC_{50} values and regression parameters of SFE in antioxidant assays

Assay Type	Concentration Range ($\mu\text{g/mL}$)	Maximum Inhibition (% $\pm$ SD)	IC_{50} ($\mu\text{g/mL} \pm \text{SD}$)	Regression Equation	R^2
DPPH Radical Scavenging	3.125 – 200	45.25 $\pm$ 0.61	229.91 $\pm$ 4.42	$y = 0.2078x + 20.567$	0.9786
H_2O_2 Scavenging	3.125 – 500	93.96 $\pm$ 1.25	234.08 $\pm$ 4.20	$y = 0.1694x + 10.355$	0.9900

* IC_{50} : concentration required to inhibit 50% of free radicals. R^2 : coefficient of determination indicating model fit. All assays showed dose-dependent inhibition, with H_2O_2 scavenging displaying stronger antioxidant capacity.

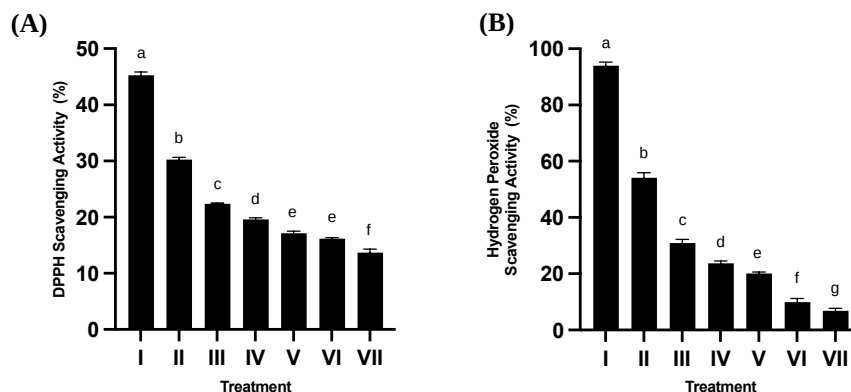


Figure 1 The Effect of SFE concentrations on scavenging DPPH (A) and H₂O₂ (B) scavenging activities

*Distinct superscript letters (a–g) indicate statistically significant differences among concentrations as determined by one-way ANOVA followed by Tukey’s post-hoc test ($p < 0.05$). For the DPPH assay (A), SFE was tested at concentrations of 200 (I), 100 (II), 50 (III), 25 (IV), 12.5 (V), 6.25 (VI), and 3.13 $\mu\text{g/mL}$ (VII). For the H₂O₂ scavenging assay (B), SFE was evaluated at concentrations of 500 (I), 250 (II), 125 (III), 62.5 (IV), 31.25 (V), 15.63 (VI), and 3.13 $\mu\text{g/mL}$ (VII).

3.2 Collagenase activity assay

The collagenase inhibitory activity of strawberry extract was assessed at concentrations from 3.91 to 250 $\mu\text{g/mL}$ (Figure 2). The highest inhibition ($86.31\% \pm 0.10$) was observed at 250 $\mu\text{g/mL}$, with a gradual decrease in inhibition at lower concentrations, reaching $16.23\% \pm 0.29$ at 3.91 $\mu\text{g/mL}$. Statistical evaluation using the Mann–Whitney test demonstrated significant differences ($p < 0.05$) between the highest concentration and all lower concentrations, with no significant difference between 15.625 and 7.81 $\mu\text{g/mL}$, indicating a plateau. The IC_{50} value was $112.81 \pm 1.96 \mu\text{g/mL}$, with the regression equation $y = 0.2741x + 19.244$ and $R^2 = 0.99$, indicating a strong correlation. These findings suggest that strawberry extract is a promising candidate for collagenase inhibition in therapeutic applications.

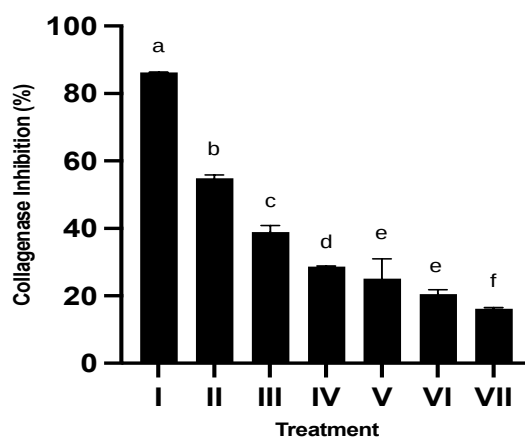


Figure 2 The effect of SFE concentrations on collagenase inhibition

*Superscript letters (a–f) denote statistically significant differences among concentrations as determined by the Mann–Whitney test ($p < 0.05$). The experimental groups consisted of SFE administered at concentrations of 250 $\mu\text{g/mL}$ (I), 125 $\mu\text{g/mL}$ (II), 62.5 $\mu\text{g/mL}$ (III), 31.25 $\mu\text{g/mL}$ (IV), 15.625 $\mu\text{g/mL}$ (V), 7.81 $\mu\text{g/mL}$ (VI), and 3.91 $\mu\text{g/mL}$ (VII).

3.3 Elastase activity assay

The elastase inhibitory activity of strawberry extract was evaluated at varying concentrations, specifically from 1.04 to 66.67 $\mu\text{g/mL}$ (Figure 3). The highest inhibition ($90.48\% \pm 0.31$) was observed at 66.67 $\mu\text{g/mL}$, with a decrease in inhibition at lower concentrations, reaching $16.28\% \pm 0.21$ at 1.04 $\mu\text{g/mL}$. The results of the Mann–Whitney test demonstrated statistically significant differences ($p < 0.05$) between the highest concentration and lower concentrations, with no significant difference between 4.17 and 2.08 $\mu\text{g/mL}$, suggesting a plateau. The IC_{50} value was $28.03 \pm 0.68 \mu\text{g/mL}$, with the regression equation $y = 1.1061x + 18.605$ and $R^2 = 0.99$, demonstrating

a strong correlation. These results suggested that strawberry extract is a potential natural inhibitor for elastase, particularly for conditions involving elastase-related tissue damage.

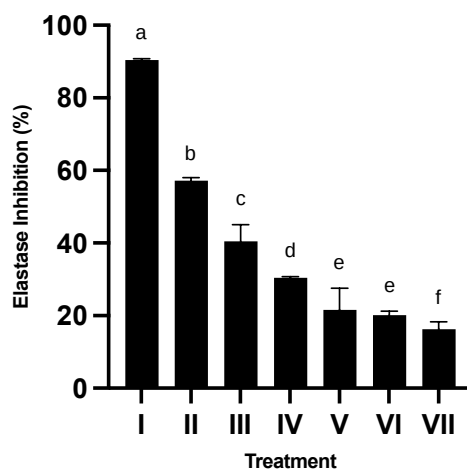


Figure 3 The effect of SFE concentrations on elastase inhibition

*Superscript letters (a–f) indicate statistically significant differences among concentrations according to the Mann–Whitney test ($p < 0.05$). The experimental groups comprised SFE at concentrations of 66.67 $\mu\text{g/mL}$ (I), 33.33 $\mu\text{g/mL}$ (II), 16.67 $\mu\text{g/mL}$ (III), 8.33 $\mu\text{g/mL}$ (IV), 4.17 $\mu\text{g/mL}$ (V), 2.08 $\mu\text{g/mL}$ (VI), and 1.04 $\mu\text{g/mL}$ (VII).

3.4 Molecular docking

Molecular docking was carried out to examine the molecular associations among four bioactive compounds derived from strawberries including cyanidanol, cyanidin-3-glucoside (C3G), ellagic acid, and flavan-3-ols with key target proteins involved in oxidative stress, inflammation, and tissue degradation including KEAP1, MMP1, and elastase. The binding affinity data, summarized in Table 2, delivered a comprehensive insight into the possible therapeutic applications of these compounds in the management of diseases associated with cellular damage.

Table 2 Binding affinity of strawberry fruit-derived ligands with protein complexes

Ligands	ΔG (kcal/mol)		
	KEAP1	MMP1	Elastase
Cyanidanol	-7.7	-9.8	-6.1
Cyanidin-3-glucoside	-9.6	-8.1	-6.4
Ellagic Acid	-7.9	-7.8	-6.0
Flavan-3-ols	-7.2	-9.0	-5.8

*Ligands included: Cyanidanol Compound CID: 9064; Cyanidin-3-glucoside Compound CID: 441667; Ellagic Acid Compound CID: 5281855; and Flavan-3-ols Compound CID: 3707243. Proteins included: KEAP1 (PDB ID: 4L7B), MMP-1(PDB ID: 966C), and elastase (PDB ID: 6E69).

Cyanidin-3-glucoside showed the highest predicted binding affinity to KEAP1 (-9.6 kcal/mol), forming hydrogen bonds with VAL604, LEU365, GLY364, SER363, ASN414, and ARG415, and hydrophobic interactions with GLY603, highlighting its potential to modulate the KEAP1–NRF2 pathway. Cyanidanol showed a slightly weaker binding (-7.7 kcal/mol), with interactions at SER508 and ILE461. Ellagic Acid and Flavan-3-ols displayed lower affinities (-7.9 and -7.2 kcal/mol, respectively), with interactions including $\text{Pi}-\pi$ stacking and Pi -Cation. These results suggested cyanidin-3-glucoside as the most promising candidate for targeting KEAP1 in oxidative stress-related therapies (Figure 4).

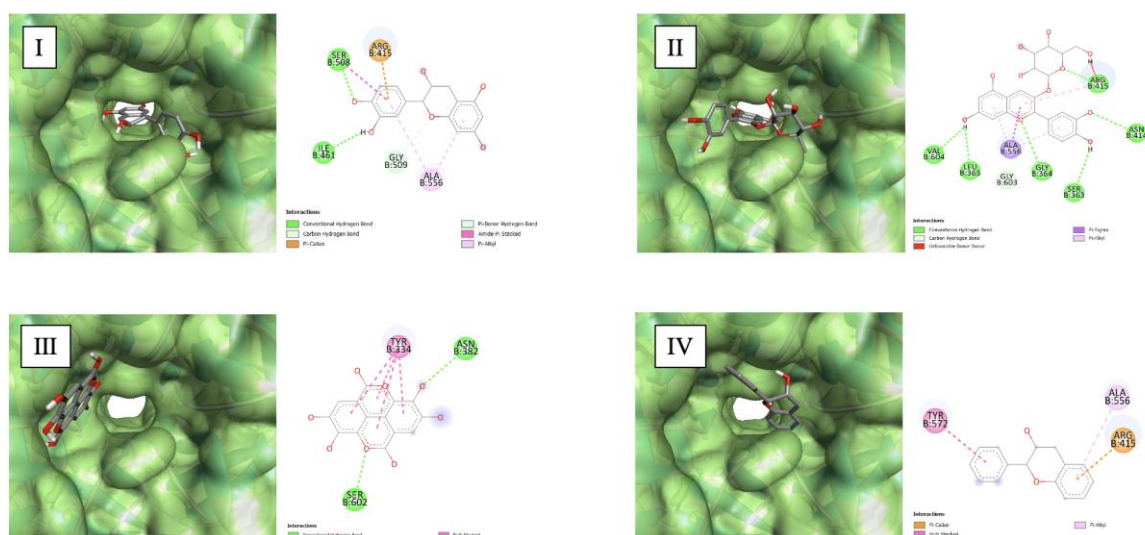


Figure 4 KEAP1– ligands interaction visualization

*Ligands included: Cyanidanol (I); Cyanidin-3-glucoside (II); Ellagic Acid (III); and Flavan-3-ols (IV).

Cyanidanol demonstrated the highest predicted binding affinity to MMP1 (-9.8 kcal/mol), with CvHB interactions at THR241, LEU235, and ALA182. Flavan-3-ols (-9.0 kcal/mol) also showed strong binding, while Cyanidin-3-glucoside (-8.1 kcal/mol) and Ellagic Acid (-7.8 kcal/mol) showed weaker binding. Cyanidanol is the most promising compound for inhibiting MMP1, which is key in tissue remodelling and inflammation (Figure 5).

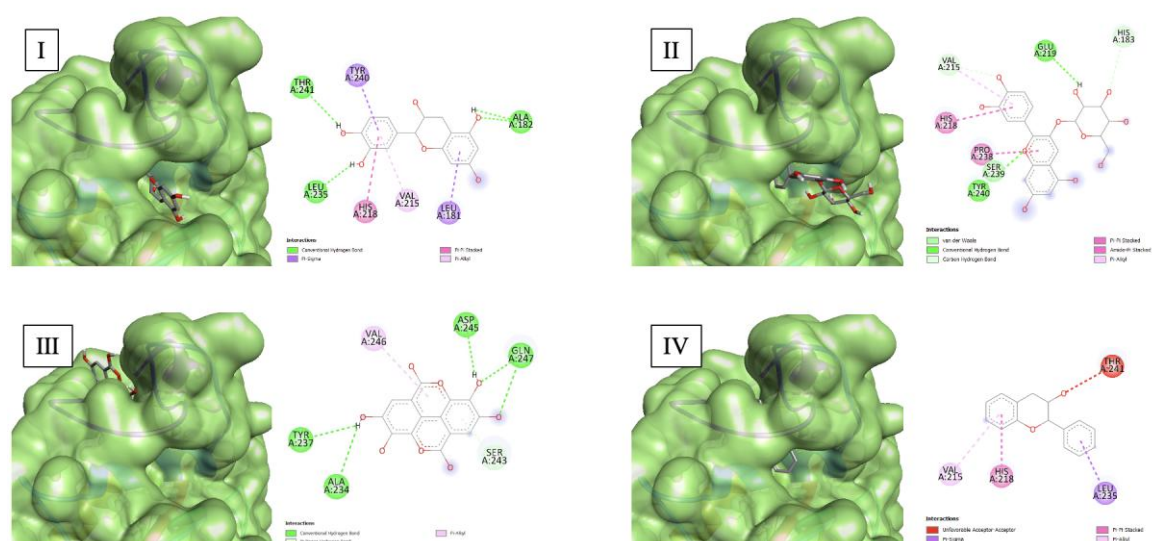


Figure 5 MMP1– ligands interaction visualization

*Ligands included: Cyanidanol (I); Cyanidin-3-glucoside (II); Ellagic Acid (III); and Flavan-3-ols (IV).

Cyanidanol exhibited the highest binding affinity for elastase (-6.1 kcal/mol) with interactions at VAL2016, suggesting strong inhibition potential. Cyanidin-3-glucoside (-6.4 kcal/mol) also showed significant binding at SER195 and VAL216. Ellagic acid and flavan-3-ols had weaker affinities (-6.0 and -5.8 kcal/mol, respectively). Cyanidanol emerges as the leading compound for elastase inhibition in conditions involving elastin degradation (Figure 6).

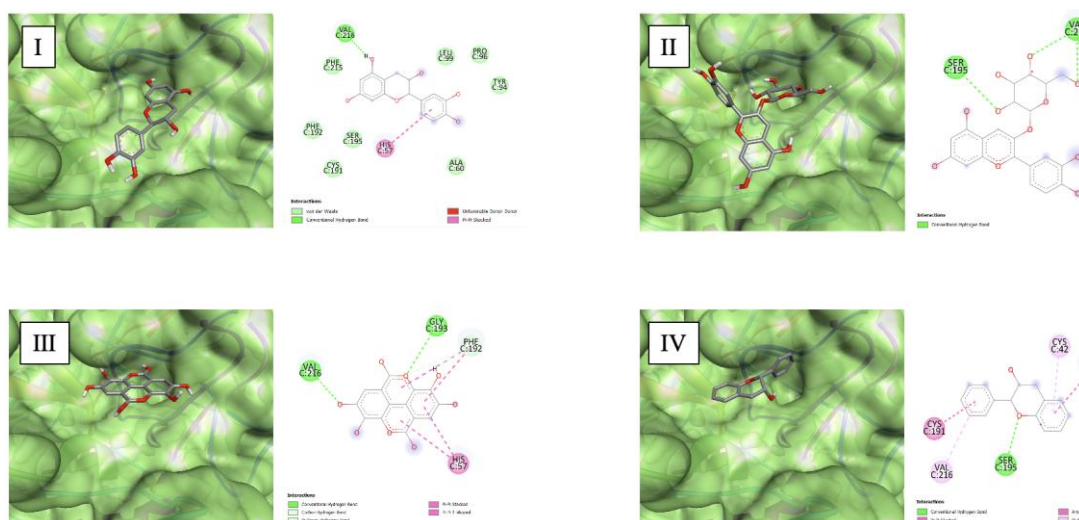


Figure 6 Elastase– ligands interaction visualization

*Ligands included: Cyanidanol (I); Cyanidin-3-glucoside (II); Ellagic Acid (III); and Flavan-3-ols (IV).

4. Discussion

Photoaging is primarily driven by ultraviolet-induced reactive oxygen species (ROS), such as superoxide anions (O_2^-) and H_2O_2 contributes to oxidative damage in extracellular matrix (ECM) components, notably elastin and collagen, resulting in skin sagging, wrinkles, and reduced elasticity [18]. Strawberry extract, rich in bioactive compounds, offers antioxidant properties that may mitigate such damage by modulating cellular redox pathways [19]. Key molecular targets in this process include the KEAP1–NRF2 signaling axis, MMP1, and elastase, which are critically involved in UV-induced skin aging [20].

The DPPH scavenging activity of SFE showed a dose-dependent increase. The highest activity was observed at 200 $\mu\text{g/mL}$ (45.25%), while the lowest was at 3.125 $\mu\text{g/mL}$ (13.70%). The IC_{50} value was 124.62 $\mu\text{g/mL}$, indicating moderate antioxidant potential. Compared to previous findings by Ayunda and Etika (2024), who reported a much lower IC_{50} (33.48 ppm) for strawberry petiole extract, the higher IC_{50} in this study may result from differences in plant parts used, extraction methods, and phenolic content. The moderate antioxidant activity in the current study is likely due to lower phenolic concentrations in the fruit extract [21]. Strawberry extract demonstrated antioxidant potential through its DPPH (2,2-diphenyl-1-picrylhydrazyl) scavenging activity. This effect is mainly attributed to bioactive compounds such as cyanidin-3-glucoside (C3G) and ellagic acid [22,23]. This activity not only neutralizes free radicals but also activates redox-regulating pathways, particularly the KEAP1–NRF2 axis [8]. C3G can inhibit KEAP1, allowing NRF2 to translocate into the nucleus. This leads to the upregulation of key antioxidant enzymes, such as catalase, glutathione peroxidase (GPx), superoxide dismutase (SOD), and heme oxygenase-1 (HO-1) [24,25]. Normally, KEAP1 binds NRF2 to prevent unnecessary antioxidant gene expression [7,26]. Under oxidative stress, NRF2 dissociates from KEAP1 and dimerizes with small musculoaponeurotic fibrosarcoma (MAF) proteins. The NRF2–MAF complex then binds to Antioxidant Response Elements (AREs), promoting the expression of antioxidant defenses and protecting skin from ROS-induced collagen and elastin degradation [27].

The H_2O_2 scavenging activity of strawberry fruit extract was evaluated across concentrations ranging from 3.125 to 500 $\mu\text{g/mL}$, showing a dose-dependent increase. Maximum inhibition was observed at 500 $\mu\text{g/mL}$ ($93.96\% \pm 1.25$), and the lowest at 3.125 $\mu\text{g/mL}$ ($6.90\% \pm 0.79$), with an IC_{50} value of 234.08 ± 4.20 $\mu\text{g/mL}$. Previous studies have shown that anthocyanin-enriched strawberry fractions reduce H_2O_2 -induced DNA damage in human leukocytes at lower concentrations (15–20 $\mu\text{g/mL}$), highlighting the antioxidant role of anthocyanins [28]. This supports the current findings, although the higher IC_{50} suggests lower potency in whole fruit extract. Catalase plays a critical role in detoxifying H_2O_2 into water and oxygen, especially in UV-exposed skin cells, thereby reducing oxidative stress and preventing photoaging [29]. Activation of the NRF2 pathway induces catalase expression and enhances antioxidant defense mechanisms in skin cells [30]. Cyanidin-3-glucoside (C3G) from strawberry extract enhances NRF2 activation by inhibiting KEAP1, leading to upregulation of catalase and accelerated H_2O_2 clearance [28]. This mechanism contributes to reduced oxidative damage and protection against UV-induced skin aging.

The present study demonstrated that strawberry extract significantly inhibits collagenase activity, with the highest inhibition of $86.31\% \pm 0.10$ observed at 250 $\mu\text{g/mL}$ and the lowest ($16.23\% \pm 0.29$) at 3.91 $\mu\text{g/mL}$. The IC_{50} value was 112.81 ± 1.96 $\mu\text{g/mL}$. Compared to raspberry extract, which showed only 18.4% and 32.3%

inhibition at 100 and 300 $\mu\text{g/mL}$ respectively, strawberry extract exhibits superior collagenase inhibitory potential, particularly at higher concentrations [31]. Matrix metalloproteinase-1 (MMP1), a collagenase that degrades type I and III collagen in the extracellular matrix (ECM), is upregulated by UV-induced oxidative stress and inflammation. Excess MMP1 activity leads to collagen loss, reduced skin elasticity, and wrinkles. Cyanidanol, a major bioactive in strawberry extract, has been shown to inhibit MMP1 expression and activity by downregulating the Nuclear Factor kappa B (NF- κ B) pathway [32,33]. Through MMP1 inhibition, cyanidanol protects collagen structure and mitigates photoaging-related skin damage caused by UV exposure and oxidative stress.

Strawberry extract exhibited strong elastase inhibitory activity, with the highest inhibition ($90.48\% \pm 0.31$) observed at $66.67 \mu\text{g/mL}$ and the lowest ($16.28\% \pm 2.01$) at $1.04 \mu\text{g/mL}$, resulting in an IC_{50} value of $28.03 \pm 0.68 \mu\text{g/mL}$. These findings indicate the extract's potent ability to inhibit elastase, a key enzyme in skin aging. Compared to raspberry extract, which showed only 17.1% and 25.6% inhibition at 100 and 300 $\mu\text{g/mL}$, respectively, strawberry extract demonstrated significantly stronger activity at much lower concentrations, highlighting its superior efficacy as a natural elastase inhibitor [31]. Elastin is essential for skin elasticity and flexibility but is degraded by elastase, especially under oxidative stress and UV exposure. Increased elastase activity contributes to loss of skin firmness and the formation of wrinkles. Cyanidanol, a key compound in strawberry extract, inhibits elastase activity, thereby protecting elastin fibers from UV-induced degradation [34]. This inhibition supports skin structure, maintains elasticity, and helps delay signs of photoaging [35].

Thus, strawberry extract, through its bioactive compounds like C3G, offers a multifaceted defense against oxidative stress, MMP1-induced collagen degradation, and elastase-mediated elastin loss, providing a promising natural intervention for counteracting the visible effects of photoaging, while enhancing skin resilience against UV-induced damage. This study has several limitations. The biological activities of strawberry extract were evaluated primarily through *in vitro* assays and *in silico* molecular docking, which may not fully represent *in vivo* or clinical conditions. The complex interactions of bioactive compounds within biological systems, including bioavailability, metabolism, and skin penetration, were not assessed. In addition, the study focused on selected enzymes and molecular targets related to photoaging, while other signaling pathways involved in skin aging may also play important roles. Future studies involving *in vivo* models, formulation development, and clinical evaluations are recommended to further validate the anti-photoaging potential of strawberry extract and to support its practical application in skincare or nutraceutical products.

5. Conclusion

The strawberry extract demonstrated notable antioxidant activity. The IC_{50} values were $229.91 \pm 4.42 \mu\text{g/mL}$ for DPPH scavenging and $234.08 \pm 4.20 \mu\text{g/mL}$ for H_2O_2 scavenging. In addition, the extract exhibited significant inhibitory effects on collagenase and elastase, with IC_{50} values of $112.81 \pm 1.96 \mu\text{g/mL}$ and $28.03 \pm 0.68 \mu\text{g/mL}$, respectively. Molecular docking analysis indicated that key bioactive compounds, including cyanidin-3-glucoside and cyanidanol, interact with enzymes involved in oxidative stress regulation and extracellular matrix remodeling. Collectively, these findings suggest that strawberry extract may play a promising role as an anti-photoaging agent by protecting against oxidative damage and preserving extracellular matrix integrity. These findings indicate the potential application of strawberry extract in skincare formulations or dietary supplements, this research requires further *in vivo* and clinical studies to confirm its efficacy and safety.

6. Acknowledgments

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7. Conflict of Interest

The authors have no conflict of interest to disclose.

8. Author Contributions

Wahyu Widowati was responsible for conceptualization, supervision, project administration, and funding acquisition. Hendra Subroto contributed to methodology, investigation, formal analysis, and data curation. Imelda Imelda contributed to investigation, data curation, and validation. Dian Puspitasari contributed to formal analysis, visualization, and validation. Yenny Noor contributed to resources, investigation, and validation. Vini Ayuni contributed to data curation and investigation. Reyhan Natadilandes contributed to investigation and data curation. All authors contributed to writing the manuscript and have read and approved the final version of the manuscript.

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