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Phytochemical Study and Evaluation of Toxicity and Antioxidant Properties of *Allium ascalonicum* Leaf Extracts on Cell Line HepG2

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Abstract:

Allium ascalonicum, a leafy vegetable belonging to the Liliaceae family, is widely cultivated and consumed in several West African countries, including Ghana, Benin, and Nigeria. The leaves of this plant are utilized both as a fresh salad ingredient and as a cooked component in sauces. In addition to its culinary uses, *Allium ascalonicum* is traditionally consumed in concoctions for managing various health conditions, including diabetes and hypertension. While numerous global studies have explored the medicinal properties of this plant, there is a notable lack of research specifically addressing its therapeutic potential within Nigeria. This study investigates the phytochemical composition, antioxidant activities, and cytotoxic properties of *Allium ascalonicum* leaf extracts, with a focus on methanol and aqueous preparations. Phytochemical analysis identified key bioactive constituents such as phenolics, flavonoids, alkaloids, and tannins, with the methanol extract demonstrating higher concentrations of phenolics (82.4 mg GAE/g) and flavonoids (54.7 mg QE/g) compared to the aqueous extract. Antioxidant efficacy was evaluated using 2,2-diphenyl-1-picrylhydrazyl (DPPH), ferric reducing antioxidant power (FRAP) assay, and total antioxidant capacity (TAC) assays, wherein the methanol extract exhibited superior performance. The methanol extract showed a lower 2,2-diphenyl-1-picrylhydrazyl (DPPH) IC_{50} value (42.8 µg/mL) and a higher FRAP value (310.5 µM ascorbic acid equivalents), indicating robust free radical scavenging and reducing capabilities. Cytotoxicity was assessed against HepG2 liver cancer cells, revealing an IC_{50} of 72.4 µg/mL for the methanol extract, indicative of significant anticancer potential. Conversely, the aqueous extract demonstrated comparatively lower cytotoxicity, with an IC_{50} value of 145.6 µg/mL. These findings underscore the potential of *Allium ascalonicum* leaf extracts, particularly the methanol preparation, as a promising natural source of antioxidants and anticancer agents. Further research is warranted to elucidate the molecular mechanisms underpinning these bioactivities and to evaluate the plant's potential applications in pharmaceutical and therapeutic contexts.

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INTRODUCTION

For decades, medicinal plants have served as an invaluable foundation for drug discovery, offering a vast array of bioactive compounds with significant therapeutic potential. Among these, *Allium ascalonicum* (commonly known as shallot) has garnered attention due to its phytochemical richness, including flavonoids, phenolics, and sulfur-containing compounds [1]. Widely utilized in both culinary and traditional medicinal practices, *A. ascalonicum* demonstrates a broad spectrum of pharmacological activities, such as antimicrobial, anti-inflammatory, and antioxidant properties, which have piqued the interest of researchers globally [2].

Oxidative stress, a condition arising from an imbalance between the generation of reactive oxygen species (ROS) and the body's antioxidant defenses, plays a pivotal role in the etiology of numerous chronic diseases, including cancer, cardiovascular disorders, and neurodegenerative diseases [3]. Natural antioxidants derived from plant sources have emerged as safer and more effective alternatives to synthetic counterparts, which are often associated with adverse effects. As such, the assessment of antioxidant properties in plant extracts has become a critical focus area in the field of natural product pharmacology.

In parallel, advancements in cancer therapy have increasingly emphasized the exploration of natural products with selective cytotoxicity against cancer cells. The HepG2 cell line, derived from human liver cancer, has been extensively used as a robust model for evaluating the cytotoxic effects and underlying mechanisms of action of plant-derived compounds. Research has highlighted that phytochemicals, including phenolic acids, flavonoids, and sulfur-containing compounds, can induce apoptosis, inhibit cellular proliferation, and regulate oxidative stress, signaling pathways, and cell cycle progression in cancer cells [4].

Despite the documented traditional and pharmacological relevance of *A. ascalonicum*, comprehensive phytochemical profiling and biological evaluations of its leaf extracts remain scarce. This study seeks to address this gap by investigating the phytochemical composition of *A. ascalonicum* leaf extracts and evaluating their antioxidant properties and cytotoxic effects on HepG2 cell lines. By elucidating these bioactivities, this research aims to advance the understanding of the therapeutic potential of *A. ascalonicum* and its viability as a natural source of bioactive compounds for future pharmaceutical development.

MATERIALS AND METHODS

Plant Material

Fresh leaves of *Allium ascalonicum* were collected from a local market in (mandate) Ilorin, Nigeria, and identified at the Department of Botany, University of Ilorin, and assigned the voucher number ULH/1335/2024

Ethical Approval

The study protocol was approved by the Institutional Ethical Committee of Al-Hikmah University, Ilorin, Nigeria, under the reference number HUI/REC/FHS/2024/25

Cell Lines

HepG2 (Human hepatocellular carcinoma) cell line was obtained from [Institution or Supplier].

Collection, Preparation and Plant Extracts

Fresh *Allium ascalonicum* leaves were carefully harvested, thoroughly cleaned, and air-dried at room temperature for one week. Once dried, the leaves were finely powdered using a mechanical grinder to ensure uniformity for subsequent extraction processes. The powdered leaves were then subjected to two extraction methods. For the methanol extract, the powdered leaves were macerated in methanol for 72 hours at room temperature with intermittent agitation to enhance the extraction process. The mixture was filtered through Whatman No. 1 filter paper, and the solvent was evaporated under reduced pressure using a rotary evaporator, yielding the methanol extract in a semi-solid form. For the aqueous extract, the powdered leaves were boiled in distilled water for 30 minutes to extract water-soluble phytochemicals. The boiled mixture was filtered to remove solid particles, and the filtrate was concentrated by evaporating the water under reduced pressure, resulting in the aqueous extract.

Phytochemical Screening

The phytochemical analysis of both methanol and aqueous extracts was performed to identify the presence of bioactive compounds [5]. The following

tests were conducted: alkaloids, tannins. Flavonoids, phenolic and saponins.

Antioxidant Assays

DPPH (2,2-Diphenyl-1-picrylhydrazyl) Radical Scavenging Activity

The antioxidant activity of the extracts was measured using the DPPH assay. A 100 µL of the extract (at various concentrations) was mixed with 3 mL of 0.004% DPPH solution. The mixture was incubated in the dark for 30 minutes, and the absorbance was measured at 517 nm [6].

FRAP (Ferric Reducing Antioxidant Power)

The FRAP assay was performed by mixing 1 mL of the extract with 3 mL of the FRAP reagent. The absorbance was measured at 593 nm, and the antioxidant power was expressed as µM equivalents of ascorbic acid [6].

TAC (Total Antioxidant Capacity)

The total antioxidant capacity was determined using the phosphomolybdenum assay, where the extract was added to a reagent containing ammonium molybdate, and the absorbance was measured at 695 nm [6].

Cytotoxicity Assay

Cell Culture

HepG2 cells were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS), 100 U/mL penicillin, and 100 µg/mL streptomycin. The cells were incubated at 37°C in a 5% CO_2 incubator [7].

MTT Assay (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) Assay

HepG2 cells (1×10^4 cells/well) were seeded in 96-well plates and allowed to adhere for 24 hours. After treatment with various concentrations of *Allium ascalonicum* leaf extracts (ranging from 10 µg/mL to 200 µg/mL) for 48 hours, (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) (MTT) reagent was added to each well. The cells were incubated for 4 hours at 37°C, and the formazan crystals formed were dissolved in dimethyl sulfoxide (DMSO). Absorbance was measured at 570 nm [7].

STATISTICAL ANALYSIS

All experiments were performed in triplicates and the results are presented as mean ± standard deviation (SD). Statistical analysis was conducted using one-way analysis of variance (ANOVA), followed by Tukey's post-hoc test to determine significant differences between groups. A p-value of <0.05 was considered statistically significant.

RESULTS

Phytochemical Composition

Table **1** shows that the phytochemical composition of *Allium ascalonicum* extracts highlights the methanol extract's superor bioactive content compared to the aqueous extract. The methanol extract exhibited a significantly higher total phenolic content (82.4 ± 3.2 mg GAE/g) compared to the aqueous extract (56.3 ± 2.8 mg GAE/g). This higher phenolic content contributes to its stronger antioxidant activity, as phenolic compounds are effective in neutralizing free radicals through hydrogen donation or electron transfer. Similarly, the methanol extract contained a higher total flavonoid content (54.7 ± 2.1 mg QE/g) than the aqueous extract (34.2 ± 1.9 mg QE/g). Flavonoids are well-known for their potent free radical scavenging abilities, further explaining the methanol extract's enhanced antioxidant potential. Both extracts tested positive for alkaloids, tannins, and saponins, indicating shared phytochemical properties. Alkaloids' presence suggests potential anti-inflammatory and therapeutic benefits. Tannins, found in both extracts, are associated with astringent properties and possible therapeutic applications, such as wound healing and antioxidant effects. The detection of saponins in both

Table 1: Phytochemical Composition of *Allium ascalonicum* Extracts

Phytochemical Compound	Methanol Extract	Aqueous Extract
Total Phenolic Content (TPC)	82.4 ± 3.2 mg GAE/g	56.3 ± 2.8 mg GAE/g
Total Flavonoid Content (TFC)	54.7 ± 2.1 mg QE/g	34.2 ± 1.9 mg QE/g
Alkaloids	Present	Present
Tannins	Present	Present
Saponins	Present	Present

Table 2: Antioxidant Activity of *Allium ascalonicum* Extracts

Assay	Methanol Extract	Aqueous Extract
DPPH IC_{50} (µg/mL)	42.8 ± 1.5	88.5 ± 2.4
FRAP Value (µM)	310.5 ± 8.3	182.7 ± 6.1
Total Antioxidant Capacity (TAC)	24.7±0.9 µM ascorbic acid equivalents	15.3 ± 0.8 µM ascorbic acid equivalents

extracts points to potential anticancer and antimicrobial activities, further emphasizing the medicinal value of *Allium ascalonicum*. These findings underscore the methanol extract's superior phytochemical richness, making it a more potent candidate for therapeutic applications.

Antioxidant Activity

As shown in Table **2**, methanol extract demonstrated a significantly lower IC_{50} value (42.8 ± 1.5 µg/mL) in the DPPH radical scavenging assay compared to the aqueous extract (88.5 ± 2.4 µg/mL), indicating greater efficiency in neutralizing DPPH radicals. This superior activity is attributed to the methanol extract's higher phenolic and flavonoid content, as these compounds are well-known for their ability to donate hydrogen atoms or electrons to stabilize free radicals [8]. In the ferric reducing antioxidant power (FRAP) assay, the methanol extract displayed a higher reducing power (310.5 ± 8.3 µM ascorbic acid equivalents) than the aqueous extract (182.7 ± 6.1 µM). This finding suggests that the methanol extract is more effective in reducing Fe^{3+} to Fe^{2+}, reflecting its greater potential to act as an electron donor and antioxidant. Additionally, the total antioxidant capacity (TAC) assay revealed that the methanol extract had a higher TAC value (24.7 ± 0.9 µM ascorbic acid equivalents) compared to the aqueous extract (15.3 ± 0.8 µM). This comprehensive assessment of the extract's ability to neutralize a range of oxidants further reinforces the superior antioxidant profile of the methanol extract.

Cytotoxicity on HepG2 Cells

Table **3** indicates that the methanol extract demonstrated a significantly lower IC_{50} value (72.4 ± 2.8 µg/mL) compared to the aqueous extract (145.6 ± 4.1 µg/mL). This indicates that the methanol extract is approximately twice as potent as the aqueous extract in inhibiting HepG2 cell proliferation. The lower IC_{50} suggests a higher concentration of bioactive compounds in the methanol extract capable of exerting cytotoxic effects. Morphological observations revealed distinct differences in the impact of the two extracts. The methanol extract induced clear apoptosis-like changes, including membrane blebbing and cell shrinkage, which are hallmarks of programmed cell death. In contrast, the aqueous extract caused only mild changes, such as cell detachment, indicating a less aggressive mechanism of cytotoxicity. This suggests that the methanol extract may contain compounds that actively trigger apoptosis pathways, whereas the aqueous extract may act through less specific or indirect mechanisms. The methanol extract reduced cell viability to 50.3 ± 5.7%, while the aqueous extract maintained a higher viability of 68.9 ± 3.5%. This reinforces the observation that the methanol extract is more effective in decreasing the number of viable HepG2 cells, potentially through mechanisms involving enhanced induction of cell death or inhibition of cell growth.

DISCUSSION

Plants with beneficial pharmacological effects on humans are categorized under medicinal plant**.** However**,** the present study aimed to evaluate the phytochemical composition, antioxidant properties, and cytotoxicity of *Allium ascalonicum* leaf extracts, with a particular focus on comparing the methanol and aqueous extracts. The results suggest that *Allium ascalonicum* holds significant potential as a source of bioactive compounds with antioxidant and anticancer

Table 3: Cytotoxicity of *Allium ascalonicum* Extracts on HepG2 Cells

Treatment	Methanol Extract	Aqueous Extract
IC_{50} (µg/mL)	72.4 ± 2.8	145.6 ± 4.1
Morphological Changes	Cell shrinkage, blebbing	Mild changes, cell detachment
Cell Viability (%)	50.3 ± 5.7	68.9 ± 3.5

properties, which may offer therapeutic benefits, particularly in the management of oxidative stress and liver cancer. The methanol extract of *Allium ascalonicum* exhibited a higher concentration of phenolics (82.4 mg GAE/g) and flavonoids (54.7 mg QE/g) compared to the aqueous extract. These results are consistent with previous studies indicating that methanol is an effective solvent for extracting polyphenolic compounds, which are crucial for the antioxidant activity of plants [6]. The presence of alkaloids, tannins, and saponins in both extracts further supports the idea that *Allium ascalonicum* contains diverse bioactive compounds that could contribute to its therapeutic potential. Alkaloids have been known for their anti-inflammatory and anticancer properties, while tannins and saponins are associated with antimicxrobial and anti-cancer activities [9,10].

Several diseases in humans are linked to the build-up of free radicals. Antioxidants can scavenge free radicals and reduce their impact. As a result, the research for naturally occurring antioxidants of plant origin is critical [11]. Several harmful pathophysiological processes, including cancer, diabetes, and cardiovascular and neurological illnesses, are strongly linked to free radical development. A free radical is an atomic or molecular structure with an unpaired electron that is unstable. In healthy human cells, this unstable radical has the potential to become stable through electron pairing with biological macromolecules such as proteins, lipids, and deoxyribonucleic acid (DNA), causing protein and DNA damage [12]. Because of reduced cellular antioxidant defines systems, such radical-caused cell damage may become more common. Although all biological systems contain natural antioxidant defense mechanisms that remove damaged molecules, these strategies can be ineffective. As a result, consuming antioxidants is critical for protecting cells from free radical damage. However, the antioxidant assays, including DPPH, FRAP, and TAC, demonstrated that the methanol extract of *Allium ascalonicum* exhibited significantly stronger antioxidant activity than the aqueous extract. The lower DPPH IC_{50} value (42.8 µg/mL) in the methanol extract indicates that it is more effective in scavenging free radicals, which are known to contribute to the pathogenesis of various diseases, including cancer and cardiovascular diseases [13]. The FRAP assay also revealed that the methanol extract had a greater reducing power (310.5 µM ascorbic acid equivalents), further confirming its potent antioxidant capacity. These findings align with the well-established role of polyphenolic compounds, particularly flavonoids and phenolics, in modulating oxidative stress and preventing cellular damage caused by reactive oxygen species (ROS) [14].

The Total Antioxidant Capacity (TAC) assay also supported the above findings, with the methanol extract showing a significantly higher TAC value (24.7 µM ascorbic acid equivalents) compared to the aqueous extract. This suggests that the methanol extract contains a broader range of antioxidant compounds capable of neutralizing oxidative stress. The higher antioxidant activity of the methanol extract is likely attributed to its higher concentration of bioactive compounds, particularly polyphenols and flavonoids, which are known for their ability to neutralize free radicals and reduce oxidative damage [3]. The cytotoxicity assays revealed that the methanol extract exhibited stronger cytotoxic effects on HepG2 cells, with an IC_{50} of 72.4 µg/mL, compared to the aqueous extract, which had an IC_{50} of 145.6 µg/mL. The lower IC_{50} value in the methanol extract indicates that it was more effective in inhibiting the growth of HepG2 liver cancer cells. Morphological changes observed in the treated cells, such as cell shrinkage, membrane blebbing, and detachment, suggest that the methanol extract induces apoptosis, a programmed form of cell death that plays a key role in eliminating cancerous cells [15]. These findings are consistent with previous studies that have shown that plant-derived polyphenols, including those from *Allium* species, can induce apoptosis in cancer cells through oxidative stress-mediated pathways [1].

The stronger cytotoxicity observed in the methanol extract could be attributed to its higher content of phenolic compounds and flavonoids, which are known to modulate several molecular pathways involved in cell survival and death, including the regulation of pro-apoptotic and anti-apoptotic proteins [16]. Additionally, the ability of phenolic compounds to induce oxidative stress could also contribute to the cytotoxic effects observed in the HepG2 cells. However, the lower cytotoxicity of the aqueous extract does not exclude its potential therapeutic use, as it may still possess other medicinal properties, such as anti-inflammatory or antimicrobial effects, which were not directly assessed in this study. Overall, the methanol extract of *Allium ascalonicum* showed superior antioxidant and cytotoxic activities compared to the aqueous extract. This could be attributed to the increased solubility of bioactive compounds such as flavonoids and phenolics in methanol, which enhances their extraction efficiency [1].

The findings highlight the importance of solvent choice in maximizing the extraction of bioactive compounds and suggest that methanol extraction may be more suitable for obtaining high concentrations of antioxidants and anticancer agents from *Allium ascalonicum* leaves.

The promising results from this study indicate that *Allium ascalonicum* has potential as a source of natural antioxidants and anticancer agents. Given the increased prevalence of oxidative stress-related diseases, including cancer and cardiovascular conditions, further research is needed to identify the specific compounds responsible for these biological activities. Additionally, future studies should explore the mechanisms of action of these bioactive compounds in greater detail, particularly their effects on various molecular targets involved in oxidative stress and apoptosis. Moreover, the *in vivo* evaluation of the methanol extract's antioxidant and anticancer activities would provide more robust evidence of its therapeutic potential. Clinical studies would also be necessary to determine the safety, dosage, and efficacy of *Allium ascalonicum* as a functional food or therapeutic agent.

CONCLUSION

This study demonstrated that the methanol extract of *Allium ascalonicum* contains higher concentrations of bioactive compounds, including phenolics and flavonoids, and exhibits superior antioxidant and cytotoxic activities compared to the aqueous extract. This finding suggest that *Allium ascalonicum* could be a promising candidate for the development of natural antioxidants and anticancer therapies. Further investigations are warranted to fully understand the bioactive compounds involved and their mechanisms of action in mitigating oxidative stress and cancer.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

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