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The Antioxidant and Anticancer Efficacy of Tea Tree (*Melaleuca alternifolia*) Oil and Casein Polymer Against Melanoma Skin Cancer

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Abstract

One of the most widespread global health problems is cancer, specifically skin cancer. These problems are attributed to environmental and immunological causes and can be associated with other disease conditions. According to the statistical increase of the disease, the need has become urgent to reach an alternative formula for chemotherapy due to its side effects on the body's organs. One of the most important anticancer agents is essential oils, especially tea tree oil, which has been extracted from the plant's dry leaves using the steam distillation method by Clevenger apparatus, then analysed using gas chromatography mass technique which revealed the presence of many important compounds such as (4-terpineol 22.45%, cymene 14.10%, γ-terpinene 6.69%, α-pinene 5.79%, α-terpineol 3.48%, sabinene 2.54% and α-terpinolene 2.33%); the oil was polymerized with casein to compare its effectiveness as an antioxidant and anticancer agent. The study proved that casein polymer compared to ascorbic acid scored highest inhibitory activity at concentration 100 (mg/ml) (34.34±11.92 and 54.08±15.89) and 80 (mg/ml) (27.15±10.92 and 38.77±12.83) and lowest inhibitory activity at concentration 40 (mg/ml) (14.26±4.98 and 20.91±8.92) and 20 (mg/ml) (14.89±6.29 and 18.36±6.87); meanwhile tea tree oil scored highest anticancer activity at doses 0, 31.25, and 62.5 µg/ml (100 ± 1.92, 92.20 ± 1.98, and 91.96 ± 1.95) and lowest anticancer activity at doses 250 and 500 µg/ml (53.6 ± 1.80 and 10.37 ± 2.86), while casein scored highest anticancer activity at doses 0, 7.81 and 31.25 µg/ml (100 ± 4.09, 89.94 ± 0.66 and 89.35 ± 3.30) and lowest anticancer activity at doses 250 µg/ml (74.09 ± 1.78) which considered the highest skin anticancer value for the polymer.

Keywords: tea tree oil, γ-terpinene, A375 cell line, DPPH method, casein polymerization.

فعالية زيت شجرة الشاي وبوليمر الكازين كمضاد للاكسدة ومضاد للسرطان في مكافحة سرطان الجلد الميلانيني

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الخلاصة

من اهم المشاكل الصحية الواسعة الانتشار في العالم هو مرض السرطان وخصوصا سرطان الجلد. حيث ان هذه المشاكل الصحية تعزى الى مختلف الاسباب البيئية والمناعية بالاضافة الى ارتباطها بامراض وحالات صحية اخرى, ونظرا للاحصائيات المتزايدة لهذا المرض كانت هناك حاجة ملحة لوجود تراكيب دوائية مغايرة للعلاج الكيماوي نظرا لاعراضه الجانبية المؤثرة على مختلف اعضاء الجسم. ومن اهم مضادات الاصابة بالسرطان هي الزيوت الاساسية المستخلصة من النباتات ولاسيما زيت شجرة الشاي حيث تم استخلاصه بطريقة التقطير البخاري باستخدام جهاز الكلافنجر وتم الحصول على الزيت والكشف عنه بطريقة Gas–chromatography mass وتم تشخيص المركبات المهمة الموجودة فيه وظهرت بالنسب التالية(4–terpineol 22.45%, cymene 14.10%, γ–terpinene 6.69%, α–pinene 5.79%, α–terpineol 3.48%, sabinene 2.54% and α–terpinolene 2.33%) كما تم ربط الزيت مع مركب الكازيين لتكوين بوليمر وذلك لزيادة فعاليته وقد تم مقارنة مركب الزيت المستخلص مع البوليمر المحضر من ناحية الفعالية المضادة للاكسدة وكذلك الفعالية ضد الخلايا السرطانية المسببة لسرطان الجلد وقد أثبتت الدراسة أن بوليمر الكازئين مقارنةً بحمض الأسكوربيك سجل أعلى نشاط تثبيطي عند تركيز 100 ملغم/مل (34.34±11.92 و54.08±15.89) و80 ملغم/مل (27.15±10.92 و38.77±12.83)، وسجل أدنى نشاط تثبيطي عند تركيز 40 ملغم/مل (14.26±4.98 و20.91±8.92) و20 ملغم/مل (14.89±6.29 و18.36±6.87) وفي الوقت ذاته، سجل زيت شجرة الشاي أعلى نشاط مضاد للسرطان عند الجرعات 0 و31.25 و62.5 ميكروغرام/مل (100 ± 1.92، 92.20 ± 1.98، و91.96 ± 1.95)، وأدنى نشاط عند الجرعات 250 و500 ميكروغرام/مل (53.6 ± 1.80 و10.37 ± 2.86) أما الكازئين فقد سجل أعلى نشاط مضاد للسرطان عند الجرعات 0 و7.81 و31.25 ميكروغرام/مل (100 ± 4.09، 89.94 ± 0.66، و89.35 ± 3.30)، وأدنى نشاط عند جرعة 250 ميكروغرام/مل (74.09 ± 1.78)، والتي اعتُبرت أعلى قيمة مضادة لسرطان الجلد بالنسبة للبوليمر.

1. Introduction

Melanoma is the most lethal form of skin cancer, frequently arising from a pigment-producing cell called a melanocyte, located in the lowest layer of the epidermis [1]; approximately 132,000 new cases are diagnosed annually, with at least 6,500 of those resulting in patient death. It is most commonly associated with excessive exposure to ultraviolet radiation (UVR) during childhood [2]. Various genetic changes underlying the initiation and progression of melanoma necessitate the constant search for new strategies in the fight against this cancer [3]. The 5-year survival rate for average melanoma patients is now over 90 percent. However, serious cases of skin cancer have a considerably higher fatality rate. When skin melanomas have invaded adjacent skin, the 5-year survival rate drops to 64 percent [4]. Patients with melanomas larger than 4 millimeters, which have passed beyond the skin to invade other areas of the body, are given a 46 percent chance of surviving for five years. This drop in survival demonstrates the importance of early detection and therapy in saving the lives of individuals with advancing skin cancer [5].

Different genetic and environmental factors contribute to the development of skin cancer. People with a family history of skin cancer, blonde hair, fair skin, and light-colored eyes are more likely to get skin cancer. Melanomas may start to grow in areas of the body that are protected from the sun, such as within the intestines or in the reproductive and urinary tracts [6].

Recent research follows the rationale that the elucidation of the biological processes involved in the development of melanocytic tumors is likely to provide a blueprint for the dissection of other human cancers [7]. Although many specialized tumor cell lines exist, the most extensively studied is A375, as it has been associated with the rapid iteration of melanoma metastases, as well as having a predisposition to the brain [8].

A375 is a widely studied malignant melanoma skin cancer cell line. It grows in vitro both as adherent cells in a monolayer and in suspension, and in general appears like the classical fast-growing melanoma cells, with a bipolar, elongated spindle shape. The cells are arranged in parallel, often giving a "railroad tract" look [9].

Historically, chemotherapy was the mainstay modality in treating metastatic seminoma of all sites, including the skin. Since the 1970s, several classes of cytotoxic chemotherapeutic drugs, such as alkylating agents, platinum analogs, antimetabolites, and Vinca alkaloids, have been used either as single agents or in combination regimens, mainly for patients with relatively high general condition [10]. Most of the currently used chemotherapeutic agents act by interfering with DNA synthesis and replication or by inhibiting the formation of microtubules that are required for mitosis, leading to disruption of cellular division and death of rapidly dividing cells like cancer, resulting in inhibition of skin cancer growth [11]. Because the chemotherapeutic agents are developed to target rapidly dividing cells, they tend to also affect normal cells that divide rapidly, leading to corresponding side effects [12,13].

One of the alternatives to chemotherapy against cancer is the use of essential oils and their polymers. Essential oils (EOs) extracted from aromatic and medicinal plants have shown great potential for managing a number of diseases, including efficacy in different cancers [14]. One of these effective essential oils against skin cancer is tea tree oil (TTO), which is extracted from *Melaleuca alternifolia*, also known as tea tree, the most renowned of the species belonging to the Myrtaceae family, which is native to Australia [15].
Tea tree oil (TTO) is considered to have antimicrobial, antiseptic, anticancer, and bactericidal properties. These properties are primarily due to thymol, terpinen-4-ol, and sabinene found within it [16]; TTO contains approximately 90% terpenes, irrespective of the country of origin. Camphor, 1,8-cineole, eucalyptol, terpinen-4-ol, and α-terpinene are the major terpenes in the oil [17]. Terpenes are lipophilic and have a range of antimicrobial activities as they act on the cell membranes of microorganisms, which helps to decrease the incidence of microorganism antibiotic resistance [18]. It has been suggested that terpenes inactivate the substrate, making the cell membrane more permeable; as it takes action over the permeability barrier, which helps to cause a loss of hydrogen ions and reduced adenosine triphosphatase activity [19].
Natural polymers have garnered significant attention in various food, pharmaceutical, and material applications due to their multifaceted physicochemical properties. Casein, one of the three major proteins present in milk, is an example of a biocompatible biopolymer that is extensively used in a wide range of pharmaceutical and food products [20]. Compared to casein, some synthetic polymers have inherent limitations, such as non-biodegradability. These limitations are addressed by the use of natural polymers, such as casein, which are abundant, inexpensive, renewable, and have superior biodegradability and biocompatibility, among other favorable characteristics [21].

The aim of this study is to investigate the activity of tea tree essential oil and its active compounds polymerized with casein as an antioxidant and anticancer against A375 skin cancer *in vitro*.

2. Materials and methods

2.1 collection and extraction of tea tree plant

The plant specimens used in this study consisted of the above-ground portions of *Melaleuca alternifolia* (commonly known as tea tree), which were obtained from a local market and classified according to the classification certificate No. 1337 dated 1 June 2025 by assistant professor Dr. Sukaina Abbas at University of Baghdad/ Department of Biology Herbarium

center. Following collection, the plants underwent a thorough cleaning process, including rinsing with tap water, and were subsequently air-dried at room temperature. They were then stored in pristine conditions until they were ready for use [22].

A total of 250 g of dried plant parts underwent the steam distillation method (Clevenger apparatus) to obtain the essential oil. The plant material, along with 1.2L of distilled water, was brought to a boil and simmered for a duration of 3 hours [23]. Subsequently, the essential oil was stored at a temperature of 4 °C until it was ready for utilization. To create the stock solution, the concentrated oil extract was combined with Dimethyl sulfoxide (DMSO) and diluted. Subsequently, various concentrations (7.81, 15.62, 31.25, 62.5, 125, 250, and 500 µg/ml) were prepared by mixing specific volumes of the stock solution with specific volumes of DMSO.

2.2 Investigate the phytochemical compounds of tea tree oil using the GC-MS technique

The Chemical Analysis Center in Iraq scientific laboratories conducted Gas Chromatography-Mass (GC-MS) analysis on *Melaleuca alternifolia* essential oil using a Shimadzu gas chromatograph. The procedure for this analysis was performed in the same manner as outlined by Abd-alkadhem and Mohammed [24] in 2022.

2.3 Polymerization of tea tree oil with casein

2.3.1 Synthesis of compound Z1 (terpene-diallyl maleate adduct)

To create the Z1 compound, combine 12 ml of TTO and 4g of maleic anhydride with 40 ml of dimethylformamide (DMF) in a 250 ml four-necked flask. This flask should be equipped with an electric agitator, a thermometer, a reflux condenser, and a dropping funnel. Gently heat the mixture until the maleic anhydride melts, and then continue heating it at 145°C. Next, 0.96 g of p-toluene sulfonic acid catalyst was added to the flask. The reaction is considered complete after heating at 149°C for 2 hours. To obtain the pure terpene maleic adduct, extract the mixture with distilled water and separate the compound using a vacuum to concentrate the mixture into a powdered polymer [25].

2.3.2 Synthesis of Z2 polymer (terpene-diallyl-grafted- maleate adduct anhydride) with casein

Ten ml of Z1 polymer was added to 3.3 g of casein compound with 46 ml of DMF. Then, the mixture was refluxed for 6 hours and then re-crystallized using vacuum at 40 °C [26].

2.4 Analyses the polymerized compound using FT-IR

The Shimadzu Fourier Transform Infrared Spectrophotometer (FTIR) device was used to examine the pure crystals of acrylamide, casein, and polyvinyl alcohol polymers. These specific polymers were chosen to construct a calibration curve that illustrates the intensity (absorbance) of the vibrational modes associated with the distinctive bonds present in each polymer [27].

2.5 Identification of Anticancer Activity using Cell Line by MTT assay

In 96-well plates, a confluent Vero cell monolayer was seeded with a cell density of 4 × 104 cells/well. Following incubation at 37 °C in a 5% environment, after incubating the CO_2 incubator for 24 hours, 100 µL of each extract, which had been serially diluted in two-fold increments (ranging from 640 to 5 µg/mL), was added to the wells containing maintenance medium (DMEM with 1% FBS). In order to establish a comparison, blank medium and cells without extract treatment were also included in the same plates. The plates were then placed in a 5% CO_2 incubator and further incubated for 72 hours at a temperature of 37 °C. Following this, 20 µL of microculture tetrazolium test (MTT) solution (5 mg/mL in phosphate buffered saline (PBS)) was carefully added to each well, after which a 3-hour incubation period was

initiated in the 5% CO_2 incubator at 37 °C. Subsequently, 70% of the mixture was removed and replaced with 150 µL of dimethyl sulfoxide, which was added to the wells to dissolve the MTT formazan. The absorbance of the samples was then measured at 550 nm using a microplate reader. It is important to note that the results were obtained from three independent experiments, with each experiment being conducted in duplicate [28].

2.6 Determination of Antioxidant Activity by DPPH Free Radical Scavenging Assay

Radical scavenging activity (RSA) was measured according to [29] as follows in brief: Prepare a DPPH solution with a series of reference ascorbic acid concentrations, make a series of concentrations of the substance whose effectiveness is to be measured, add equal amounts of the violet DPPH reagent and the solution whose effectiveness is to be measured, leave the mixture in a dark environment for 30 minutes and notice the color of the violet reagent changing to yellow or transparent depending on the strength of the compound in preventing oxidation. Then the absorbance is measured with a spectrophotometer at 517 nm, and then the value of the antioxidant activity is extracted according to the equation below:

$$\mathrm{RSA}(\%) = \left[\frac{(\mathrm{Ac} - \mathrm{As})}{\mathrm{Ac}}\right] \times 100 \text{ or } \mathrm{RSA}(\%) = \left[1 - \frac{\mathrm{Ac}}{\mathrm{As}}\right] \times 100$$

Ac: control reaction absorbance.
As: testing specimen absorbance.

2.7 Statistical Analysis

The present data were programmed by SPSS v. 20.0 and GraphPad Prism v.6 statistical software. Ordinal data were detected by the Pearson-Chi-square test. Scale data showed at Mean±St. Error. The differences among means were detected by the Duncan test (ANOVA). $P \leq 0.05$ was used for the calculation.

3. Results and Discussion

3.1 GC-MS and FT-IR results

Tea tree essential oil was obtained through a Clevenger apparatus, and its active ingredient was polymerized with casein to create the TTO polymer.

The results demonstrated significant differences in the levels of active compounds found in the tea tree oil, as evidenced by Malik and Upadhyay in 2022. This study revealed the presence of the following compounds with higher percentages (4-terpineol 22.45%, cymene 14.10%, γ-terpinene 6.69%, α-pinene 5.79%, α-terpineol 3.48%, sabinene 2.54%, and α-terpinolene 2.33%), these differences in the levels of active compounds are according to the differences in the environmental factors leading to the composition of these compounds as secondary metabolites found in the tea tree oil as evidenced by Kapse *et al.,* [31] in 2024. α-Pinene was evaluated for its effectiveness against various strains of both Gram-negative and Gram-positive bacteria, revealing activity against methicillin-resistant *Staphylococcus aureus* (MRSA) with an IC50 of 68.6 ± 7.9 µg/mL [32]. Additionally, 4-terpineol has been shown to exhibit antibacterial, antioxidant, and anticancer properties, as demonstrated by Calcabrini *et al.,* who found it to be more effective against Candida species than the reference fungicide clotrimazole [33]. The presence of these compounds resulted in a decrease in the number of blastoconidia and inhibited the transition to pseudo-hyphae, which are key virulence factors of Candida [34].

The TTO polymer was prepared using what was mentioned in the material and method by mixing oil with casein compound. After completing their manufacture, a sample of the casein polymer was sent for analysis using FT-IR technology to clarify the changes in the functional groups of the oil after being reacted with the polymer.

3.1.1 FT-IR analysis of compound Z2 (terpene-diallyl-grafted- maleate adduct anhydride with casein)

This part featured the production of superimposed polymers with the initial stage of the reaction including the nucleophilic attack of the amine group in casein on the carbon of the carbonyl group in the phthalic anhydride ring. The second stage involves a (co-polymer) of chitosan, phthalic anhydride and casein, concerning the infrared spectra of the compound showed the high intensity at the range of (3450) cm-1 vibrations of hydroxyl groups, the stretching vibrations of (3332)cm-1refer to the(N-H), show bands at (2958,2873) cm-1 due to the stretching vibrations of (CH) Alph, band at (1774,1720) cm-1 medium the stretching vibrations of(C=O ester), while at (1600) cm-1 which refers to(C=O amide), (1550,1454) cm-1 which refer to the (C=C) of aromatic ring for these compound as stretching vibrations appeared at (1264) cm-1 of (C-N) and (1219) cm-1 were due to the bending vibrations of (C-O). The structural characterization was done by FT-IR, which showed a broad band at about 3329 cm-1 due to (NH) stretching. (2934, 2866) cm-1 assigned to aliphatic (CH and CH_2) stretching showed peaks at (1797) cm-1 assigned to (C=O) stretching of casein, at (1600) cm-1 assigned to characteristic absorption of (C=O) amide. On the other hand, the 1546 cm-1 peak of (C=C).

3.2. Measurement of Anticancer Activity using the Cell Line by MTT Assay

The results showed that the TTO anticancer activity increased with the concentration, reaching its optimum at 500 µg/ml. In contrast, casein polymer reached its maximum viability at a concentration of 250 µg/ml compared to the control. The present findings showed there are significant differences ($p<0.05$) among different concentrations of treatments (TTO and casein), and anticancer activity. TTO scored highest anticancer activity at doses 0, 31.25, and 62.5 µg/ml (100 ± 1.92, 92.20 ± 1.98, and 91.96 ± 1.95) and lowest anticancer activity at doses 250 and 500 µg/ml (53.6 ± 1.80 and 10.37 ± 2.86). Casein scored highest anticancer activity at doses 0, 7.81, and 31.25 µg/ml (100 ± 4.09, 89.94 ± 0.66, and 89.35 ± 3.30) and lowest anticancer activity at doses 250 µg/ml (74.09 ± 1.78).

In additionally, present study showed at 7.81 and 500 (µg/ml) casein scored highest activity (89.94 ± 0.66 and 80.80 ± 2.320), at 15.62, 31.25 and 62.5 (µg/ml) while TTO scored (88.37 ± 3.55, 92.20 ± 1.98, and 91.96 ± 1.95) at the same concentrations (Table 1 and Figures 1 and 2).

Table 1: MTT assay results of TTO and casein polymer.

Dose (µg/ml) Three replicates for each dose	TTO	Casein Polymer
	Mean ± St. error	Mean ± St. error
0	100 ± 1.92 [a] A	100 ± 4.09 [a] A
7.81	81.08 ± 4.96 [b] C	89.94 ± 0.66 [a] B
15.62	88.37 ± 3.55 [a] B	83.38 ± 2.38 [b] C
31.25	92.20 ± 1.98 [a] B	89.35 ± 3.30 [a] B
62.5	91.96 ± 1.95 [a] B	81.44 ± 2.79 [b] C
125	88.70 ± 2.67 [a] B	84.61 ± 0.759 [a] C
250	53.6 ± 1.80 [d] D	74.09 ± 1.78 [b] D
500	10.37 ± 2.86 [c] E	80.80 ± 2.320 [a] C
	E	C

Small letters show differences among treatments for each dose, and large letters show differences among doses for each treatment. Different letters refer to significant differences at $p<0.05$. The Duncan test was utilized to detect differences among means.

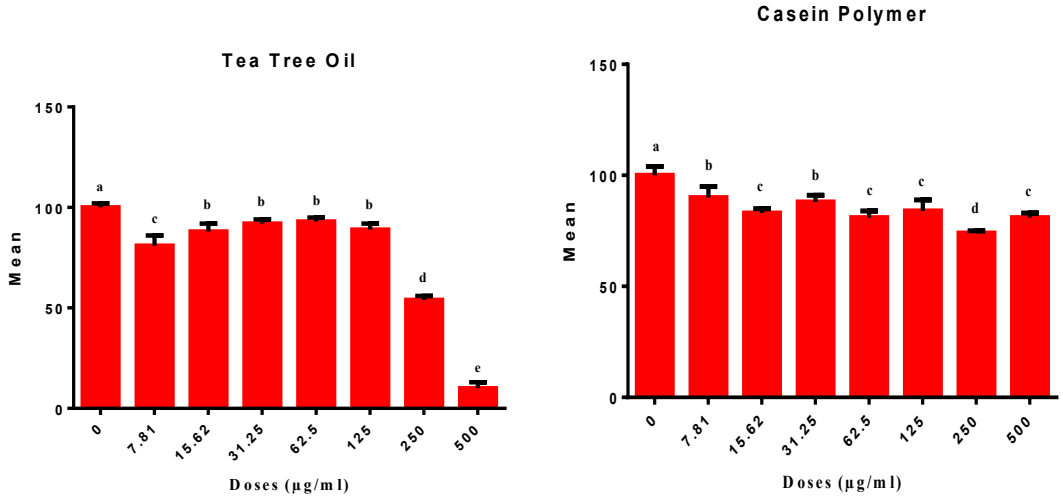
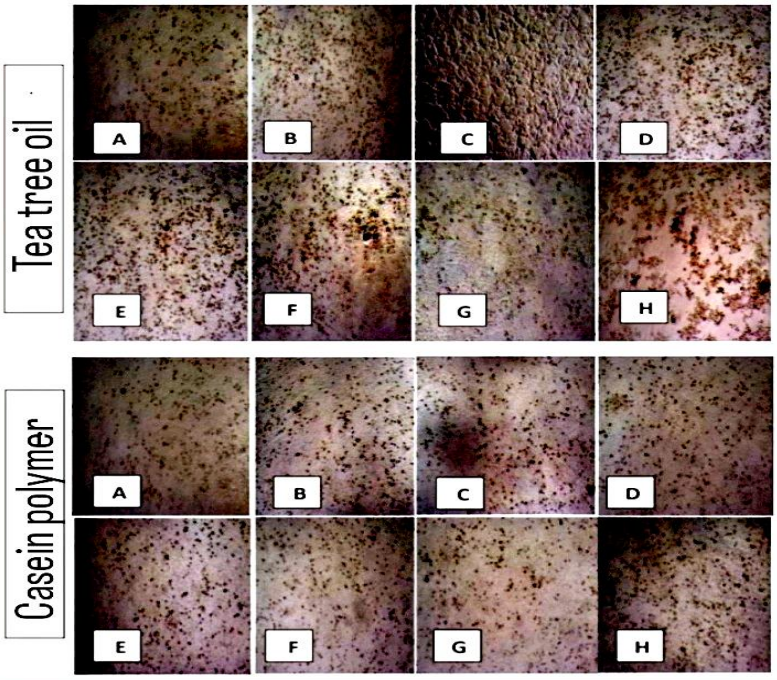


Figure 1: Anticancer activity of TTO and casein polymer



*A=ZERO, B= 7.81, C= 15.62, D= 31.25, E=62.5, F= 125, G= 250, H= 500 (µg/ml).

Figure 2: Cell viability results of TTO and casein polymer**.**

Compared with many essential oils obtained from various plants within the Myrtaceae family, for example, thyme oil and clove oil, TTO has been shown to have the strongest *in vitro* cytolytic activity against human melanomas [35]. It has also been demonstrated that TTO is the only essential oil of the seven tested that displays a significant in vitro cytotoxic activity in a panel of murine leukemia cell lines. Furthermore, *in vivo* studies suggest that TTO, when applied to skin containing excision wounds, regresses implanted murine leukemia. These observations suggest that TTO may be effective in treating large melanomas [36]. In another study, TTO has been proposed as a promising and new therapeutic compound in the prevention,

pre-exposure, and alleviation of UVA-irradiated skin carcinogenesis [37]. The beneficial effect of tea tree oil was demonstrated at different stages of the process of experimentally initiated cutaneous preneoplastic lesions becoming malignant. This observation adds to the list of previously reported beneficial properties of tea tree oil in treating other cancers and infections of the skin [38].

3.2 The Results of Antioxidant Activity Using DPPH Free Radical Scavenging Assay

As antioxidants play a vital role in human health, they are capable of inhibiting or delaying the oxidation of lipids, proteins, or DNA, playing a critical role in the prevention of serious diseases, including several types of cancer, cardiovascular diseases, neurodegenerative diseases, and diabetes, among others. Therefore, the use of antioxidants isolated from different sources has become vital [39].

As shown in Table 2 and Figure 3, the present findings showed there is significant differences ($p<0.05$) among different concentrations of treatments casein (CAS) and ascorbic acid (AA) and inhibitory activity, where it is found that CAS and AA treatments scored highest inhibitory activity at concentration of 100 (mg/ml) (34.34±11.92 and 54.08±15.89) and 80 (mg/ml) (27.15±10.92 and 38.77±12.83) and lowest inhibitory activity at concentration of 40 (mg/ml) (14.26±4.98 and 20.91±8.92) and 20 (mg/ml) (14.89±6.29 and 18.36±6.87); so these results demonstrate the efficacy of TTO and casein polymer in preventing cancer as an antioxidant and provide a reference for its future application in cancer treatment, these results agree with other studies [40, 41].

Table 2: Antioxidant levels of TTO and casein polymers by using the DPPH method.

Concentration (mg/ml) Three replicates for each concentration	**TTO Tea tree oil**	**CAS Casein polymer**	**Ascorbic acid AA**
	Mean ± St. error	Mean ± St. error	Mean ± St. error
100	26.23±7.32 ^{c} A	34.34±11.92 ^{b} A	54.08±15.89 ^{a} A
80	25.54±5.90 ^{b} A	27.15±10.92 ^{b} B	38.77±12.83 ^{a} B
60	23.90±8.43 ^{b} A	25.63±9.80 ^{b} B	31.12±14.29 ^{a} C
40	0.00±0.00	14.26±4.98 ^{b} C	20.91±8.92 ^{a} D
20	0.00±0.00	14.89±6.29 ^{b} C	18.36±6.87 ^{a} D

Small letters show differences among treatments for each concentration; large letters show differences among concentrations for each treatment. Different letters refer to significant differences at $p<0.05$. The Duncan test was utilized to detect differences among means.

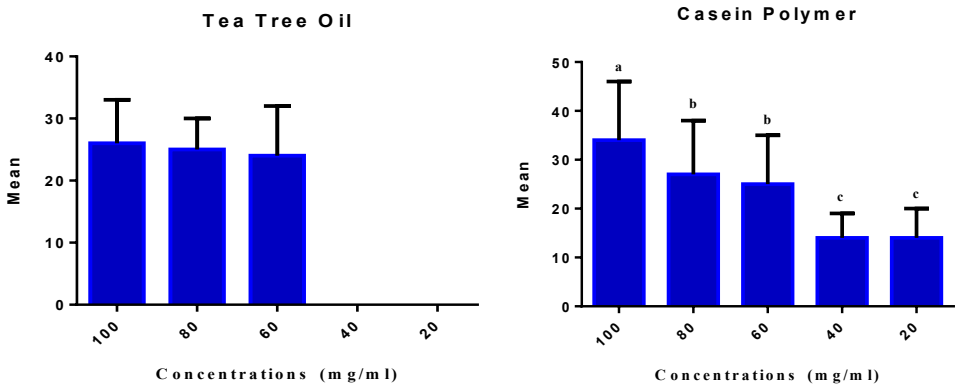


Figure 3: Antioxidant levels of TTO and casein polymer by using the DPPH method.

4. Conclusion

In conclusion, skin cancers may be prevented through public awareness and health promotion regarding the adverse effects of UV radiation and the signs of skin cancer. However, pharmacological interventions that focus on chemoprevention are needed. Tea tree oil is an essential oil that has shown numerous benefits as a topical treatment for skin diseases, including skin cancer. The essential oil appeared to work by initiating the programmed cell death process, known as apoptosis, which is a characteristic of unwanted intruders to the human skin that are subject to cell-mediated immunity or T cell killing or, in the case of carcinogenic cells, self-destruction. Moreover, tea tree oil showed cell proliferation regulation and antitumor activity. The bioactive component terpinen-4-ol was found to exhibit these properties independently of tea tree oil, supporting these observations, given its effectiveness as an antibacterial agent, it may be that tea tree oil reduces the incidence of secondary bacterial infection in skin tissue stressed by exposure to UV radiation in reasonable environmental conditions; considering the damages and risks associated with excessive sun exposure, tea tree oil has the potential to enhance the photoprotective properties of sun-care products. However, serious discussions about the inclusion of this natural essential oil in commercially available products are necessary prior to actual implementation, requiring further clinical comparative studies to investigate its efficacy and compare it to other products containing synthetic chemical UV filters. It is essential to study further and isolate the active compounds in tea tree oil, and then test them as a complementary therapy in conjunction with chemotherapy to mitigate or alleviate the side effects of these chemotherapeutic agents used in skin cancer cases.

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Disclosure and Conflict of Interest

The authors declare that they have no conflicts of interest.

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