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Antimutagenic, Antioxidant and Anti-inflammatory Evaluation of Selected Seed Oils: Potential Application for Skin Cancer Chemoprevention

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ABSTRACT

Background: Skin cancer is a major global health concern driven by ultraviolet radiation (UVR)-induced DNA damage, oxidative stress, and chronic inflammation. Targeting these interconnected processes is critical for effective chemoprevention. This study aimed to evaluate the antimutagenic, antioxidant, and anti-inflammatory potential of selected seed oils (*Citrullus lanatus, Cocos nucifera, and Vitellaria paradoxa*) and to explore their relevance in mitigating key pathways involved in skin carcinogenesis.

Methods: Seed oils were extracted using Soxhlet extraction and assessed using established in vitro assays. Antimutagenic activity was determined using the Ames test with -Ve-His-*Salmonella typhimurium*. Antioxidant capacity was evaluated via 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging, hydroxyl radical scavenging, and lipid peroxidation inhibition assays. Anti-inflammatory activity was determined by protein denaturation and proteinase inhibition assays. All experiments were conducted in triplicate, and statistical significance was determined using one-way ANOVA at $P < 0.05$.

Results: The results demonstrated significant, concentration-dependent biological activities across all oils. *Citrullus lanatus* seed oil exhibited the strongest antimutagenic effect, reducing revertant colonies to 32.0 ± 1.41(75.18% inhibition) at 2.5% compared to 130 ± 19.79 in the positive control. In antioxidant assays, *Cocos nucifera* seed oil showed the highest DPPH radical scavenging activity (73.03% at 125 µml/ml; IC_{50} = 144.1 µml/ml), while *Citrullus lanatus* oil demonstrated superior hydroxyl radical scavenging (45.65% at 125 µml/ml) and lipid peroxidation inhibition (55.58%). Anti-inflammatory assays revealed strong inhibition of protein denaturation, with *Citrullus lanatus* oil reaching 91.78% at 125 µml/ml, alongside notable proteinase inhibition (56.19%). *Vitellaria paradoxa* showed moderate but consistent activity across all assays.

Conclusion: The studied seed oils exhibit multi-targeted chemopreventive properties, acting through suppression of mutagenesis, attenuation of oxidative stress, and modulation of inflammatory responses. *Citrullus lanatus* seed oil demonstrated the most consistent and potent activity, highlighting its potential as a promising natural agent for skin cancer prevention.

Keywords: Skin carcinogenesis; Chemoprevention; *Vitellaria paradoxa*; *Cocos nucifera*; His-*Salmonella typhimurium*; *Citrullus lanatus*.

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INTRODUCTION

Cancer remains a major global health burden and a leading cause of morbidity and mortality worldwide. Recent global cancer statistics indicate a continuous rise in incidence, largely driven by population growth, aging, and increased exposure to environmental and lifestyle-related risk factors (Sung *et al*., 2021). Although significant advances have been made in cancer diagnosis and treatment, current therapeutic approaches are often limited by adverse side effects, high treatment costs, multidrug resistance, and tumor recurrence (Dagogo-Jack and Shaw, 2018; Vasan *et al*., 2019). These challenges underscore the urgent need for safer, more effective, and accessible strategies, particularly those that can prevent or delay cancer development.

Skin carcinogenesis unfolds through a complex, multistage process initiation, promotion, and progression, shaped by an interplay of environmental exposures and genetic vulnerabilities. Ultraviolet radiation (UVR) stands out as the dominant environmental trigger, driving skin cancer development through multiple converging mechanisms. At the molecular level, UVR inflicts direct DNA damage, notably the formation of cyclobutene pyrimidine dimers and other mutagenic lesions that, when left unrepaired, can set carcinogenesis in motion (Cadet and Douki, 2018). Beyond its genotoxic effects, UVR also fuels excessive reactive oxygen species (ROS) production, unleashing oxidative stress that degrades lipids, proteins, and nucleic acids (Rinnerthaler et al., 2015; Liu et al., 2023). When this oxidative burden persists, it compounds DNA damage and erodes genomic stability, creating fertile ground for malignant transformation.

Closely linked to oxidative stress is chronic inflammation, which plays a pivotal role in tumor development and progression. Inflammatory processes contribute to carcinogenesis by generating reactive species, promoting cell proliferation, and inhibiting apoptosis (Greten and Grivennikov, 2019). Prolonged inflammatory signaling has been shown to enhance mutagenesis and facilitate tumor promotion through the activation of various molecular pathways, including NF-κB and cytokine-mediated signaling cascades (Nowsheen *et al*., 2012). The interplay between DNA mutation, oxidative stress, and inflammation therefore represents a critical axis in skin carcinogenesis, providing key targets for chemopreventive interventions.

Chemoprevention encompasses the strategic use of natural or synthetic agents to interrupt, slow, or reverse carcinogenesis at any stage of its progression. Natural products have emerged as particularly compelling candidates in this space, attracting growing scientific interest for their favorable safety profiles, broad accessibility, and capacity to engage multiple molecular targets at once (Sporn, 2022). Phytochemicals — including flavonoids, phenolic acids, and vitamins — have shown remarkable antioxidant, antimutagenic, and anti-inflammatory activity, equipping them to meaningfully counteract the cellular and molecular events that drive carcinogenesis (Liu, 2020). Their protective effects operate through several coordinated mechanisms: neutralizing free radicals, bolstering the cell's own antioxidant defenses, fine-tuning detoxification enzyme activity, and dampening pro-inflammatory signaling pathways.

Plant-derived seed oils constitute an important source of these bioactive compounds and have been widely utilized for nutritional, cosmetic, and medicinal purposes. These oils are rich in unsaturated fatty acids, phytosterols, tocopherols, and phenolic compounds, all of which contribute to their biological activities (Ganesan *et al*., 2018). *Cocos nucifera* (coconut), *Vitellaria paradoxa* (shea butter), *Citrullus lanatus* (watermelon) seed oils are commonly consumed and extensively used in traditional medicine across various regions. Emerging studies have reported that these oils possess antioxidant and anti-inflammatory properties, which may contribute to their protective effects against oxidative stress-related diseases (Orsavova *et al*., 2015). However, their potential roles in modulating mutagenesis and their integrated effects on key pathways involved in skin carcinogenesis remain insufficiently explored.

Despite increasing interest in natural oils as therapeutic agents, there is still limited comprehensive evidence evaluating their combined antimutagenic, antioxidant, and anti-inflammatory effects within the framework of skin carcinogenesis. Most existing studies focus on isolated biological activities without integrating these

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interconnected mechanisms. Therefore, a systematic evaluation of these properties is necessary to better understand their chemopreventive potential.

Accordingly, this study aims to investigate the biological activities of selected seed oils (*Cocos nucifera*, *Vitellaria paradoxa*, and *Citrullus lanatus*) by assessing their antimutagenic potential using the Ames test, alongside their antioxidant and anti-inflammatory activities using established in vitro assays. By targeting key processes involved in carcinogenesis; mutation, oxidative stress, and inflammation, this study seeks to provide insights into the potential application of these oils as natural chemopreventive agents against skin cancer.

MATERIALS AND METHODS

Chemicals and Reagents

All chemicals and reagents used were of analytical grade (≥99% purity). Key reagents included DPPH, ascorbic acid, gallic acid, 2-deoxyribose, thiobarbituric acid (TBA), trichloroacetic acid (TCA), ethylenediaminetetraacetic acid (EDTA), ferric chloride ($FeCl_3$), ferrous sulfate ($FeSO_4$), hydrogen peroxide (H_2O_2), sodium dodecyl sulfate (SDS), Folin–Ciocalteu reagent, sodium hydroxide, Hydrochloric acid (HCl), Sodium carbonate (Na_2CO_3) and trypsin.

Plant Materials and Oil Extraction

Seeds of *Cocos nucifera*, *Vitellaria paradoxa*, and *Citrullus lanatus* were procured from local markets in Ogbomosho (Oyo State) and Ede (Osun State), Nigeria. The plant materials were authenticated prior to use. The seeds were cleaned, air-dried, and pulverized.

Oil extraction was carried out using Soxhlet extraction following AOAC (1998) guidelines. Briefly, 1000 g of pulverized seed material was extracted with n-hexane for 12 h. The solvent was removed using a rotary evaporator, and the extracted oil was oven-dried at 75 °C for 1 h, then stored in airtight containers at 4 °C until further analysis.

Antimutagenic Assay (Ames Test)

The antimutagenic activity of the seed oils was evaluated using the Ames test as described by Ames *et al*. (1973, 1975), employing the TA98 strain of *Salmonella typhimurium* histidine-dependent (His^-) strains.

Briefly, bacterial suspensions were prepared in phosphate buffer and exposed to a known mutagen (2-aminofluorene) in the presence or absence of varying concentrations of the oil samples. A small amount of histidine was included to allow initial bacterial growth. Two control suspension of His-ve *Salmonella typhimurium* was also prepared, with histidine (positive control) and without histidine (negative control). The mixtures were incubated at 37 °C for 20 min, plated on agar, and further incubated at 37 °C for 48 h. Revertant colonies were counted, and antimutagenic activity was expressed as percentage inhibition relative to the positive control.

Antioxidant Assays

DPPH Radical Scavenging Assay: The free radical scavenging activity of the oil samples was evaluated using the stable 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical, a widely employed model for assessing the hydrogen atom or electron donation capacity of antioxidant compounds (Brand-Williams et al., 1995). The principle of this assay is based on the reduction of the purple-colored DPPH radical to a yellow-colored DPPH-H molecule in the presence of a hydrogen-donating antioxidant, with the degree of discoloration reflecting the radical scavenging potential of the test sample. Absorbance was measured at 518 nm, and radical scavenging activity was expressed as percentage inhibition, calculated as:

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$$\% \text{ Inhibition} = [(A \text{ control} - A \text{ test}) / A \text{ control}] \times 100$$

Hydroxyl radical scavenging activity was assessed by the 2-deoxyribose degradation method, which exploits the ability of hydroxyl radicals — generated through the Fenton reaction — to oxidatively degrade 2-deoxyribose into malondialdehyde-like fragments that condense with thiobarbituric acid (TBA) to yield a pink chromogen measurable at 532 nm (Halliwell et al., 1987). The underlying principle relies on the capacity of antioxidant compounds to compete with 2-deoxyribose for the generated hydroxyl radicals, thereby attenuating chromogen formation. Percentage inhibition was calculated as:

$$\% \text{ Inhibition} = [(A \text{ control} - A \text{ test}) / A \text{ control}] \times 100$$

The inhibition of lipid peroxidation was determined using the thiobarbituric acid reactive substances (TBARS) method, with egg yolk serving as the lipid-rich substrate (Ruberto et al., 2000). The assay is based on the principle that Fe^{2+}-induced oxidation of polyunsaturated fatty acids generates malondialdehyde (MDA) and other reactive aldehydes, which react with TBA under acidic and high-temperature conditions to produce a pink-colored MDA–TBA adduct quantifiable at 532 nm. The extent to which test samples suppress this chromogen formation serves as an index of their lipid peroxidation inhibitory capacity, and percentage inhibition was calculated relative to the control using the formula described above.

Anti-inflammatory Activity

The anti-inflammatory potential of the oil samples was evaluated through inhibition of heat-induced protein denaturation and proteinase activity, both of which are well-established in vitro surrogates for inflammation-associated molecular events (Mizushima and Kobayashi, 1968). The protein denaturation assay is grounded in the principle that denaturation of endogenous proteins is a hallmark of inflammation, and agents capable of preventing this process may exert meaningful anti-inflammatory effects in vivo. Using egg albumin as the model protein, heat-induced turbidity was measured at 660 nm, and the percentage inhibition of denaturation was calculated as:

$$\% \text{ Inhibition} = [(A \text{ control} - A \text{ test}) / A \text{ control}] \times 100$$

The proteinase inhibition assay was employed to further characterize the anti-inflammatory activity of the samples, based on the principle that proteolytic enzymes such as trypsin contribute to tissue damage and inflammatory cascades by degrading structural proteins and activating pro-inflammatory mediators (Oyedapo and Famurewa, 1995). The capacity of the oil samples to inhibit trypsin-mediated proteolysis was quantified spectrophotometrically at 660 nm following treatment with Folin–Ciocalteu reagent, and percentage inhibition was determined relative to a control prepared without the test sample, using the formula described above.

Statistical Analysis

All experiments were performed in triplicate, and results were expressed as mean ± standard deviation. Statistical analysis was conducted using one-way analysis of variance (ANOVA) by GraphPad Prism software (version 9; GraphPad Software Inc., California, USA), with significance set at $P < 0.05$.

RESULTS

The antimutagenic, antioxidant, and anti-inflammatory activities of the selected seed oils are presented below. All oils were pale yellow and remained liquid at room temperature. The biological activities of *Citrullus lanatus, Cocos nucifera, and Vitellaria paradoxa* oils were evaluated using the Ames test, DPPH radical scavenging assay, hydroxyl radical scavenging assay, lipid peroxidation inhibition assay, protein denaturation assay, and proteinase inhibition assay.

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Antimutagenic effects of selected seed oils

Table 1: Colony count for -Ve His-*Salmonella typhimurium* growth in the presence of selected seed oils

Concentration (µl/ml)	*Cocos nucifera* oil	*Vitellaria paradoxa* oil	*Citrullus lanatus* seed oil	+C	-C
2.5%	42.5±9.89	78±12.72	32±1.41		
5.0%	49±9.89	78.5±7.78	57±21.21	130±19.79	15.5±0.71
7.5%	78±4.24	146.5±12.02	66.5±14.85		
10.0%	93.5±7.78	159.5±14.85	75±5.66		

Table 2: Percentage Inhibition of -Ve His-*Salmonella typhimurium* growth by selected seed oils

Concentration (µl/ml)	*Cocos nucifera*oil (%Inhibition)	*Vitellaria paradoxa* oil (%Inhibition)	*Citrullus lanatus* seed oil (%Inhibition)
2.5%	67.9 ± 1.36	40.05 ± 0.33	75.18 ± 1.35
5.0%	62.45 ± 0.95	39.37 ± 1.63	56.90 ± 4.88
7.5%	39.55 ± 2.97	-	47.37 ± 9.72
10.0%	26.77 ± 0.57	-	41.30 ± 6.65

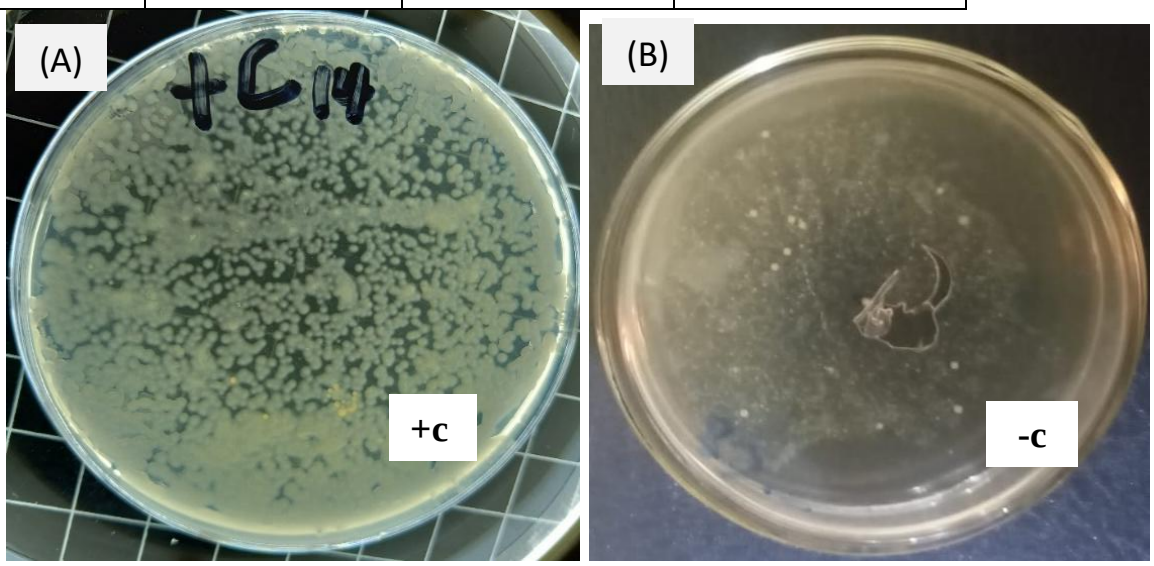

Plate 1: Anti-mutagenic test control plates (Ames test**). (**A) Positive control: contains *S. typhimurim*, histidine and all test reagents without sample
(B) Negative control: contains *S. typhimurim*, and all test reagents without histidine and sample

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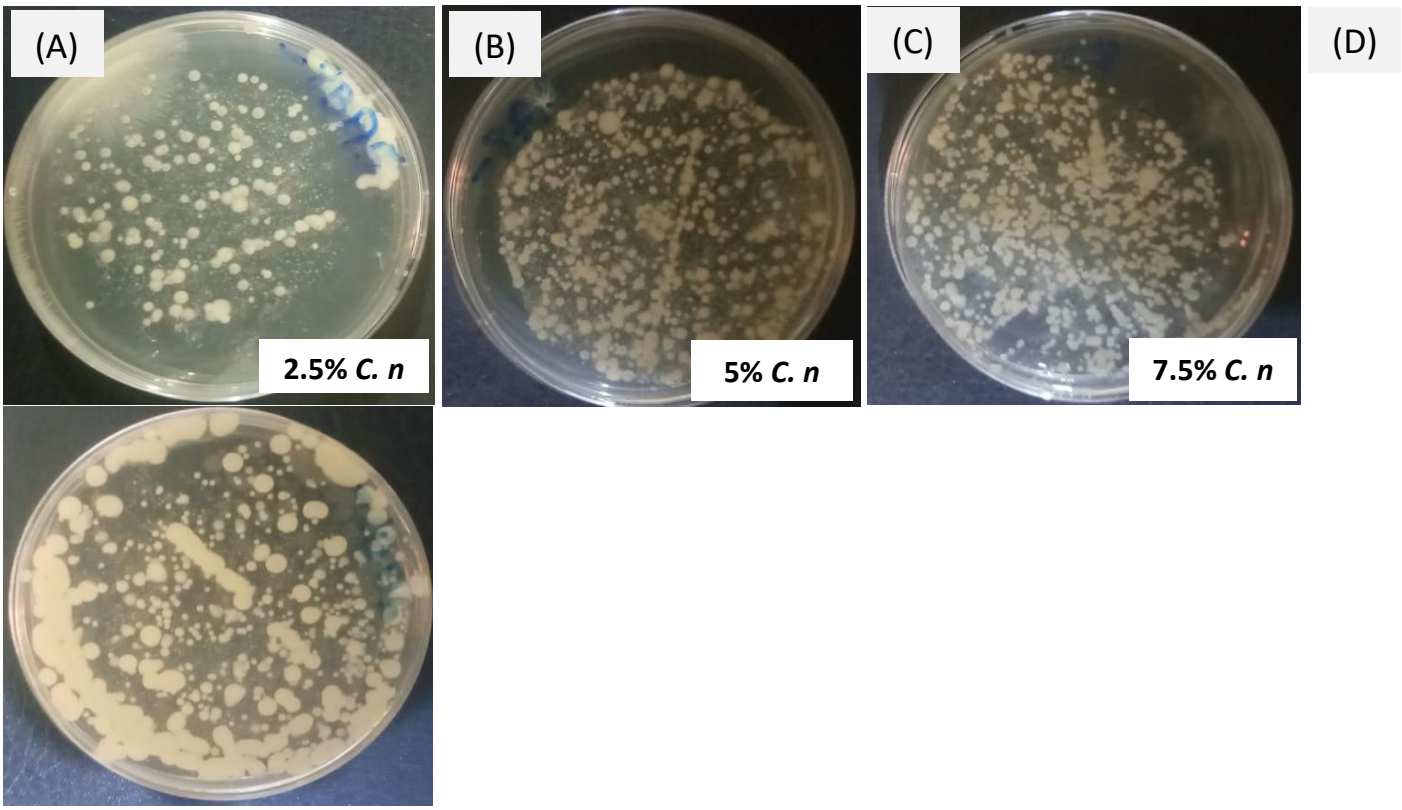

Plate 2 Anti-mutagenic effect of *Cocos nucifera* oil against -Ve His-*Salmonella typhimurim* (A) 2.5% (B) 5% (C) 7.5% (D) 10%

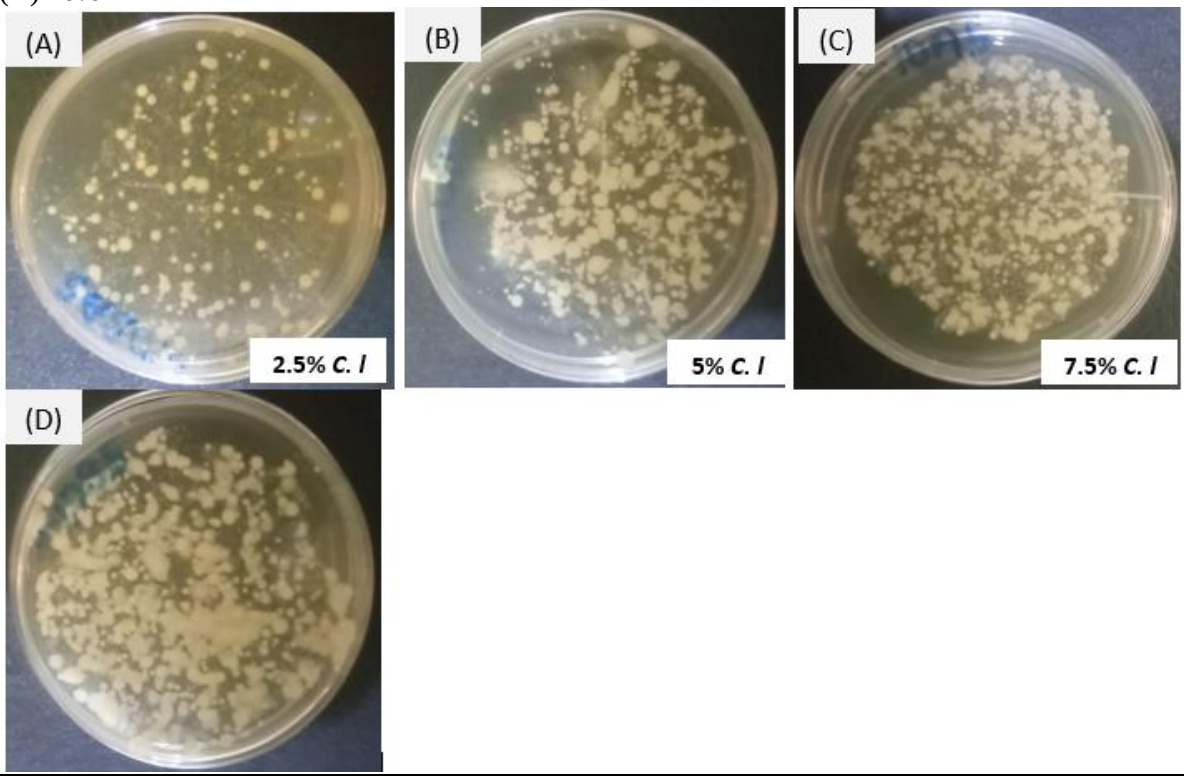

Plate 3: Anti-mutagenic effect of *Citrullus lanatus* seed oil against -Ve His-*Salmonella typhimurim.* (A) 2.5% (B) 5% (C) 7.5% (D) 10%

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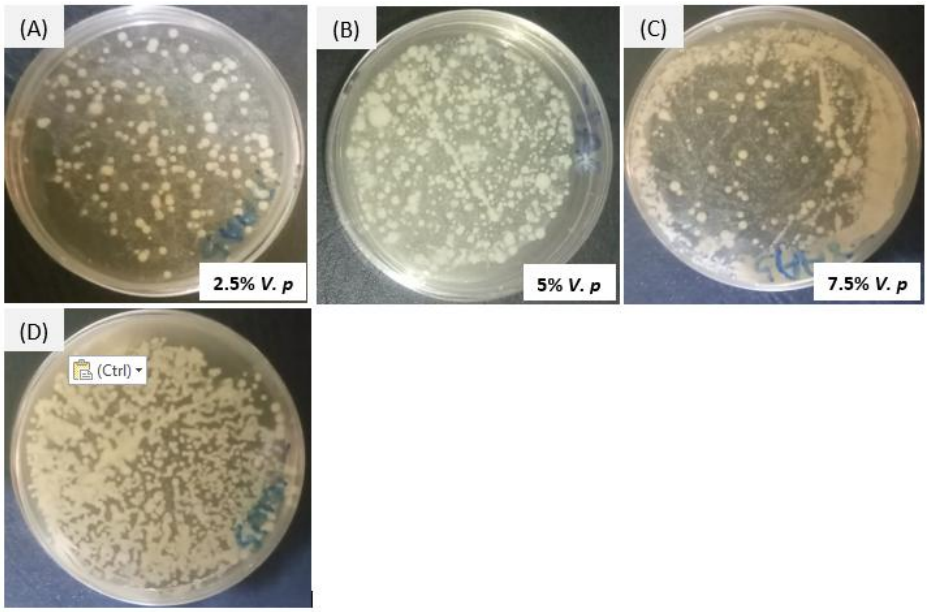

Plate 4: Anti-mutagenic effect of *Vitellaria paradoxa* oil against -Ve His-S*almonella typhimurim* (A) 2.5% (B) 5% (C) 7.5% (D) 10%

Result of Antioxidant Capacity of Selected Seed Oils

The radicals scavenging capacity of selected seed oils against DPPH and OH radicals are presented as percentage inhibition.

Percentage Inhibition of DPPH Radical Scavenging Activities.

The DPPH radical scavenging activities of the selected seed oils are presented in Table 3. All oils demonstrated concentration-dependent increases in radical scavenging activity across the tested range (25–125 µl/ml). At the highest concentration (125 µl/ml), *Cocos nucifera* oil exhibited the strongest activity (73.03%), followed by *Vitellaria paradoxa* (58.60%) and *Citrullus lanatus* (53.35%). The corresponding IC_{50} values further confirmed this trend, with *Cocos nucifera* showing the lowest IC_{50} (144.1 µl/ml), indicating higher antioxidant potency.

Table 3: Percentage Inhibition of DPPH Radical Scavenging Activities

Percentage Inhibition of DPPH radical scavenging activity			
Concentrations (µl/ml)	*Citrullus lanatus* seeds oil (%Inhibition)	*Cocos nucifera* oil (%Inhibition)	*Vitellaria paradoxa* oil (%Inhibition)
25	$26.77^{a} \pm 2.74$	$45.67^{a} \pm 1.61$	$41.39^{a} \pm 5.73$
50	$29.85^{a} \pm 1.94$	$57.62^{b} \pm 2.07$	$49.11^{a} \pm 3.38$
75	$41.04^{b} \pm 0.04$	$64.95^{c} \pm 2.49$	$50.29^{a} \pm 0.87$
100	$46.45^{b} \pm 3.16$	$71.09^{d} \pm 1.32$	$58.37^{b} \pm 2.55$
125	$53.35^{c} \pm 2.20$	$73.03^{d} \pm 1.38$	$58.60^{b} \pm 1.79$

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Percentage Inhibition of Hydroxyl (OH) -Radicals Scavenging Effects of Selected Seed Oil.

Hydroxyl radicals scavenging effect of selected oils (*Citrullus lanatus* seeds oil, *Cocos nucifera* oil, and *Vitellaria paradoxa* oil) are illustrated in Table 4 with comparison to a standard (gallic acid). The concentrations of the oils tested ranges from 25-125 µl/ml against hydroxyl radical.

The results revealed that all three oils exerted dose-dependent scavenging ability against hydroxyl radical, and at 125 µl/ml, all three oils have the highest inhibitory effect. *Citrullus lanatus* seed oil at 125 µl/ml showed a 45.65% inhibition while *Cocos nucifera* oil and *Vitellaria paradoxa* at 125 µl/ml oil had 43.18% and 35.04% inhibitory effects against. the standard utilized, Gallic acid showed better inhibitory effects against OH- radicals, with 88.24% inhibition recorded at 125 µl/ml concentration.

Table 4: Percentage Inhibition of OH-Radicals Scavenging Effects of Selected Seed Oil

	Percentage Inhibition of OH-radicals scavenging activity			
Concentrations (µl/ml)	Standard (Gallic acid) (%Inhibition)	*Citrullus lanatus* seeds oil (%Inhibition)	*Cocos nucifera* oil (%Inhibition)	*Vitellaria paradoxa* oil (%Inhibition)
25	$32.22^{a} \pm 1.92$	$25.39^{a} \pm 0.76$	$11.18^{a} \pm 0.41$	$8.19^{a} \pm 0.50$
50	$42.74^{b} \pm 1.50$	$28.97^{a} \pm 4.36$	$17.93^{b} \pm 0.54$	$15.48^{a} \pm 6.25$
75	$68.76^{c} \pm 1.37$	$33.31^{b} \pm 5.72$	$34.30^{c} \pm 2.52$	$33.63^{b} \pm 1.75$
100	$77.74^{d} \pm 1.37$	$44.05^{c} \pm 0.57$	$38.71^{c} \pm 3.32$	$33.50^{b} \pm 2.73$
125	$88.24^{e} \pm 0.85$	$45.65^{c} \pm 4.72$	$43.19^{d} \pm 3.19$	$35.04^{b} \pm 1.19$

Percentage Inhibition of Protein Denaturation by Selected Oils

The percentage inhibition in protein denaturation using egg albumin by the selected oil samples are displayed in Table 5. The result shows significant inhibition protein denaturation by all three oils. At all concentrations tested (25-125 µl/ml), above 50 % inhibitions were recorded.

The highest concentration tested (125 µl/ml) had the highest inhibitory effect, with *Citrullus lanatus* seed oil (91.78%), *Cocos nucifera* oil (66.78%), and *Vitellaria paradoxa* (65.05%) recording excellent inhibition of protein denaturation activities. The regression curve analyses revealed an IC_{50} of 16.6 µl/ml, 7.84 µl/ml, 1.85 µl/ml for *Citrullus lanatus* seed oil, *Cocos nucifera* oil and *Vitellaria paradoxa* oil respectively.

Table 5: Percentage Inhibition of Protein Denaturation by Selected Oils

Percentage Inhibition of Protein Denaturation by Selected Oils			
Concentrations (µl/ml)	*Citrullus lanatus* seeds oil (%Inhibition)	*Cocos nucifera* oil (%Inhibition)	*Vitellaria paradoxa* oil (%Inhibition)
25	$62.38^{a} \pm 0.06$	$58.82^{a} \pm 0.68$	$60.10^{a} \pm 1.50$
50	$72.08^{b} \pm 1.36$	$59.89^{a} \pm 1.29$	$60.76^{a} \pm 1.69$
75	$79.99^{c} \pm 3.19$	$65.45^{b} \pm 0.79$	$64.39^{b} \pm 0.26$

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100	$89.33^{d} \pm 1.41$	$64.79^{b} \pm 0.61$	$64.84^{b} \pm 0.28$
125	$91.78^{d} \pm 1.06$	$66.78^{b} \pm 0.73$	$65.05^{b} \pm 0.07$

Percentage Inhibition of Lipid Peroxidation by Selected Oils

The results for the percentage inhibition of lipid peroxidation (Table 6) revealed excellent inhibition of egg yolk homogenate by all three oil samples at the concentrations assessed (25-125 µl/ml). *Citrullus lanatus* seed oils had the best inhibitory effect with 125 µl/ml showing a 55% inhibition of fe^{2+}-induced lipid peroxidation using egg York homogenate was recorded. *Cocos nucifera* oil and *Vitellaria paradoxa* oil showed significant dose-dependent inhibitory effects against fe^{2+}-induced lipid peroxidation with the highest concentration, 125 µl/ml, having a 53.05% and 53.52% inhibition respectively. The regression analyses revealed an IC_{50} value of 41.23 µl/ml, 109.8 µl/ml, 112.46 µl/ml respectively.

Table 6: Percentage Inhibition of Lipid Peroxidation by Selected Oils

Percentage Inhibition of Lipid Peroxidation by Selected Oils			
Concentrations (µl/ml)	*Citrullus lanatus* seeds oil (%Inhibition)	*Cocos nucifera* oil (%Inhibition)	*Vitellaria paradoxa* oil (%Inhibition)
25	$42.53^{a} \pm 0.39$	$24.77^{a} \pm 1.18$	$39.56^{a} \pm 1.07$
50	$52.69^{b} \pm 0.57$	$29.03^{b} \pm 1.14$	$40.32^{a} \pm 0.68$
75	$54.59^{b} \pm 0.48$	$33.23^{c} \pm 1.03$	$44.03^{b} \pm 0.77$
100	$55.28^{b} \pm 0.74$	$46.16^{d} \pm 0.87$	$47.03^{c} \pm 0.58$
125	$55.58^{b} \pm 0.53$	$53.05^{e} \pm 3.45$	$53.51^{d} \pm 1.38$

Percentage Inhibition of Proteinase Activity

The percentage inhibition of proteinase activity by selected oils are displayed in Table 7. The results show concentration-dependent inhibition of proteinase activity by all three oils. The highest concentration tested (125 µl/ml) had the highest inhibitory effect, with *Citrullus lanatus* seed oil 56%, *Cocos nucifera* oil 53%, and *Vitellaria paradoxa* 50% recording excellent inhibition of proteinase activity (above 50%) respectively. The regression curve analyses revealed an IC_{50} of 112.4 µl/ml, 117.32 µl/ml, 124.09 µl/ml for *Citrullus lanatus* seed oil, *Cocos nucifera* oil and *Vitellaria paradoxa* oil respectively.

Table 7: Percentage Inhibition of Proteinase Activity

Percentage Inhibition of Proteinase Activities by Selected Oils			
Concentrations (µl/ml)	*Citrullus lanatus* seeds oil (%Inhibition)	*Cocos nucifera* oil (%Inhibition)	*Vitellaria paradoxa* oil (%Inhibition)
25	$21.64^{a} \pm 0.78$	$17.87^{a} \pm 0.82$	$16.65^{a} \pm 1.05$
50	$26.54^{b} \pm 0.39$	$23.98^{b} \pm 0.07$	$24.23^{b} \pm 1.91$

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75	$30.91^{c} \pm 0.17$	$35.50^{c} \pm 1.87$	$33.03^{c} \pm 1.05$
100	$43.75^{d} \pm 0.67$	$43.22^{d} \pm 1.37$	$37.87^{d} \pm 1.14$
125	$56.19^{e} \pm 0.43$	$53.61^{e} \pm 1.10$	$50.34^{e} \pm 1.58$

DISCUSSION

Skin cancer remains one of the most prevalent malignancies worldwide, with its development strongly associated with cumulative ultraviolet radiation (UVR) exposure and environmental stressors. Globally, its burden continues to rise, as highlighted by recent cancer statistics (Sung *et al*., 2021; Ferlay *et al*., 2021). UVR contributes to carcinogenesis primarily through direct DNA damage and the generation of reactive oxygen species (ROS), which induce oxidative stress and activate pro-inflammatory signaling pathways (Cadet and Douki, 2018; Rinnerthaler *et al*., 2015; Liu *et al*., 2023). These processes; DNA mutation, oxidative stress, and chronic inflammation, are central to tumor initiation and progression (Greten and Grivennikov, 2019; Jomová *et al*., 2023). Notably, these mechanisms directly correspond to the biological endpoints evaluated in this study: mutagenicity (Ames test), oxidative stress (DPPH, hydroxyl radical scavenging, and lipid peroxidation), and inflammation (protein denaturation and proteinase inhibition). Thus, the integrated experimental approach employed here provides a mechanistic framework for assessing the chemopreventive potential of the selected seed oils against skin carcinogenesis.

The growing interest in plant-derived compounds for cancer prevention is driven by their structural diversity and multi-targeted biological activities. Natural products have historically played a central role in drug discovery and continue to offer promising therapeutic candidates with relatively low toxicity profiles (Atanasov *et al*., 2021). In particular, plant oils contain bioactive constituents such as phenolics, flavonoids, tocopherols, and unsaturated fatty acids, which are known to modulate oxidative stress and inflammatory pathways (Shahidi and Ambigaipalan, 2015). These properties make them especially relevant for dermatological applications, where topical or dietary interventions can directly influence skin physiology and protection.

The antimutagenic activity observed in this study, particularly in *Citrullus lanatus* seed oil, indicates a strong capacity to inhibit mutagen-induced genetic alterations. The Ames test remains a gold standard for evaluating mutagenicity and ant-imutagenicity, as it detects mutation events in *Salmonella typhimurium* strains (Mortelmans and Zeiger, 2000). The TA98 histidine dependent strain was utilized and the reduction in revertant colony formation suggests that the tested oils may interfere with mutagen activation or directly scavenge reactive intermediates responsible for DNA damage. This is consistent with previous findings that plant-derived phenolics and flavonoids can protect against genotoxicity by enhancing antioxidant defences and preventing DNA adduct formation (Shahidi and Ambigaipalan, 2015; Singh *et al*., 2023). The enhanced activity observed at lower concentrations may be attributed to improved solubility and interaction of bioactive compounds, a phenomenon previously associated with solvent-mediated bioavailability effects.

The antioxidant capacity of the selected oils, as demonstrated by DPPH and hydroxyl radical scavenging assays, further supports their protective role against oxidative stress. The concentration-dependent increase in radical scavenging activity aligns with established antioxidant mechanisms involving hydrogen atom donation and electron transfer (Brand-Williams *et al*., 1995). Among the oils, *Cocos nucifera* exhibited the highest DPPH scavenging activity, which may be attributed to its phenolic composition and synergistic interactions between its constituents (Marina *et al*., 2009). The hydroxyl radical scavenging activity observed is particularly significant, as hydroxyl radicals are highly reactive species capable of inducing severe DNA damage and mutagenesis (Liu *et al*., 2023). These findings highlight the ability of the oils to mitigate ROS-mediated cellular damage, a key factor in UV-induced skin carcinogenesis (Rinnerthaler *et al*., 2015; Jomová *et al*., 2023).

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Lipid peroxidation is another critical consequence of oxidative stress, leading to the formation of reactive aldehydes such as malondialdehyde (MDA), which can further damage DNA and proteins. The significant inhibition of Fe^{2+}-induced lipid peroxidation observed in this study indicates that the oils can effectively protect cellular membranes from oxidative degradation. This finding is consistent with established mechanisms of lipid oxidation and its role in disease progression (Ayala *et al*., 2014). The relatively higher inhibition observed in *Citrullus lanatus* oil may be attributed to its composition of polyunsaturated fatty acids and antioxidant phytochemicals, which act synergistically to stabilize membrane lipids and reduce oxidative damage.

The anti-inflammatory properties of the oils, demonstrated through protein denaturation and proteinase inhibition assays, further strengthen their chemopreventive potential. Protein denaturation is commonly associated with inflammatory conditions, and its inhibition suggests the ability of these oils to stabilize protein structures under stress. Chronic inflammation is a well-established driver of carcinogenesis, contributing to tumor promotion, angiogenesis, and metastasis (Greten and Grivennikov, 2019). The inhibition of proteinase activity observed in this study is also significant, as proteolytic enzymes play a role in tissue degradation and cancer progression. These findings suggest that the oils may modulate key inflammatory pathways involved in tumor development.

Prior *in-silico* work by Adebayo *et al.*, 2026, profiled the phytochemical composition of *Cocos nucifera*, *Vitellaria paradoxa*, and *Citrullus lanatus* seed oils using GC-FID and HPLC, identifying 45 bioactive compounds. Molecular docking against Human Dihydroorotase, a key enzyme in de novo pyrimidine biosynthesis, revealed seven lead compounds including apigenin, β-sitosterol, and ferulic acid with binding affinities (−7.3 to −8.0 kcal/mol) exceeding that of 5-fluorouracil (−6.0 kcal/mol). This computational evidence of enzyme-targeted anticancer potential provides mechanistic rationale for the present investigation into these oils' antioxidant, anti-inflammatory, and antimutagenic chemopreventive properties.

Collectively, the results of this study demonstrate that the selected seed oils possess multi-functional biological activities that target key pathways involved in carcinogenesis. By simultaneously inhibiting mutagenesis, reducing oxidative stress, and suppressing inflammation, these oils may interfere with multiple stages of cancer development, including initiation, promotion, and progression. Such multi-targeted activity is particularly advantageous in chemoprevention, given the complex and multifactorial nature of cancer biology (Atanasov *et al*., 2021).

From a biomedical perspective, these findings suggest that the studied oils may have potential applications in skin cancer prevention and management. Their antioxidant, anti-inflammatory and *in-silico* properties make them promising candidates for incorporation into topical formulations aimed at protecting against UV-induced skin damage. (Pinto *et al*., 2023).

CONCLUSION

This study provides compelling evidence that selected seed oils; *Citrullus lanatus*, *Cocos nucifera*, and *Vitellaria paradoxa*, possess significant antimutagenic, antioxidant, and anti-inflammatory activities, underscoring their potential as multi-functional agents in cancer chemoprevention. By demonstrating the ability to suppress mutagen-induced genetic alterations, neutralize reactive oxygen species, inhibit lipid peroxidation, and modulate inflammatory processes, these oils effectively target the key molecular pathways implicated in the initiation and progression of carcinogenesis.

Importantly, the integration of these biological effects highlights a coordinated mechanism through which these natural products may confer protection against skin cancer. Given that ultraviolet radiation–induced carcinogenesis is driven by oxidative stress, DNA damage, and chronic inflammation, the observed activities of the studied oils position them as promising candidates for mitigating these pathological processes. Among the

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oils investigated, *Citrullus lanatus* seed oil consistently exhibited superior or comparable efficacy across multiple assays, suggesting a particularly strong chemopreventive potential that warrants further exploration.

Beyond their mechanistic relevance, these findings carry broader biomedical significance. The growing demand for safe, accessible, and cost-effective alternatives to conventional therapeutic agents has intensified interest in plant-derived compounds. In this context, the studied oils offer a compelling advantage due to their natural origin, bioavailability, and potential for topical and dietary application. Their incorporation into dermatological formulations or preventive health strategies may represent a viable approach to reducing the burden of skin cancer, particularly in regions with high ultraviolet exposure.

In conclusion, this study advances the growing body of evidence supporting the role of plant-derived oils as potent, multi-targeted agents in cancer prevention. By addressing the fundamental processes underlying skin carcinogenesis, these oils not only reinforce the therapeutic value of natural products but also open new avenues for the development of innovative, integrative strategies in cancer prevention and skin health management.

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