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Assessing the Cytotoxic Impact of Pesticide-Contaminated Agricultural Extracts

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Abstract*: The extensive use of pesticides in conventional farming raises serious concerns about residual toxicity in food and its potential health risks. This study evaluates the cytotoxic effects of homogenates from pesticide-exposed cumin and grapes on six human cell lines: HepG2 (liver), TK6 (lymphoblastoid), THP1 (monocytic), Jurkat (T-cell leukemia), Raji, and Daudi (B-cell lymphoma). Dose-dependent cytotoxicity was observed across all cell lines, with cell viability decreasing at 5%, 10%, and 20% homogenate concentrations. THP1 cells were most sensitive, showing viability below 30% at the highest grape homogenate dose, while HepG2 cells were comparatively resistant. To benchmark toxicity, chlorpyrifos (CPF), a widely used organophosphate pesticide, was tested. CPF exposure (1–20 µM) resulted in significant viability loss, especially in Jurkat and TK6 cells. Doxorubicin (20 µM), used as a positive control, induced severe cytotoxicity across all lines, validating assay reliability. Additional tests on Raji, THP1, and Daudi cells confirmed CPF and Doxorubicin's cytotoxic potential. These findings highlight the health risks posed by pesticide residues in food and emphasize the need for stricter monitoring and safer agricultural practices. The study provides foundational evidence for further research into detoxification strategies and regulatory reforms to reduce consumer exposure.*

Keyword: Agrochemical Exposure, Immunotoxicology, Pesticide Residues, Agricultural Extracts, Chlorpyrifos (CPF)

1. Introduction

The global reliance on pesticides in conventional agriculture has significantly increased over the past few decades, driven by the need to enhance crop yields and ensure food security. However, this widespread use has raised serious concerns regarding the residual presence of these chemicals in food products and their potential impact on human health. Pesticides, by design, are biologically active compounds intended to eliminate pests, but their toxicity is not limited to target organisms. Numerous studies have demonstrated that chronic exposure to pesticide residues, whether through ingestion, inhalation, or dermal contact can lead to a range of adverse health outcomes, including endocrine disruption, neurotoxicity, reproductive dysfunction, and carcinogenicity (1).

Recent epidemiological and experimental research has highlighted the link between pesticide exposure and metabolic disorders, particularly in vulnerable populations such as children and agricultural workers. For instance, prenatal and early-life exposure to organophosphate mixtures has been associated with increased risks of obesity, insulin resistance, and cardiovascular anomalies in young adults. Similarly, neonicotinoid insecticides have been implicated in male reproductive toxicity, with evidence pointing to reduced sperm quality and hormonal imbalances. These findings underscore the urgency of evaluating the cytotoxic potential of pesticide residues in commonly consumed food items (2). In this context, the present study investigates the cytotoxic effects of homogenates derived from pesticide exposed to agricultural products specifically cumin and grapes on a panel of human cell lines representing diverse tissue origins and disease states. The selected cell lines include HepG2 (liver), TK6 (lymphoblastoid), THP1 (monocytic), Jurkat (T-cell leukemia), Raji, and Daudi (B-cell lymphoma). These models offer a comprehensive view of how pesticide residues may affect both normal and malignant cells, providing insights into tissue-specific vulnerabilities.

The current study addresses a critical gap in the literature by directly linking pesticide-contaminated food extracts to cytotoxic outcomes in human cells. It provides foundational evidence for the health hazards associated with dietary pesticide exposure and supports the need for stringent monitoring of agricultural products. Furthermore, the results advocate for the development of detoxification protocols and regulatory reforms aimed at minimizing consumer exposure to harmful residues.

By integrating cellular toxicology with real-world food contamination scenarios, this research contributes to the broader discourse on sustainable agriculture and public health. It calls for a reevaluation of pesticide usage practices and encourages the adoption of safer alternatives, such as integrated pest management (IPM), to protect both environmental and human health.

2. Literature survey

The increasing use of pesticides in agriculture has led to widespread contamination of food products, raising significant concerns about their impact on human health. Numerous studies have documented the cytotoxic effects of pesticide residues, particularly organophosphates like chlorpyrifos (CPF), on various human cell lines. These compounds are known to induce oxidative stress, DNA damage, and apoptosis, contributing to a range of chronic diseases including cancer, neurodegeneration, and immune dysfunction (1).

Cell-based toxicity assays have become a cornerstone in evaluating the health risks posed by pesticide exposure. HepG2 cells, representing hepatic metabolism, are frequently used to assess xenobiotic detoxification and bioactivation. Studies have shown that CPF and its metabolite chlorpyrifos exhibit differential cytotoxicity in HepG2 and HK-2 cells due to variations in efflux transporter expression and metabolic enzyme activity. Similarly, lymphoid and myeloid cell lines such as Jurkat, TK6, THP1, Raji, and Daudi are valuable models for studying immunotoxicity, given their relevance to immune regulation and hematological malignancies (3).

Emerging evidence links pesticide exposure to autoimmune disorders, suggesting that immunotoxicity may be a key mechanism underlying disease onset. Organophosphates, pyrethroids, and carbamates have been shown to disrupt cytokine signaling, impair immune tolerance, and promote chronic inflammation. For instance, CPF has been implicated in the suppression of T-cell proliferation and NK cell cytotoxicity, as well as the inhibition of Th1 differentiation and IL-2 signaling. These effects compromise immune surveillance and may contribute to the development of autoimmune conditions such as lupus, rheumatoid arthritis, and multiple sclerosis (4) (5).

The cell lines used in the present study THP1, Jurkat, TK6, Raji, Daudi, and HepG2 are particularly relevant for investigating these immunotoxic effects. THP1 cells, derived from monocytic leukemia, are sensitive indicators of innate immune responses and inflammation. Jurkat and TK6 cells, representing T-cell and lymphoblastoid lineages respectively, are commonly used to study genotoxicity and apoptosis. B-cell lines Raji and Daudi are instrumental in evaluating antigen presentation and cytokine modulation. The observed dose-dependent cytotoxicity in these lines upon exposure to cumin and grape homogenates, as well as CPF and doxorubicin, underscores the potential immunological risks posed by pesticide-contaminated food.

Furthermore, the literature supports the hypothesis that chronic dietary exposure to pesticide residues may exacerbate autoimmune responses by inducing cellular stress and immune dysregulation. This study contributes to the growing body of evidence advocating stricter regulatory oversight, improved residue monitoring, and the development of detoxification strategies to mitigate health risks (6).

3. Problem Solving Objectives

1) Evaluate Cytotoxicity of Pesticide-Contaminated Food Products.
2) Compare Toxicological Profiles of Food Extracts and Known Pesticides.
3) Identify Cell Line-Specific Sensitivities to Pesticide Exposure.
4) Explore Immunotoxic and Autoimmune-Relevant Effects.
5) Support Regulatory and Public Health Interventions.
6) Establish a Screening Framework for Food Safety Assessment.

4. Methodology

Cell line and culture conditions:
Human cancer cell lines were selected to represent hepatic, lymphoid, and monocytic origins e.i. HepG2 (human hepatocellular carcinoma), TK6 (human B-lymphoblastoid), THP1 (human monocytic leukemia) and Raji and Daudi (human Burkitt's lymphoma). All cell lines were obtained from authenticated sources (e.g., ATCC) and cultured under recommended conditions. HepG2 cells were maintained in DMEM supplemented with 10% fetal bovine serum (FBS), 1% penicillin-streptomycin. TK6, THP1, Raji, and Daudi cells were cultured in RPMI-1640 medium with 10% FBS and antibiotics. Cultures were incubated at 37°C in a humidified atmosphere with 5% CO_2.

Preparation of test substances:
Chlorpyrifos (CPF), deltamethrin (DM), and cypermethrin (CPM) were procured from certified chemical suppliers in analytical grade purity (>98%). Dimethyl sulfoxide (DMSO, molecular biology grade) was used as the solvent for stock preparation. All reagents were stored and handled according to manufacturer safety guidelines. Each pesticide was initially dissolved in DMSO to prepare a 20 mM stock solution. The stock solutions were vortexed thoroughly and stored at −20°C in amber vials to prevent photodegradation. Fresh working dilutions were prepared prior to each experiment. To achieve final concentrations of 1, 2, 5, 10, and 20 µM in cell culture media, serial dilutions were performed using complete RPMI-1640 or DMEM (depending on the cell line) supplemented with 10% foetal bovine serum (FBS) and 1% penicillin-streptomycin. The final DMSO concentration in all treatment groups, including controls, was maintained at 0.5% (v/v) to ensure solvent consistency and minimize cytotoxic effects from DMSO itself. Cells were treated with 0.5% DMSO in culture media without any pesticide to account for solvent effects. Doxorubicin (20 µM) was used as a known cytotoxic agent to validate assay sensitivity. Untreated cells cultured in complete media served as baseline controls.

Plant Homogenates:
Wheat grains, grapes, and cumin seeds were sourced from nearby shops suppliers. Samples were washed with sterile distilled water, air-dried, and homogenized in sterile phosphate-buffered saline (PBS) using a mechanical homogenizer under aseptic conditions. Homogenates were filtered through sterile gauze and centrifuged at 3,000 rpm for 10 min to remove debris. Supernatants were collected and used at 5%, 10%, and 20% (v/v) concentrations in culture medium. All preparations were performed fresh and stored at 4°C for no longer than 24 h before use.

Cytotoxicity Assay (MTT Assay):
Cell viability was assessed using the MTT assay, which measures mitochondrial metabolic activity. In brief, Cells were seeded in 96-well plates at a density of 1×10^4 cells/well in 100 µL of complete medium. After 24 h stabilization, cells were treated with either pesticides or plant homogenates at specified concentrations for 24 h. Following treatment, 20 µL of MTT solution (5 mg/mL in PBS) was added to each well and incubated for 4 h at 37°C. Formazan crystals were solubilized using 100 µL of DMSO, and absorbance was

measured at 570 nm using Epoch microplate reader. Cell viability (%) was calculated as against 0.5 % DMSO control. Each treatment was performed in triplicate wells and repeated in three independent experiments. Negative and positive controls were included in every plate to ensure assay consistency. Data were expressed as mean ± standard deviation (SD). • Graphs and dose-response curves were generated using GraphPad Prism v9.0.

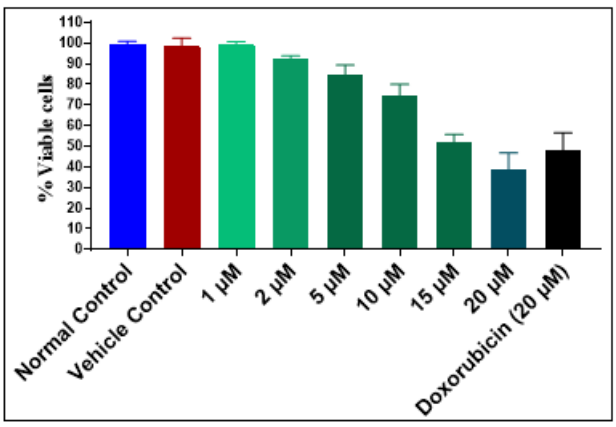
5. Results and Discussion

In all experiments in cell line HepG2 (human hepatocellular carcinoma), TK6 (human B-lymphoblastoid), THP1 (human monocytic leukemia) and Raji and Daudi (human Burkitt's lymphoma) and in wheat, cumin and grape homogenates the Normal Control and Vehicle Control (0.5% DMSO) groups-maintained viability near 100%, confirming that the culture conditions and solvent exerted negligible cytotoxicity. Conversely, the Doxorubicin (20 µM) group exhibited a pronounced reduction in viability, validating its role as a robust positive control for cell death. The cytotoxicity assay was conducted on three human cell lines HepG2 (hepatic), TK6 (human lymphoblastoid), and THP1 (monocytic) to evaluate the effect of wheat, cumin and grapes homogenate at concentrations of 5%, 10%, and 20%. Cell viability was assessed after 24 hours of exposure using an MTT assay, and results were normalized against vehicle control.

Cytotoxic effect of Chlorpyrifos

Exposure to CPF elicited a concentration-dependent decline in cellular viability across all tested cell lines. At the lowest concentration (1 µM), viability remained relatively high (>85%), whereas at the highest concentration (20 µM), viability dropped significantly (<30%). This dose-response pattern was consistent, indicating that CPF exerts measurable cytotoxicity even at micromolar levels.

Although all cell lines demonstrated similar trends, HepG2 cells exhibited marginally higher viability at intermediate concentrations (5–10 µM) compared to Jurkat and Tk6 cells. This observation may reflect intrinsic differences in metabolic capacity, detoxification pathways, or membrane transporter activity. Nonetheless, the overall cytotoxic effect was broadly comparable, suggesting that CPF targets fundamental cellular processes rather than tissue-specific mechanisms (Figure 1).



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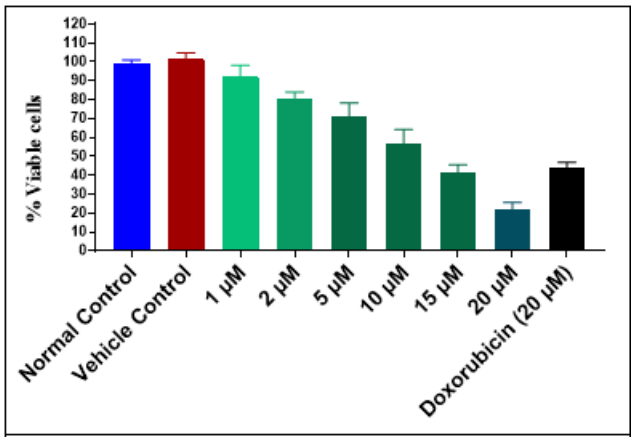

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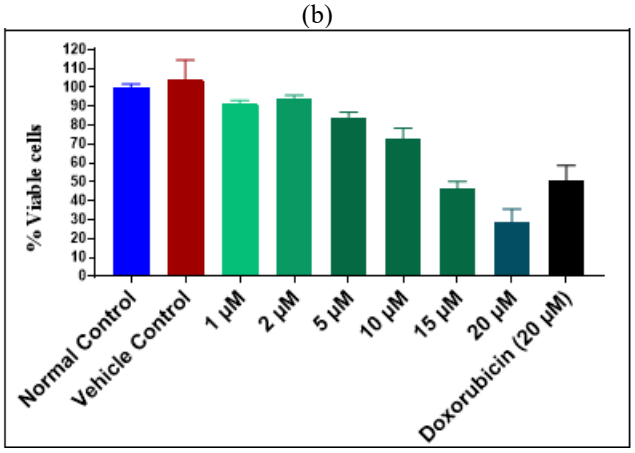

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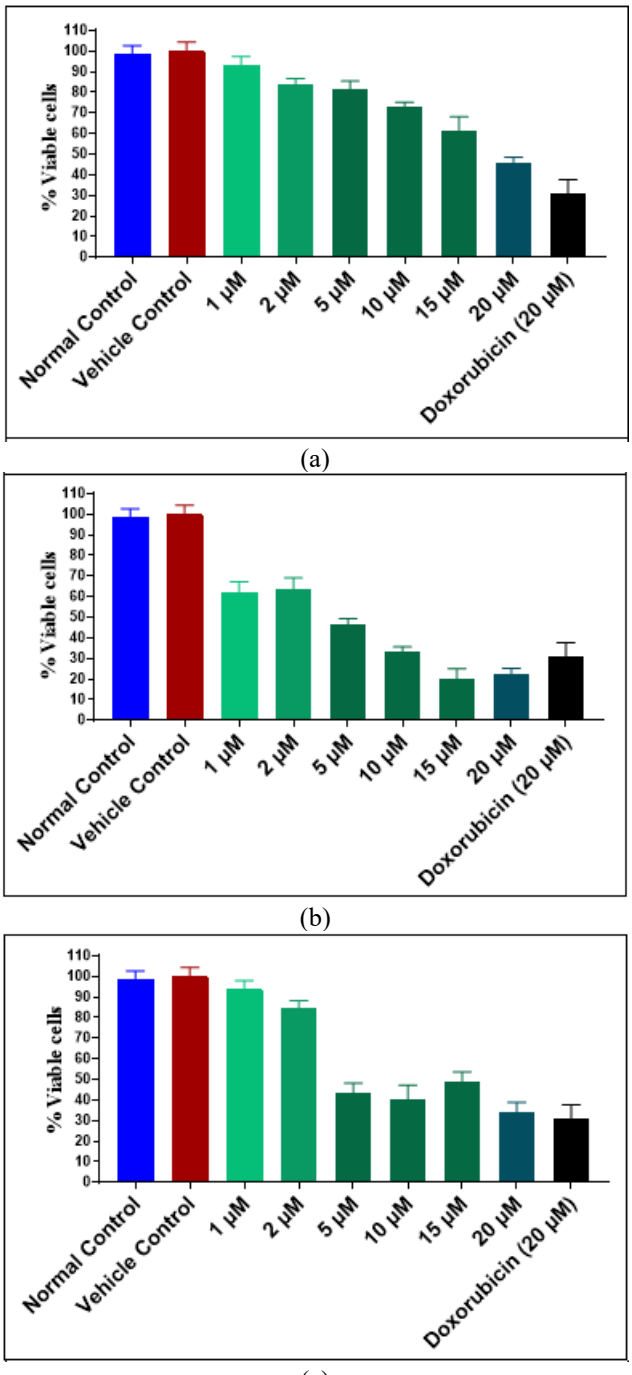
Figure 1: Cell viability in HepG2 (a), Jurkat (b) and Tk6 (c) cells with Chlorpyrifos after 24 hr of exposure.

The present findings establish that CPF induces cytotoxicity in HepG2, Jurkat, and Tk6 cells in a dose-dependent manner, a hallmark of compounds with toxicological and pharmacological relevance. The observed decline in viability with increasing CPF concentration aligns with prior evidence implicating organophosphate pesticides in mitochondrial dysfunction, oxidative stress, and apoptotic signaling (7). Mechanistically, CPF has been reported to disrupt mitochondrial membrane potential, elevate reactive oxygen species (ROS), and activate caspase-dependent apoptotic pathways in hepatic cells (7). Furthermore, CPF and its oxon metabolite can interfere with efflux transporters, leading to intracellular accumulation and enhanced toxicity (3). Recent systematic reviews highlight CPF's ability to modulate MAPK and ERK signaling cascades, contributing to apoptosis and inflammatory responses (8). The comparable sensitivity of hepatic and lymphoid cell lines suggests that CPF's cytotoxicity is not confined to a single tissue type, raising concerns about systemic toxicity following exposure. These findings underscore the necessity for in vivo studies and mechanistic investigations to delineate CPF's toxicodynamics and evaluate its potential risk to human health (9).

Cytotoxic effect of Deltamethrin

Raji cells displayed a clear dose-dependent decline in viability upon exposure to the test compound. At the lowest concentration (1 µM), viability remained relatively high (~90%), but as the concentration increased, a progressive reduction was observed, culminating in viability below 40%

at 20 µM. This trend indicates that the compound exerts significant cytotoxicity at higher doses. THP1 cells exhibited the most pronounced sensitivity among the tested lines. Viability decreased sharply from approximately 65% at 1 µM to nearly 20% at 20 µM. This steep decline suggests that THP1 cells may possess intrinsic vulnerabilities, such as higher uptake of the compound or reduced detoxification capacity, making them particularly susceptible to its cytotoxic effects. Daudi cells followed a similar dose-dependent pattern, with viability decreasing from ~85% at 1 µM to less than 40% at 20 µM. The response closely mirrored that of Raji cells, indicating comparable sensitivity and reinforcing the compound's broad cytotoxic potential across B-cell lymphoma lines (Figure 2).



(a)

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Figure 2: Cell viability in Raji (a), THP1 (b) and Daudi (c) cells with Deltamethrin after 24 hr of exposure.

The findings unequivocally demonstrate that the tested compound induces concentration-dependent cytotoxicity in Raji, THP1, and Daudi cell lines after 24 hours of exposure. This dose-response relationship is a hallmark of pharmacologically active agents and suggests interference with critical cellular processes such as mitochondrial integrity, oxidative homeostasis, and apoptotic signaling pathways (10).

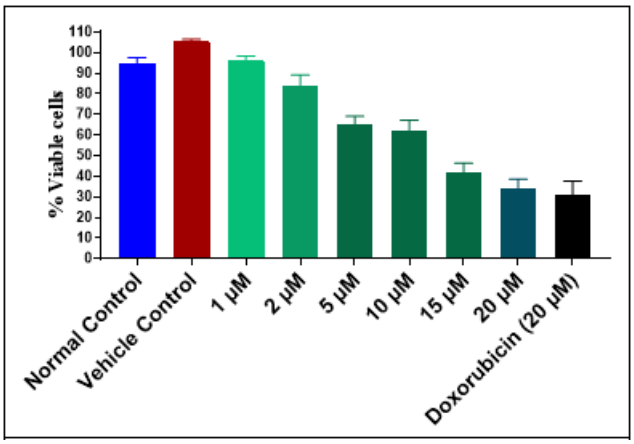
The heightened sensitivity of THP1 cells compared to Raji and Daudi may reflect lineage-specific metabolic differences or variations in membrane transport mechanisms. Previous studies on lymphoid malignancies have reported that cytotoxic compounds often trigger apoptosis through caspase activation, mitochondrial membrane potential disruption, and reactive oxygen species (ROS) generation (10). Additionally, research on anticancer agents targeting hematological cancers indicates that these pathways converge on MAPK/ERK signaling cascades, DNA fragmentation, and cell cycle arrest, ultimately leading to programmed cell death (11).

The comparable cytotoxicity observed in Raji and Daudi cells both derived from Burkitt's lymphoma suggests that the compound may have therapeutic relevance for B-cell malignancies. However, the pronounced effect on THP1 cells (monocytic lineage) indicates broader applicability across hematological cancers. These observations warrant further mechanistic studies to elucidate the molecular targets and signaling pathways involved (12).

Cytotoxic effect of Cypermethrin

Raji cells demonstrated a clear dose-dependent decline in viability upon Cypermethrin exposure. At 1 µM, viability remained high (~90%), but progressively decreased with increasing concentrations, reaching below 40% at 20 µM. This trend indicates significant cytotoxicity at higher doses. THP1 cells exhibited the greatest sensitivity among the tested lines. Viability dropped sharply from approximately 65% at 1 µM to nearly 20% at 20 µM. This pronounced decline suggests intrinsic vulnerabilities, possibly linked to differences in metabolic activity or membrane transport mechanisms. Daudi cells followed a similar dose-dependent pattern, with viability decreasing from ~85% at 1 µM to less than 40% at 20 µM. The response closely mirrored that of Raji cells, indicating comparable sensitivity and reinforcing Cypermethrin's broad cytotoxic potential across B-cell lymphoma lines (Figure 3).

The findings unequivocally demonstrate that Cypermethrin induces concentration-dependent cytotoxicity in Raji, THP1, and Daudi cell lines after 24 hours of exposure. This dose-response relationship is characteristic of cytotoxic agents and suggests interference with essential cellular processes such as mitochondrial integrity, oxidative homeostasis, and apoptotic signaling (13).



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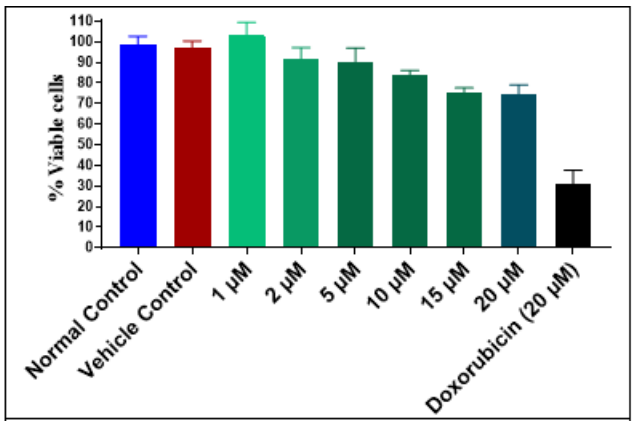

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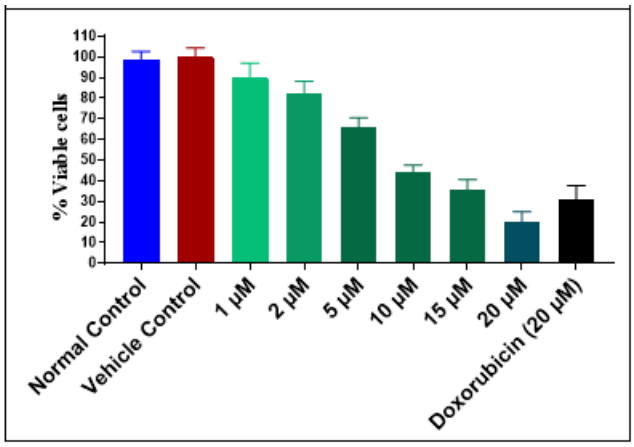

(c)

Figure 3: Cell viability in Raji (a), THP1 (b) and Daudi (c) cells with Cypermethrin after 24 hr of exposure.

Previous studies have shown that Cypermethrin exerts toxic effects on lymphocytes through oxidative stress, mitochondrial dysfunction, and activation of apoptotic pathways. Mechanistic investigations reveal that Cypermethrin can induce G1 cell cycle arrest, DNA damage, and apoptosis mediated by ROS-dependent activation of JNK/ERK signaling pathways. These pathways converge on caspase activation and PARP cleavage, hallmarks of programmed cell death (14).

The heightened sensitivity of THP1 cells compared to Raji and Daudi may reflect lineage-specific metabolic differences or variations in detoxification capacity. The comparable cytotoxicity observed in Raji and Daudi cells both derived from Burkitt's lymphoma suggests that Cypermethrin may have therapeutic relevance for B-cell malignancies. However, its pronounced effect on THP1 cells (monocytic lineage) indicates broader applicability across hematological cancers (15).

Importantly, Cypermethrin's cytotoxicity raises dual concerns: while it demonstrates potential as an anti-cancer agent, its widespread use as an agricultural pesticide underscores the need for toxicological risk assessment in human exposure scenarios (16).

Cytotoxic effect of Wheat Homogenates

HepG2 cells demonstrated a modest reduction in viability with increasing homogenate concentration. At 5%, viability was approximately 90%, decreasing to ~80% at both 10% and 20%. This suggests that HepG2 cells are relatively resistant to wheat homogenate-induced cytotoxicity compared to the other cell lines. TK6 cells exhibited a more pronounced dose-dependent response. Viability decreased from ~80% at 5% homogenate to ~70% at 10%, and further to ~60% at 20%. This indicates higher sensitivity of TK6 cells, possibly due to their lymphoid origin and differences in metabolic or oxidative stress handling mechanisms. THP1 cells showed intermediate sensitivity. Viability declined from ~85% at 5% to ~78% at 10%, and ~63% at 20%. The pattern suggests that wheat homogenate exerts significant cytotoxic effects on monocytic cells, potentially through pathways involving oxidative stress or membrane disruption (Figure 4).

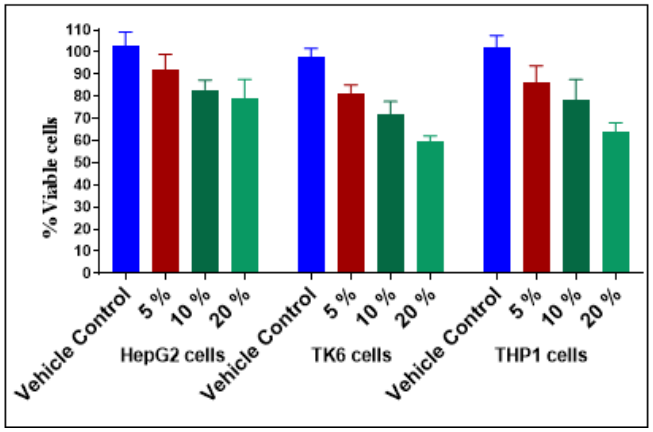

Figure 4: Cell viability in HepG2 (a), Tk6 (b) and THP1 (c) cells with wheat homogenates after 24 hr of exposure.

The data clearly indicates that wheat homogenate possesses dose-dependent cytotoxic properties, as evidenced by the progressive decline in cell viability across all tested cell lines. The vehicle control results confirm that the observed cytotoxicity is intrinsic to the wheat homogenate rather than the solvent. The differential sensitivity among cell lines is noteworthy. TK6 and THP1 cells were more susceptible than HepG2 cells, suggesting that lymphoid and monocytic cells may have less robust defense mechanisms against bioactive compounds present in wheat homogenate. These differences could be attributed to variations in cellular metabolism and detoxification pathways, membrane composition and permeability and presence of specific receptors or transporters interacting with wheat derived compounds.

Previous studies on wheat germ and bran extracts have demonstrated anticancer and cytotoxic effects mediated by bioactive components such as benzoquinones, phenolic acids, and wheat germ agglutinin, which can induce apoptosis, oxidative stress, and cell cycle arrest in cancer cells. Fermented wheat germ extract (FWGE), for example, has been shown to activate caspase-dependent pathways and synergize with chemotherapeutic agents in vitro. Wheat germ agglutinin, a lectin, exhibits selective cytotoxicity through carbohydrate-binding mechanisms, making it a candidate for targeted drug delivery (17).

Cytotoxic effect of Cumin Homogenates

HepG2 cells exhibited minimal sensitivity to cumin homogenate. Viability remained high, with only a slight decrease at the highest concentration: ~95% at 5%, ~96% at 10%, and ~91% at 20%, compared to ~97% in the vehicle control. This suggests that HepG2 cells are relatively resistant to the cytotoxic effects of cumin homogenate. TK6 cells showed a more pronounced dose-dependent response. Viability decreased from ~98% in the vehicle control to ~84% at 5%, ~70% at 10%, and ~60% at 20%. This indicates significant cytotoxicity at higher concentrations and suggests that TK6 cells are moderately sensitive to cumin homogenate. THP1 cells were the most sensitive among the tested lines. Viability declined sharply from ~100% in the vehicle control to ~74% at 5%, ~65% at 10%, and ~50% at 20%. This steep reduction suggests that cumin homogenate exerts strong cytotoxic effects on monocytic cells (Figure 5).

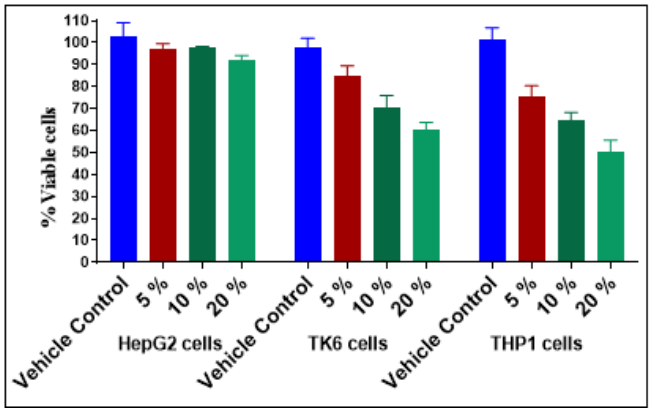

Figure 5: Cell viability in HepG2 (a), Tk6 (b) and THP1 (c) cells with cumin homogenates after 24 hr of exposure.

The data demonstrate that cumin homogenate induces dose-dependent cytotoxicity in all three cell lines, with varying degrees of sensitivity. The differential sensitivity among cell lines is a key observation. THP1 cells exhibited the greatest susceptibility, followed by TK6, while HepG2 cells were relatively resistant. These differences may be attributed to cellular metabolism and detoxification capacity (HepG2 cells possess robust metabolic pathways) membrane composition and permeability, influencing compound uptake and presence of specific receptors or signaling pathways targeted by bioactive components in cumin (18).

Previous studies have reported that cumin seeds contain bioactive phytochemicals such as terpenes, phenolic compounds, and flavonoids, which exhibit antioxidant, anti-inflammatory, and anticancer properties. These compounds can induce oxidative stress, mitochondrial dysfunction, and apoptosis in cancer cells through caspase activation and modulation of signaling pathways like MAPK and NF-κB (18). The modest cytotoxicity observed in HepG2 cells suggests that hepatic cells may metabolize or detoxify cumin-derived compounds more efficiently. In contrast, the pronounced effect on THP1 cells indicates potential therapeutic relevance for hematological malignancies.

Cytotoxic effect of Grape Homogenates

HepG2 cells exhibited moderate sensitivity to grape homogenate. Viability decreased from ~92% in vehicle control to ~61% at 20% concentration, indicating a dose-dependent cytotoxic effect. TK6 cells showed a more pronounced reduction in viability. The control group maintained ~99% viability, which dropped to ~40% at 20% concentration. This suggests that TK6 cells are more susceptible to grape homogenate compared to HepG2. THP1 cells demonstrated the highest sensitivity. Viability declined sharply from ~99% in the control group to ~28% at 20% concentration, indicating strong cytotoxicity at higher doses. Overall, the data reveals a clear dose-dependent cytotoxic effect of grape homogenate across all tested cell lines, with THP1 being the most sensitive (Figure 6).

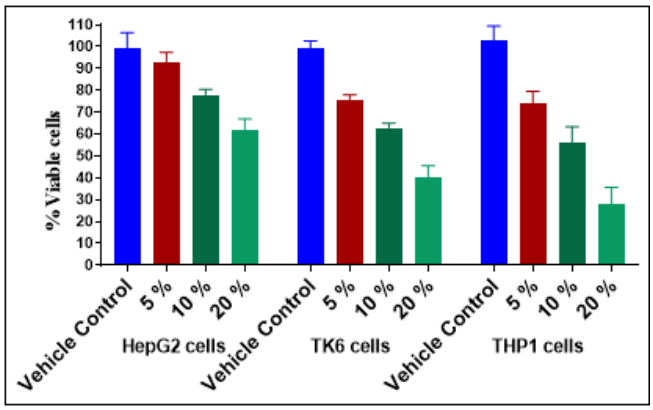

Figure 6: Cell viability in HepG2 (a), Tk6 (b) and THP1 (c) cells with grape homogenates after 24 hr of exposure.

The findings confirm that grape homogenate exerts concentration-dependent cytotoxicity on HepG2, TK6, and THP1 cells. This aligns with previous studies reporting that grapes contain bioactive compounds such as polyphenols, flavonoids, resveratrol, and proanthocyanidins known for their anticancer properties. The observed cytotoxicity likely involves mechanisms such as induction of apoptosis via caspase activation and mitochondrial dysfunction (19) (20), oxidative stress mediated by reactive oxygen species (ROS) (21) (19) or cell cycle arrest through modulation of signaling pathways like MAPK and PI3K/Akt (20). Previous research supports these findings. Grape-derived polyphenols have been shown to inhibit proliferation and induce apoptosis in hematological malignancies and solid tumors. For example, resveratrol and proanthocyanidins can activate intrinsic apoptotic pathways and suppress survival signaling in cancer cells (22) (19) (20).

6. Conclusion

This study provides compelling evidence that both synthetic and plant-derived substances exhibit significant, dose-dependent cytotoxicity against human cancer cell lines.

Cypermethrin demonstrated potent cytotoxic effects on lymphocytic cells, raising critical concerns about its environmental and occupational exposure risks despite its potential anticancer activity. Among natural treatments, grape homogenate emerged as the most effective, followed by cumin and wheat, suggesting that these dietary sources harbor bioactive compounds with promising chemo preventive and therapeutic potential.

The differential sensitivity observed THP1 cells being most susceptible, TK6 moderately sensitive, and HepG2 relatively resistant highlights the importance of cellular context in determining treatment efficacy. Mechanistic insights point toward oxidative stress, mitochondrial dysfunction, and caspase-mediated apoptosis as key pathways underlying cytotoxicity. These findings underscore the dual nature of these agents: while they offer opportunities for anticancer drug development, their safety profiles must be rigorously evaluated.

Future research should focus on isolating and characterizing active phytochemicals, elucidating molecular mechanisms of action, and assessing selectivity against normal cells. In vivo studies and toxicological risk assessments are essential to translate these findings into clinically relevant strategies. Ultimately, this work lays the foundation for leveraging natural bioactive and understanding pesticide toxicity in cancer biology, bridging the gap between food science, toxicology, and oncology.

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