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Research Article

Enhancing Quality Characteristics of Cold-Pressed Sesame Oil with Ethanolic Extract of Quince (*Cydonia oblonga*), alongside with Exploring the Interaction of Trans Fatty Acids with Key Proinflammatory Cytokines via Molecular Docking

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Currently, there is a growing trend of replacing synthetic antioxidants with natural alternatives to prevent the oxidation of edible oils. Herein, we assessed the phenolic compounds and antioxidant properties of ethanolic extracts that are obtained from *Cydonia oblonga* (SQ). Furthermore, we incorporated SQ at two different concentrations (1% and 2%) into cold-pressed sesame oil, storing it for 30 days under ambient conditions. We then assessed the peroxide value (PV), acid value (AV), oxidative stability using the Rancimat apparatus, and the fatty acid (FA) composition. Additionally, we performed the molecular docking analyses to explore the interaction between trans fatty acids (TFAs; C18:1 and C18:2) and key proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP). The total phenol, flavonoid content, and antioxidant activity of SQ were found to be 95.33 ± 5.03 mg GAE/g, 343.67 ± 16.44 mg QE/g, and 465.67 ± 5.51 mmol Fe^{2+}/g, respectively. The presence of SQ exhibited a significant impact on reducing PV and AV when compared to the control group. Furthermore, the addition of SQ resulted in a significant increase in the induction period (IP) compared to the control. The predominant FAs in the samples were 18:2n-6, 18:1n-9, 16:0, and 18:0, respectively. The levels of TFAs in all samples at 30 days were higher than those at 0 day. TNF-α and IL-6 showed a higher binding affinity for the trans-C18:1 ligand, with a docking score of -6.81 and -5.82, respectively, compared to the trans-C18:2 ligand. In this context, SQ can be proposed as a natural antioxidant to enhance the oxidative stability of sesame oil. Additionally, the binding preferences and specific interactions of TFAs with these proinflammatory cytokines indicate their potential role in modulating inflammation.

1. Introduction

Sesame oil is a consumable vegetable oil derived from the seeds of the *Sesamum indicum* Linn plant. Due to its great resistance to oxidation during storage and frying, it distinguishes itself from other vegetable oils. This exceptional stability can be due to its rich content of antioxidants, including tocopherols and lignans [1, 2]. Sesame oil is usually produced using the cold-pressing technique, which requires less processing and preserves the seed's natural deliciousness. Cold-pressed sesame oil is a preferred option in culinary uses and food preparations because of its distinctive flavor and distinctive nutty scent [3, 4].

Beyond its culinary appeal, sesame oil is also recognized for its potential health-enhancing properties. It contains a high concentration of unsaturated FAs, which are lipid

mediators involved in many physiological functions [5]. The composition of sesame oil consists of approximately 14% saturated FAs, 39% monounsaturated FAs, and 46% polyunsaturated FAs [6]. The high antioxidant activity of sesame oil arises from its primary components, notably γ-tocopherol and three essential lignan compounds including sesamin, sesamolin, and sesamol, and these compounds contribute to the potent antioxidant properties exhibited by sesame oil [7].

However, oil is susceptible to oxidation upon exposure to various elements, including light, heat, trace metals, and oxygen. This vulnerability stems from the presence of unsaturated bonds within its chemical structure. The process of oxidation has detrimental effects on both the nutritional integrity and shelf life of the oil [8]. Lipid peroxidation is a multifaceted process that unfolds in distinct stages, swiftly giving rise to a multitude of compounds. These compounds play a pivotal role in the development of lipid rancidity. Among them, hydroperoxides emerge as prominent primary oxidation products, which subsequently undergo additional oxidation steps, culminating in the formation of secondary oxidation products. Examples of these secondary oxidation products encompass various organic compounds such as alkanes, alkenes, aldehydes, and ketones [9]. To decrease the level of lipid oxidation and extend shelf life, the application of antioxidants can be effective. These compounds act as safeguards against the autoxidation of oils and fats by bestowing their hydrogen atoms upon free radicals, thereby diminishing the likelihood of oil oxidation and the subsequent development of rancidity [8, 10].

The consumption of oils and oily foods containing oxidative metabolites comprising reactive oxygen species can inflict damage on various organs within the body. These damages exert their effects through the generation of cytotoxic and genotoxic compounds that can lead to develop the chronic diseases. These repercussions include perturbation of the body's redox equilibrium, compromising the robustness of the antioxidant network. As a consequence, they increase the risk of various diseases such as atherosclerosis, diabetes, obesity, and cancer. Oxidative stress can be associated with initiation and development of myeloma and lymphoma via DNA damage. Moreover, oxidative stress is able to induce the aging process, augmenting plasma total cholesterol levels, fostering larger atherosclerotic lesions, and promoting atherogenesis that impacts arterial walls and precipitates heart diseases, ultimately culminating in cell death [9, 11–13].

TFAs are a type of unsaturated FAs that are characterized by the presence of one or more unconjugated double bonds in the trans configuration. The majority of TFAs are produced during industrial processing, particularly through the partial hydrogenation of vegetable oils that are abundant in polyunsaturated fatty acids (PUFAs) [14]. Partially hydrogenated vegetable oils can contain as much as 60% TFAs, primarily composed of various isoforms of trans-octadecenoic acid (trans-C18:1), which typically constitute 80–90% of the total TFA content. Several studies suggested that specific TFAs exert their effects via targeting various crucial physiological processes including lipid metabolism, inflammation, oxidative stress, endoplasmic reticulum stress, autophagy, and apoptosis. Disruption of these biological pathways by TFAs serves as a potential underlying mechanism contributing to the detrimental impacts of TFAs on cardiometabolic health [15, 16]. Furthermore, recent evidences highlighted a potential link between TFAs and the regulation of proinflammatory cytokines, such as TNF-α, IL-6, and CRP [17, 18]. Studies have indicated that elevated levels of TFAs in the diet have been associated with increased circulating levels of proinflammatory cytokines that can lead to the activation of inflammatory pathways [19, 20]. Proinflammatory cytokines play key roles in the immune responses and are involved in the development and progression of various inflammatory diseases, ranging from cardiovascular diseases and cancer to diabetes and obesity [21–23]. Therefore, understanding the molecular interactions between TFAs and proinflammatory cytokines may shed light on the mechanisms underlying the harmful effects of TFAs on cardiometabolic health and further emphasize the importance of discovering potential interventions to alleviate their impact.

C. oblonga Mill., commonly known as quince, belongs to the Rosaceae family. This plant is utilized for both nutritional and medicinal purposes due to its substantial polyphenol content. The polyphenols found in the quince predominantly comprise hydroxycinnamic acids (such as caffeoyl and coumaroyl derivatives), flavonols (including quercetin and kaempferol derivatives), and, to a lesser extent, flavanols (such as catechin and epicatechin). Quince serves as a dietary source of health-enhancing compounds, contributing to its antioxidant capacity. Moreover, quince shows various beneficial properties, encompassing antiulcerative, anticarcinogenic, anti-inflammatory, antiallergic, and antimicrobial activities [24–26].

Hence, the aim of this study was to investigate the impact of an ethanolic extract derived from *C. oblonga* on the quality attributes of sesame oil obtained through cold pressing over a span of 30 days under ambient storage conditions (ranging from 25 to 30°C). Furthermore, limited research has been conducted on the molecular binding processes of TFAs with various targets in inflammation-related pathways. Therefore, we conducted molecular docking analyses to explore the interaction between TFAs (specifically trans-C18:1 and trans-C18:2) and key proinflammatory cytokines, aiming to elucidate the potential molecular mechanisms by which TFAs may contribute to inflammation-related processes. This aspect represents the novelty of our study.

2. Material and Methods

2.1. Preparation of Oil Sample and Quince Extract. Fresh sesame oil and quince were procured from Rosalita Company and a local fruit shop, respectively, located in Kashan, Iran. The quince fruit samples were carefully air-dried in shaded conditions for a period of 2 weeks. Subsequently, the dried quince samples were finely powdered utilizing a mixer grinder. Each batch of powdered quince was subjected to extraction using 80% ethanol employing the maceration technique. Specifically, 100 grams of the powdered quince material was mixed with 400 milliliters of 80% ethanol and

left to undergo extraction at room temperature for a duration of 8 hours [27]. The sesame oil was divided into 3 different categories: sesame oil without extract (control; C), sesame oil treated with 1% quince extract (SQ1), and sesame oil treated with 2% quince extract (SQ2).

2.2. Estimation of Total Phenolics, Flavonoids, and Total Antioxidant Activity. The quantification of total phenolic and flavonoid constituents was conducted on ethanolic extracts using colorimetric methods, as described in previous studies [28]. The determination of the overall antioxidant activity of the plant extract was carried out through iron reduction, employing the ferric reducing antioxidant power assay (FRAP), as detailed in a prior study [29].

2.3. Peroxide Value. The PV serves as a measure to assess the concentration of peroxides and hydroperoxides that emerge during the initial phases of the lipid oxidation process. As the oil initiates the oxidation process, peroxides begin to develop, subsequently liberating iodine from potassium iodide. The resulting iodine can then be quantified through titration using standard sodium thiosulfate, employing the methodology outlined in the AOCS Cd 8–53 standard methods. This analysis offers valuable insights into the oxidative status of the oil [30]. In summary, the procedure involved adding 30 ml of acetic acid-chloroform solution to a 250 ml flask containing 5 g of oil sample and shaking to ensure complete dissolution. Once the oil had completely dissolved, 0.5 ml of saturated potassium iodide solution was augmented and quickly swirled for one minute, after which 30 ml of deionized water was added. An indicator volume of one ml of starch was added to the mixture. Subsequently, the sample was titrated against 0.1 N sodium thiosulfate until the blue-gray color ceased to exist. The PV was calculated utilizing the volume of titrant as input, employing the subsequent equation: The outcomes were denoted in milliequivalents of peroxide per kilogram of oil:

$$\textbf{Peroxide value} = \frac{(S - B) \times N \times 1000}{W}, \quad (1)$$

where S is the volume consumed during titration of the sample (ml), B is the volume consumed during titration of the blank (ml), N is the normality of sodium thiosulfate solution, and W is the weight of oil (kg).

2.4. Acid Value. The AV experiment was employed in this research to determine the proportion of unbound FAs released through the hydrolysis of triglycerides. The procedure followed the methodology outlined in AOCS Cd 3d-63 [30]. In summary, in a 250 ml flask, 10 ml of ethanol and 1 g of oil were combined to dissolve the oil. Then, as an indication, two drops of phenolphthalein were added. Then, 0.1 N potassium hydroxide (KOH) was added to oil samples in titrations until a faint pink tint emerged. The free fatty AV was calculated using the volume of the titrant using the formula below:

$$\text{Acid value} = \frac{(V - B) \times N \times 56.1}{W}, \quad (2)$$

where V is the titrant volume consumed during titration of the sample, B is the titrant volume consumed during the titration of the blank, N is the normality of KOH, and W is the weight of oil (g).

2.5. Oxidative Stability. The oxidative stability of the oils was evaluated following the ISO 6886 standard method, utilizing a Rancimat 982 apparatus manufactured by Metrohm CH in Zofingen, Switzerland. The experimental conditions entailed setting the temperature to 110°C, while maintaining an air stream of 20 liters per hour [31].

2.6. Fatty Acid Composition. The FA composition of both the control and treated sesame oil samples was assessed subsequent to alkaline transesterification. In summary, a solution consisting of 200 μl of 2M KOH in methanol and 2 ml of n-heptane was combined with 100 mg of oil in a 4 ml screw vial. The mixture underwent vortexing for 30 seconds, after which the upper layer of n-heptane was extracted and transferred to a 2 ml vial for analysis using gas-liquid chromatography with flame ionization detection (GC-FID). The methodology employed for this analysis adhered to the guidelines specified in regulation EEC 2568/91 [6, 32]. Fatty acid methyl esters (FAME) along with standard compounds were subjected to analysis via gas chromatography (Agilent 6890), which was outfitted with a flame ionization detector and an Hp-88 capillary column (100 m length, 250 μm inner diameter, and 0.2 μm film thickness). The identification of FAME was established through a comparative assessment of their retention times against those of a standard FAME mixture. The quantification process was based on peak areas represented in electronic units, with the resulting fatty acid content being expressed as the relative percentage of each individual fatty acid.

2.7. Molecular Docking Analysis. The molecular docking study is useful to predict the binding interaction of the protein and small molecules [33]. We selected Autodock Vina for molecular docking and investigation of the binding interactions between TNF-α, IL-6, and CRP proteins and ligands and TFAs (trans-C18:1 and trans-C18:2). Blind docking was performed using AutoDock Vina software, which allowed the calculation of binding scores for each protein-ligand complex.

The three-dimensional crystal structure of the selected molecular targets was downloaded from a protein data bank (PDB). The PDB ID of the downloaded proteins were 2AZ5, 1ALU, and 3PVN for TNF-α, IL-6, and CRP, respectively. Ligand molecules, trans-C18:1 (elaidic acid; PubChem CID: 637517), and trans-C18:2 (linoelaidic acid; PubChem CID: 5282457) were retrieved from the PubChem database. AutoDockTools were used to prepare the structure of proteins and ligands by adding hydrogens, assigning Gasteiger charges, and to convert the ligand and protein into the pdbqt format required by AutoDock Vina [34].

A docking grid box of dimensions $40 \times 40 \times 40$ with a grid spacing of 1 Å was centered on each protein structure to cover the entire surface, with the exhaustiveness parameter of 8.

The top binding pose ranked by binding affinity was retained to investigate the interaction of each protein-ligand pair. The interaction plot analyses were carried out by using BIOVIA Discovery Studio 2020 software.

The interactions between the protein residues and ligands were analyzed and categorized based on their type. The distances between the interacting residues and ligands were calculated. The specific residues involved in each interaction were noted.

2.8. Statistical Analysis. All experiments in this study were performed in triplicate, and the data are presented as the mean ± standard deviation (SD). Statistical analysis was performed using SPSS software (version 21, Chicago, IL, USA). One-way ANOVA and the least significant difference test were employed to determine the statistically significant differences between the samples. A p value less than 0.05 was considered indicative of significant differences.

3. Results

Table 1 shows the obtained results from tests assessing total phenol and flavonoid content, as well as antioxidant activity, for the hydroethanolic extract derived from the whole fruit of *C. oblonga*.

Figure 1 depicts the PV trends for sesame oil samples, including both oil without extract and oil treated with the hydroethanolic extract from the whole fruit of *C. oblonga* (at concentrations of 1% and 2%), during a 30-day storage period. The findings revealed a notable elevation in PVs across all samples as the storage duration extends. At the initial point (zero time), no significant distinctions were observed between the control, SQ1, and SQ2 samples. However, over the course of the 10, 20, and 30-day storage intervals, the presence of quince extract exhibited a significant impact in reducing PVs when contrasted with the control group ($p < 0.05$).

The AVs for sesame oil without extract and sesame oil with the hydroethanolic extract of the whole fruit of *C. oblonga* (at concentrations of 1% and 2%) during a 30-day storage period are presented in Figure 2. At zero and 10 time points, the results indicated no significant differences among all samples. After 20 days, the AV of all samples increased compared to the initial measurement, but only SQ2 exhibited a notable difference from the other samples ($p < 0.05$). As the storage period extended to 30 days, the presence of quince extract demonstrated significance in reducing the AV when compared to the control ($p < 0.05$).

The IP results obtained using the Rancimat method for sesame oil without extract and sesame oil with the hydroethanolic extract of the whole fruit of *C. oblonga* (at concentrations of 1% and 2%) are shown in Figure 3. The addition of quince extract showed a significant increase in IP when compared to the control ($p < 0.05$).

Table 1: Total phenols, flavonoid content, and antioxidant activity of hydroethanolic extract of whole fruit of *C. oblonga*.

	Results
Total phenol content (mg GAE/g)	95.33 ± 5.03
Flavonoid content (mg QE/g)	343.67 ± 16.44
Antioxidant activity (mmol Fe^{2+}/g)	465.67 ± 5.51

Table 2 provides the results of fatty acid quantification for sesame oil without extract and sesame oil with the hydroethanolic extract of the whole fruit of *C. oblonga* (at concentrations of 1% and 2%) at both 0 and 30 days. The predominant FAs were 18:2n-6, 18:1n-9, 16:0, and 18:0, respectively. The levels of TFAs in all samples at 30 days were higher than those at 0 day ($p < 0.05$). Additionally, the quantities of 18:2n-6 and 18:1n-9 at 30 days were lower than those at 0 day ($p < 0.05$).

The docking simulations provided insights into the binding affinities of TNF-α, IL-6, and CRP with trans-C18:1 and trans-C18:2 ligands, as well as the specific interactions formed between the protein residues and ligands. The docking scores obtained for each protein-ligand complex are presented in Table 3, while Table 4 provides information on the interactions, distances, and categorization of interactions for each protein-ligand complex.

Representative protein-ligand complexes with the most favorable binding affinities are shown in Figures 4–6. TNF-α and IL-6 exhibited a higher binding affinity for the trans-C18:1 ligand with a docking score of -6.81 and -5.82, respectively, compared to the trans-C18:2 ligand (with a docking score of -6.24 and -5.84, respectively). The analysis of interactions revealed that TNF-α formed hydrogen bond interactions between residue GLY122 and trans-C18:1, as well as hydrophobic interactions involving residues TYR59, TYR119, and TYR151 with both trans-C18:1 and trans-C18:2 ligands. In the sense of IL-6, results indicated hydrogen bond interactions involving residues ARG30, ASP34, and ARG182 with trans-C18:1 ligand, while hydrophobic interactions were observed with residues ARG179, LEU33, LEU178, and SER176. For trans-C18:2 ligand, hydrogen bond interactions were formed with residues SER176, LYS66, and ARG179. CRP demonstrated slightly lower binding affinities for both ligands, with a docking score of -5.69 for trans-C18:1 and -5.77 for trans-C18:2. The interaction analysis demonstrated hydrogen bond interactions involving residues LYS69, ASP70, and PRO87 with trans-C18:1 ligand, while hydrophobic interactions were observed with residue PRO87. For trans-C18:2 ligand, hydrophobic interactions were observed with residues LYS69, VAL89, and PRO87. The distances and interaction types are detailed in Table 4.

4. Discussion

This study investigated the impact of an ethanolic extract derived from *C. oblonga* as a potential natural antioxidant on the oxidative stability of cold-pressed sesame oil over a 30-day period of environmental storage. Furthermore, a molecular docking assessment was employed to explore the

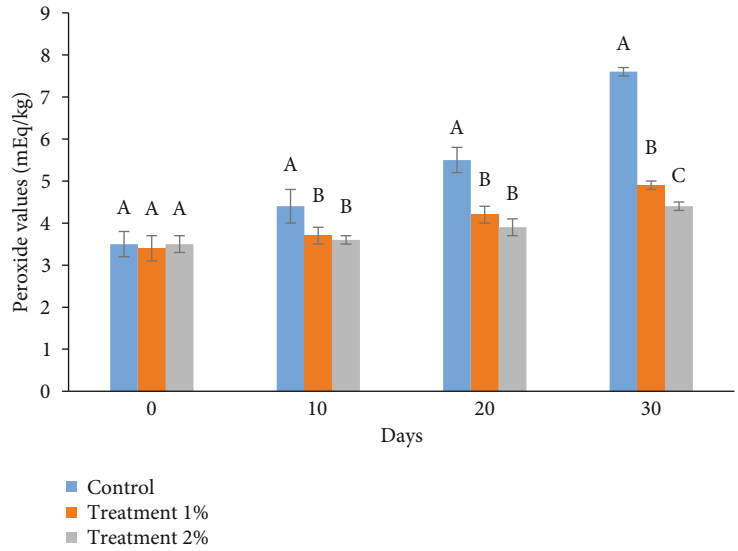


Figure 1: Peroxide value (mEq/kg) for sesame oil without extract (control) and sesame oil with hydroethanolic extract of whole fruit of *C. oblonga* (1% and 2%) during the storage period of 30 days. Different letters (A–C) in the groups indicate significant differences ($p < 0.05$).

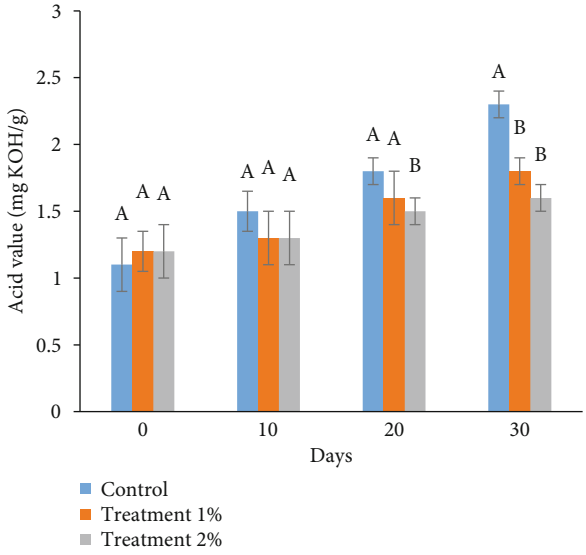


Figure 2: Acid value (mg KOH/g) for sesame oil without extract (control) and sesame oil with hydroethanolic extract of whole fruit of *C. oblonga* (1% and 2%) during the storage period of 30 days. Different letters (A and B) in the groups indicate significant differences ($p < 0.05$).

potential interactions between TFAs (trans-C18:1 and trans-C18:2) and key proinflammatory cytokines, including TNF-α, IL-6, and CRP.

The findings of this study revealed that the PVs of both the control and treated sesame oil samples remained below the CODEX standard threshold (15 meq/kg oil) over the 30-day testing period [35]. PV served as a metric to quantify the primary oxidation products generated within fats as a consequence of oxidation. Our study's results demonstrated noteworthy variations between the control samples and those treated with SQ1 and SQ2 during the storage period (Figure 1). Notably, prior research indicated that the phenolic compounds present in various extracts could potentially enhance the stability of oils [36, 37]. Soybean oil samples enriched with olive leaf extract (OLE) revealed a reduction of PV level compared to the control group. Furthermore, the oil samples supplemented with varying concentrations of OLE (1000 and 1500 ppm) demonstrated a noteworthy and statistically significant decrease ($p < 0.05$) in the presence of secondary products when compared to the control [37]. Yazdanpanah et al. [38] demonstrated that the PV of sesame oil infused with an aqueous extract of white tea was notably lower than that observed in the control group. Omidi et al. [39] similarly reported comparable findings. They showed that different concentrations of methanolic extract derived from *Spirulina microalgae* (ranging from 500 to 2000 ppm) exhibited a significant difference in terms of PV compared to the control group.

According to the results of this study, the AV of all sesame oil samples displayed a gradual increase as the storage time advanced. Nevertheless, these values remained below the permissible level set for cold-pressed virgin oils, which stands at 4 mg KOH per gram of oil [3]. The AV experiment quantifies the quantity of free FAs released through the hydrolysis of fat within the oil sample. This measurement serves as an indicator of the quality of sesame oil. A higher AV indicates a greater degree of oil oxidation, which corresponds to lower quality [3]. The upward trend in AV over time was previously documented by Zanardi et al. [40] in sesame oil, also in other oils like palm, peanut, and sunflower. In our work, there was no noteworthy disparity between the control samples and SQ1 and SQ2 at 0 and 10 days. However, a significant divergence emerged between the control samples and SQ1 and SQ2 at the 30-day mark. This result aligns with findings from another study in which sunflower oil treated with either natural or synthetic antioxidants exhibited a similar pattern [41].

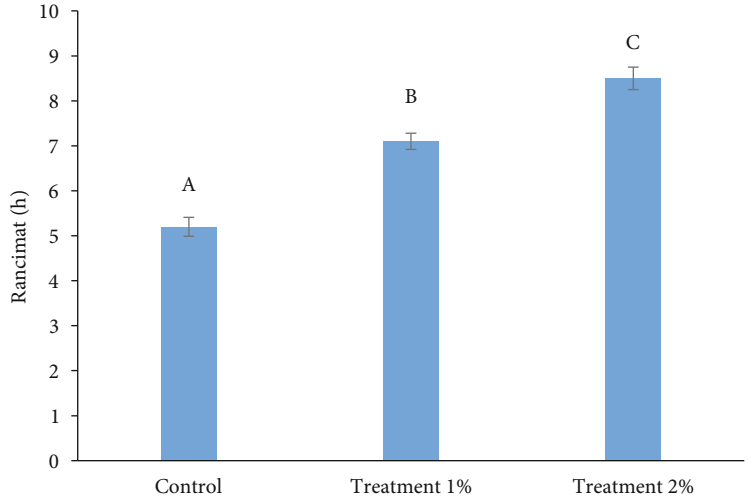


Figure 3: Evaluation of the oxidative stability of sesame oil without extract (control) and sesame oil with hydroethanolic extract of whole fruit of *C. oblonga* (1% and 2%) at 110°C, and the air stream was 20 Lit/h. Different letters (A–C) in the groups indicate significant differences ($p < 0.05$).

Table 2: Fatty acid composition expressed in mg/g of sesame oil without extract and sesame oil with hydroethanolic extract of whole fruit of *C. oblonga* (1% SQ1 and 2% SQ2) at 0 and 30 days.

Fatty acids	0 day			30 days		
	C	SQ1	SQ2	C	SQ1	SQ2
C14:0	0.12 ± 0.00^{A}	0.12 ± 0.00^{A}	0.12 ± 0.00^{A}	0.12 ± 0.00^{A}	0.12 ± 0.00^{A}	0.12 ± 0.00^{A}
C16:0	92.4 ± 0.04^{A}	92.4 ± 0.04^{A}	92.4 ± 0.04^{A}	92.6 ± 0.04^{A}	92.5 ± 0.04^{A}	92.4 ± 0.04^{A}
C16:1n-7	1.1 ± 0.02^{A}	1.1 ± 0.02^{A}	1.1 ± 0.02^{A}	1.08 ± 0.02^{A}	1.1 ± 0.02^{A}	1.1 ± 0.02^{A}
C17:0	0.33 ± 0.00^{A}	0.33 ± 0.00^{A}	0.33 ± 0.00^{A}	0.31 ± 0.03^{A}	0.30 ± 0.02^{A}	0.34 ± 0.04^{A}
C18:0	42.57 ± 0.02^{A}	42.57 ± 0.02^{A}	42.57 ± 0.02^{A}	42.54 ± 0.04^{A}	42.55 ± 0.04^{A}	42.53 ± 0.03^{A}
C18:1n-9	361.4 ± 0.08^{A}	361.4 ± 0.08^{A}	361.4 ± 0.08^{A}	354.4 ± 0.09^{B}	356.4 ± 0.07^{C}	360.5 ± 0.08^{A}
C18:1n-7	5.66 ± 0.04^{A}	5.66 ± 0.04^{A}	5.66 ± 0.04^{A}	5.57 ± 0.09^{A}	5.59 ± 0.06^{A}	5.63 ± 0.04^{A}
C18:2n-6	415.25 ± 0.05^{A}	415.25 ± 0.05^{A}	415.25 ± 0.05^{A}	409.1 ± 0.05^{B}	412.25 ± 0.03^{C}	413.1 ± 0.06^{C}
C18:3n-3	3.14 ± 0.04^{A}	3.14 ± 0.04^{A}	3.14 ± 0.04^{A}	3.12 ± 0.06^{A}	3.11 ± 0.04^{A}	3.15 ± 0.06^{A}
C20:0	4.8 ± 0.02^{A}	4.8 ± 0.02^{A}	4.8 ± 0.02^{A}	4.7 ± 0.09^{A}	4.8 ± 0.05^{A}	4.7 ± 0.08^{A}
C20:1n-9	1.6 ± 0.04^{A}	1.6 ± 0.04^{A}	1.6 ± 0.04^{A}	1.52 ± 0.03^{B}	1.58 ± 0.04^{A}	1.59 ± 0.04^{A}
C20:4n-6	0.62 ± 0.02^{A}	0.62 ± 0.02^{A}	0.62 ± 0.02^{A}	0.59 ± 0.03^{A}	0.61 ± 0.04^{A}	0.62 ± 0.06^{A}
C24:0	0.51 ± 0.04^{A}	0.51 ± 0.04^{A}	0.51 ± 0.04^{A}	0.50 ± 0.02^{A}	0.51 ± 0.06^{A}	0.50 ± 0.07^{A}
SFA	140.73 ± 0.12^{A}	$140.73 \pm .012^{A}$	$140.73 \pm .012^{A}$	$140.77 \pm .0.22^{A}$	$140.78 \pm .0.21^{A}$	$140.59 \pm .0.26^{A}$
MUFA	369.76 ± 0.18^{A}	369.76 ± 0.18^{A}	369.76 ± 0.18^{A}	362.57 ± 0.23^{A}	$364.67 \pm .0.19^{A}$	$368.82 \pm .0.18^{A}$
PUFA	419.01 ± 0.11^{A}	419.01 ± 0.11^{A}	419.01 ± 0.11^{A}	412.81 ± 0.14^{A}	$415.97 \pm .0.11^{A}$	$416.87 \pm .0.18^{A}$
Trans fatty acid	0.4 ± 0.01^{A}	0.4 ± 0.01^{A}	0.4 ± 0.01^{A}	0.5 ± 0.02^{B}	0.49 ± 0.03^{B}	0.47 ± 0.02^{B}

Mean ± standard deviation of two analyses. Different letters in the same line indicate a significant difference at 95% by the ANOVA test ($p < 0.05$).

Table 3: The binding affinities of the top docking poses.

Protein	Ligand (TFA)	Score
TNF-α	Trans-C18:1	-6.81
	Trans-C18:2	-6.24
IL-6	Trans-C18:1	-5.82
	Trans-C18:2	-5.84
CRP	Trans-C18:1	-5.69
	Trans-C18:2	-5.77

The IP in hours, determined through the Rancimat method, serves as a widely accepted measure to assess the capacity of oils and fats to withstand accelerated oxidation under stressful conditions like air and heat. Notably, the IP values for SQ1 and SQ2 significantly surpassed those of the control sample ($p < 0.05$), as depicted in Figure 2. This enhancement could be attributed to the presence of phenolic compounds within the quince extract. A prior study demonstrated a synergistic effect between phenolic compounds such as sesamol and γ-tocopherol, observed in a model

Table 4: Intermolecular interactions between the ligands and key amino acid residues in the binding site of each docked protein complex.

Protein	Interactions	Distance	Category	Type
TNF-α	A: GLY122-C18:1	2.49227	Hydrogen bond	Carbon hydrogen bond
	A: TYR59-C18:1	4.69657	Hydrophobic	Pi-Alkyl
	A: TYR59-C18:1	4.55788	Hydrophobic	Pi-Alkyl
	B: TYR119-C18:1	5.20912	Hydrophobic	Pi-Alkyl
	B:TYR151-C18:1	5.1787	Hydrophobic	Pi-Alkyl
	A: TYR151-C18:2	2.10425	Hydrogen bond	Conventional hydrogen bond
	A: SER60-C18:2	2.60046	Hydrogen bond	Conventional hydrogen bond
	B: TYR119-C18:2	5.37121	Hydrophobic	Pi-Alkyl
IL-6	ARG30-C18:1	2.75109	Hydrogen bond	Conventional hydrogen bond
	ASP34-C18:1	2.00213	Hydrogen bond	Conventional hydrogen Bond
	ARG30-C18:1	4.8115	Hydrophobic	Alkyl
	ARG179-C18:1	5.18369	Hydrophobic	Alkyl
	LEU33-C18:1	4.82652	Hydrophobic	Alkyl
	LEU178-C18:1	4.31064	Hydrophobic	Alkyl
	ARG182-C18:1	5.02992	Hydrophobic	Alkyl
	SER176-C18:2	2.33641	Hydrogen bond	Conventional hydrogen bond
	LYS66-C18:2	2.73064	Hydrogen bond	Carbon hydrogen bond
	SER176-C18:2	3.07451	Hydrogen bond	Carbon hydrogen bond
	ARG179-C18:2	4.58308	Hydrophobic	Alkyl
	SER176-C18:2	2.33641	Hydrogen bond	Conventional hydrogen bond
CRP	LYS69-C18:1	2.81528	Hydrogen bond	Conventional hydrogen bond
	ASP70-C18:1	2.08868	Hydrogen bond	Conventional hydrogen bond
	LYS69-C18:1	2.59002	Hydrogen bond	Carbon hydrogen bond
	PRO87-C18:1	4.86508	Hydrophobic	Alkyl
	LYS69-C18:2	5.38624	Hydrophobic	Alkyl
	VAL89-C18:2	4.59074	Hydrophobic	Alkyl
	PRO87-C18:2	3.86619	Hydrophobic	Alkyl

system involving linoleic acid. Arab et al. [6] demonstrated a robust correlation ($R2 = 0.84$) between the IP determined via the Rancimat method and the total phenolic compound content. This finding highlights the significant involvement of these compounds in effectively curbing oil oxidation.

The FA composition observed in sesame oil, SQ1, and SQ2 (Table 2) closely resembled or fell within the ranges previously reported in literature [2, 6, 42]. The predominant FAs identified both before and after the addition of quince extract over the 30-day period included linoleic acid (C18:2n-6; ranging from 409.1 to 415.25 ± 0.05 mg/g), oleic acid (C18:1n-9; ranging from 354.4 to 361.4 mg/g), palmitic acid (C16:0; ranging from 92.4 to 92.6%), and stearic acid (C18:0; ranging from 42.53 to 42.57 mg/g). All three samples—sesame oil, SQ1, and SQ2—contained TFAs within the range of 0.4 to 0.5 mg/g. Importantly, a significant difference ($p < 0.05$) was observed between the amounts of TFAs at 0 and 30 days, a result consistent with previous findings [43]. TFAs are known to develop under extreme conditions, particularly during prolonged heating at high temperatures, although research findings regarding the extent of TFA formation are contentious. The conversion from cis to trans configuration in unsaturated lipids is an inevitable process during autoxidation, a fundamental mechanism of lipid oxidation characterized by a free radical chain reaction comprising initiation, propagation, and termination stages. The initial step involves the formation of lipid radicals through the loss of hydrogen atoms from unsaturated lipids. Double bonds in cis configuration are inherently unstable and tend to adopt a more stable trans configuration [44]. Studies have demonstrated that the formation of TFAs can be influenced by various factors, including the type of oil, temperature, duration of heating, and cooking method (e.g., heating, frying, stir-frying) [45].

The experimental results support the findings from molecular docking simulations, which revealed the potential interaction of TFAs with proinflammatory cytokines, such as TNF-α, IL-6, and CRP. The higher binding affinities observed for TNF-α and IL-6 towards trans-C18:1 suggested that these proteins may have a stronger preference for this ligand.

The hydrogen bond interactions observed between TNF-α and IL-6 with their respective ligands indicate the involvement of specific residues, such as GLY122, TYR59, TYR119, TYR151, ARG30, ASP34, ARG182, and SER176, in stabilizing the protein-ligand complexes. In addition, the hydrophobic interactions involving TYR59, TYR119, TYR151, ARG179, LEU33, LEU178, and SER176 further contribute to the binding interactions. CRP exhibited lower binding affinities for both ligands compared to TNF-α and IL-6. However, the hydrogen bond and hydrophobic interactions observed between CRP and its ligands suggest potential binding modes and stabilization of the complexes.

The binding preferences and specific interactions of TFAs with these proinflammatory cytokines indicate their potential role in modulating inflammation. Ramos-Lopez et al. [46]

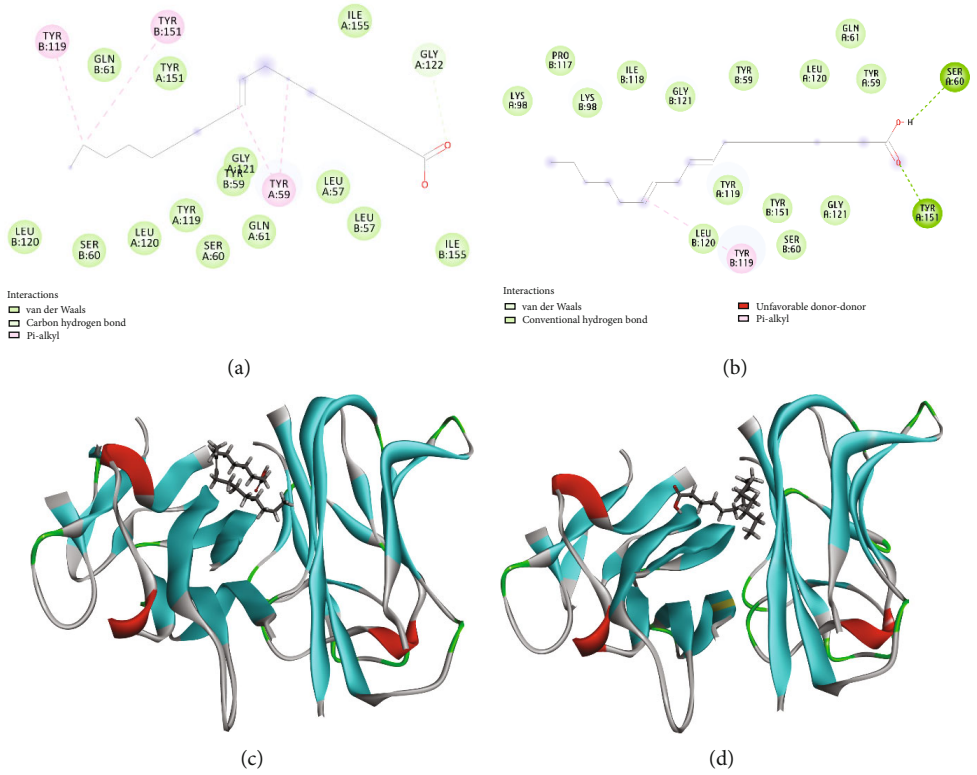


Figure 4: Representation of 2D and 3D protein-ligand interactions. (a) 2D interaction of TNF-α-trans-C18:1, (b) 2D interaction of TNF-α-trans-C18:2, (c) 3D representation of the protein-ligand complex between TNF-α-trans-C18:1 (gray), and (d) 3D representation of the protein-ligand complex between TNF-α-trans-C18:2 (gray).

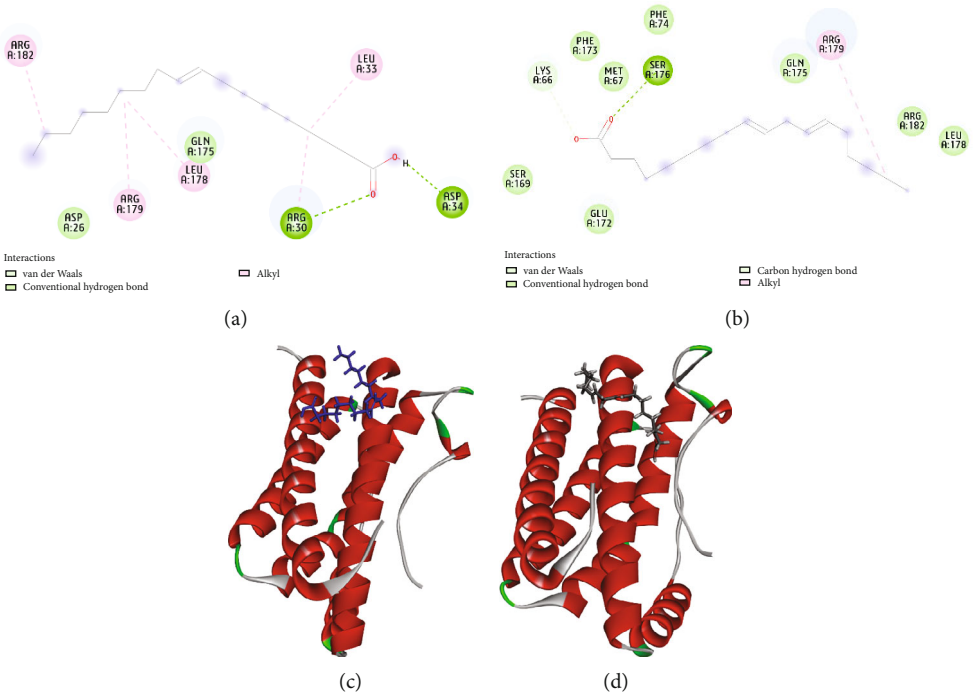


Figure 5: Representation of 2D and 3D protein-ligand interactions. (a) 2D interaction of IL 6-trans-C18:1, (b) 2D interaction of IL 6-trans-C18:2, (c) 3D representation of the protein-ligand complex between IL 6-trans-C18:1 (gray), and (d) 3D representation of the protein-ligand complex between IL 6-trans-C18:2 (gray).

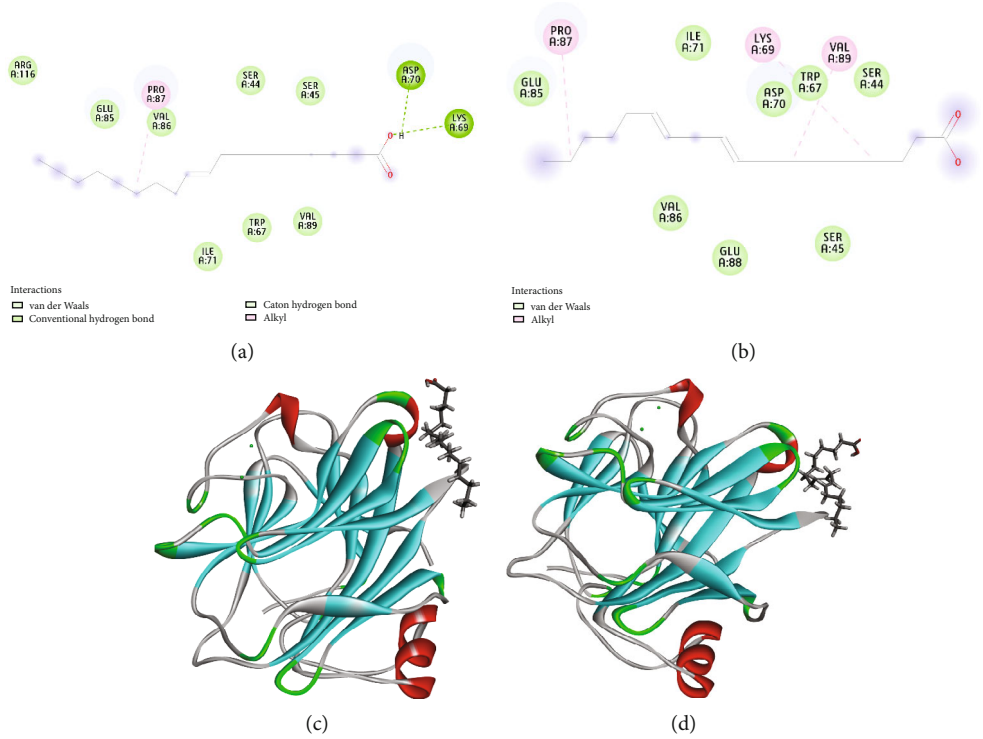


Figure 6: Representation of 2D and 3D protein-ligand interactions. (a) 2D interaction of CRP-trans-C18:1, (b) 2D interaction of CRP-trans-C18:2, (c) 3D representation of the protein-ligand complex between CRP-trans-C18:1 (gray), and (d) 3D representation of the protein-ligand complex between CRP-trans-C18:2 (gray).

found a positive correlation between TFA intake and plasma biomarkers of inflammation, such as CRP, vascular cell adhesion molecule 1, and E-selectin, in women. They also observed increased plasma levels of soluble TNF receptors 1 and 2, particularly in women with higher body mass index. Additionally, in men, serum CRP concentrations were elevated following TFA consumption (8% of total fat). Mallick and Duttaroy [47] showed that TFAs can impact the thrombotic state via the eicosanoid synthesis pathway and also impair endothelial function, contributing to their association with cardiovascular disease risk. Hirata et al. [48] demonstrated that TFAs exert toxicity by targeting signal-regulating kinase 1 (ASK1), while elaidic acid exhibited a potent proapoptotic effect upon exposure to extracellular ATP. This molecule functions as a damage-associated molecular pattern that induces apoptosis through the ASK1-p38 MAP kinase pathway.

5. Conclusion

The results of our work showed that SQ had a strong antioxidant effect due to total phenol and flavonoid contents, which could effectively improve the oxidation stability of sesame oil in an ambient condition for 30 days. All sesame oils supplemented with SQ showed low PV and AV when compared with control group. Additionally, the addition of SQ resulted in a significant increase in IP compared to the control group. The levels of TFAs in all samples at 30 days were higher than those at 0 day. Totally, the SQ at level 2% showed a good antioxidant activity when compared with other groups. Moreover, TNF-α and IL-6 exhibited a higher binding affinity for the trans-C18:1 ligand compared to the trans-C18:2 ligand. In this context, SQ can be proposed as a potential low-cost natural antioxidant to improve the oxidative stability of sesame oil or as a green alternative to chemical antioxidants. Additionally, the binding preferences and specific interactions of TFAs with these proinflammatory cytokines indicate their potential role in modulating inflammation. Therefore, further studies are needed to evaluate the interactions of the proinflammatory cytokines and TFAs both in vitro and in vivo models.

Data Availability

The datasets of the current study are available from the corresponding author on reasonable request.

Disclosure

A preprint has previously been published [49].

Conflicts of Interest

The authors declare that they have no conflict of interest.

Authors' Contributions

H.M. and R.S.C. were responsible for investigation, methodology, formal analysis, and writing of the original draft. K. S., A.J., and R.S.C. were responsible for visualization, data

curation, and supervision (equal). All of the authors were responsible for writing, reviewing, and editing.

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