

Title:

Therapeutic Perspectives of Natural Compounds from *Cymbopogon citratus* in the Management of Oxidative Stress Associated with Cancer

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Abstract

Oxidative stress is widely recognized as a critical factor in the onset and progression of cancer, largely due to the overproduction of reactive oxygen species (ROS) that inflict damage on cellular macromolecules including DNA, lipids, and proteins. The search for effective therapeutic agents to mitigate oxidative damage has increasingly focused on natural compounds derived from plants, known for their antioxidant and bio-modulatory properties. *Cymbopogon citratus* (lemongrass) is a rich source of bioactive secondary metabolites such as polyphenols, terpenoids, and flavonoids, which exhibit potent antioxidant capabilities. This review synthesizes current phytochemical and pharmacological evidence supporting the therapeutic potential of *Cymbopogon citratus* extracts in attenuating oxidative stress related to cancer pathogenesis. By scavenging free radicals, enhancing endogenous antioxidant defenses, and modulating apoptosis and cell signaling pathways, these natural compounds offer promising avenues for cancer chemoprevention and adjunctive therapy. Insights into molecular mechanisms and metabolomic profiles provide a foundation for future in vivo validation and clinical translation aimed at integrating *Cymbopogon citratus*-based phytomedicines into oncological practice.

1. Introduction

Oxidative stress, resulting from an imbalance between the production of reactive oxygen species (ROS) and the capacity of biological systems to detoxify these reactive intermediates, is widely implicated as a fundamental driver of carcinogenesis. Excessive ROS generation leads to irreversible damage of vital cellular components including DNA, lipids, and proteins, thus promoting mutagenesis and oncogenic transformation. In recent years, plant-derived natural compounds have emerged as promising chemopreventive and therapeutic agents due to their inherent antioxidant properties and capacity to modulate various molecular pathways involved in oxidative damage.

Cymbopogon citratus, commonly known as lemongrass, is a medicinal plant with a rich phytochemical profile, encompassing polyphenols, terpenoids, and flavonoids, which have demonstrated notable free radical scavenging and cytoprotective effects. Although essential oils from this plant have been extensively studied, the non-volatile fractions, particularly methanolic and chloroformic extracts, remain relatively underexplored despite their significant bioactivity. A comprehensive understanding of the phytochemical composition combined with mechanistic insights into their antioxidative properties is essential for developing effective phytomedicines targeting oxidative stress-associated cancer pathologies.

This study aims to elucidate the therapeutic potential of *Cymbopogon citratus* secondary metabolites in managing oxidative stress linked to cancer. Through integrative approaches involving advanced metabolomic profiling and functional cellular assays, we seek to clarify how these natural compounds mitigate ROS-induced damage, enhance endogenous antioxidant defenses, and regulate apoptotic pathways. The findings provide a foundation for the rational development of *Cymbopogon citratus*-based interventions as adjuncts in cancer prevention and therapy, highlighting their translational relevance for future in vivo and clinical investigations.

1.1. Study Objectives and Approach

Building upon the established antioxidant potential of *Cymbopogon citratus*, this article aims to provide an in-depth evaluation of its natural compounds as therapeutic agents against oxidative stress in cancer. Our objectives include:

- Comprehensive phytochemical profiling of methanolic and chloroformic extracts of *Cymbopogon citratus*, utilizing advanced analytical techniques such as nuclear magnetic resonance spectroscopy and chromatographic methods.
- Assessment of free radical scavenging activity through standardized in vitro assays, including DPPH and ABTS radical scavenging tests, to quantify antioxidant efficacy.
- Examination of the cytoprotective effects of these extracts in cellular models subjected to oxidative stress induced by hydrogen peroxide, focusing on intracellular reactive oxygen species levels and DNA integrity.
- Investigation of the modulation of key antioxidant enzymes and apoptotic markers through molecular assays including Western blotting and quantitative PCR, elucidating the underlying biochemical pathways affected.

This integrative strategy combines chemical, biological, and molecular analyses to unravel the multifaceted role of *Cymbopogon citratus* metabolites in attenuating oxidative stress and intervening in cancer-related pathophysiology. The study provides a scientific basis for further exploration of these compounds as phytopharmaceutical candidates and supports their potential inclusion in innovative cancer prevention and treatment regimens.

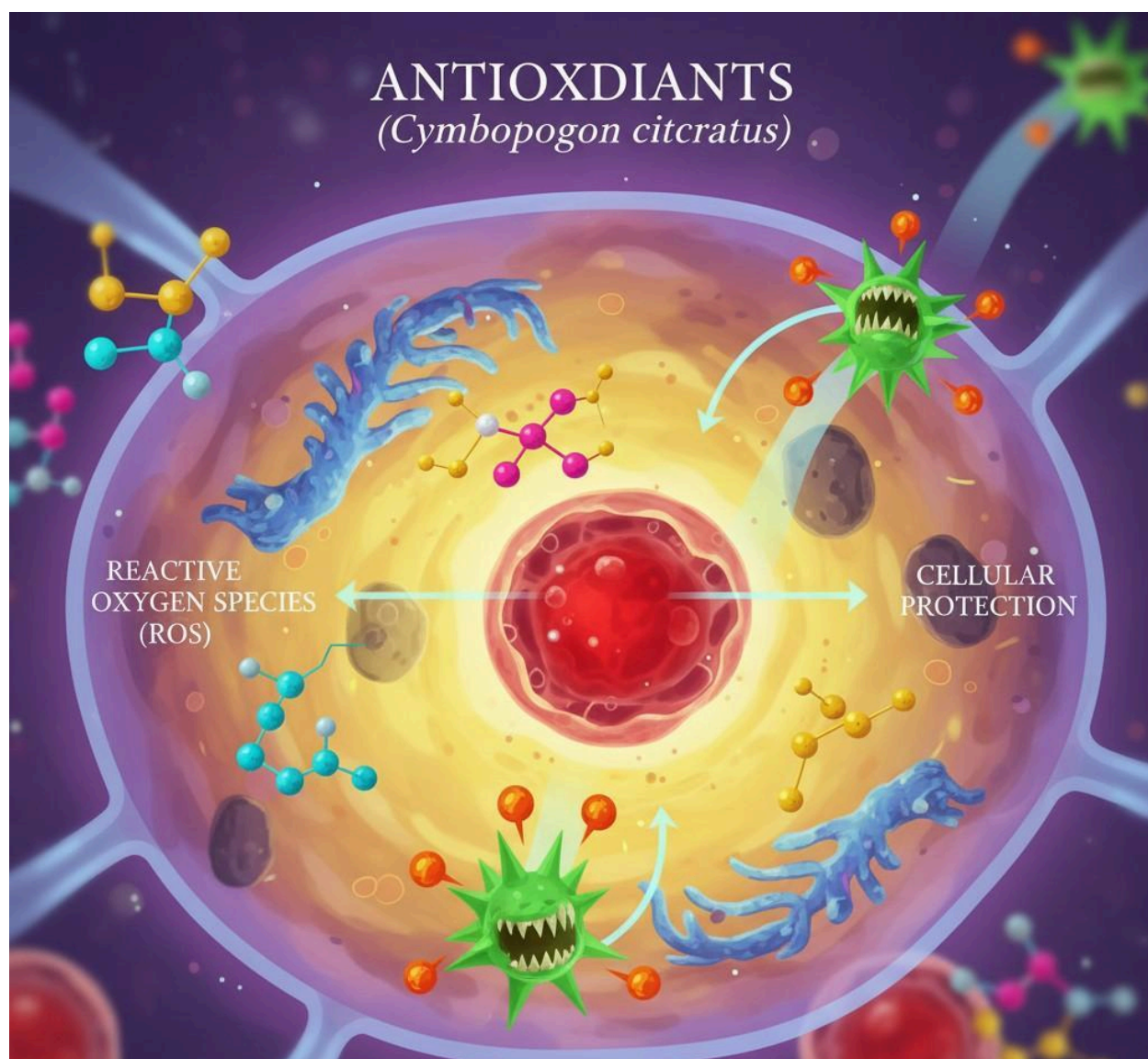


Figure X. Diagram of free radical neutralization by natural antioxidants

2. Materials and Methods

2.1. Plant Material Collection and Preparation

Fresh leaves of *Cymbopogon citratus* were collected from cultivated plants in the Kinshasa region, Democratic Republic of Congo. Leaves were thoroughly washed with distilled water to remove contaminants and allowed to air dry at ambient temperature until constant weight was reached. The dried leaves were finely ground using a mechanical grinder to produce a homogenous powder, ensuring consistency for subsequent extraction procedures.

2.2. Extraction Procedures

Sequential extraction was applied to obtain polar and non-polar fractions. Approximately 100 g of powdered leaf material underwent sonication-assisted extraction first with methanol (polar solvent) for 30 minutes at room temperature. Following filtration, the residue was then subjected to chloroform extraction (non-polar solvent) under the same conditions. Both extracts were concentrated via rotary evaporation under reduced pressure at 40°C and stored at 4°C until further phytochemical and biological analyses.



Figure X. Extraction process of compounds from *Cymbopogon citratus*

2.3. Phytochemical and Metabolomic Profiling

Chemical characterization was performed through nuclear magnetic resonance (NMR) spectroscopy using proton (^1H) and carbon (^{13}C) spectra at 600 MHz. Samples were dissolved in deuterated solvents—methanol- d_4 for methanolic extracts and chloroform- d for chloroformic extracts. Spectra were processed with Chenomx software for metabolite identification, focusing principally on polyphenols, terpenoids, and flavonoids classes. Complementary chromatographic methods, including thin layer chromatography (TLC) and liquid chromatography-mass spectrometry (LC-MS), were used to further resolve metabolite profiles.

2.4. Evaluation of Antioxidant Activity

The free radical scavenging activity of extracts was assessed using in vitro assays targeting stable radicals such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS). Serial dilutions ranging from 10 to 200 µg/mL were incubated with radical solutions, and absorbance readings were recorded spectrophotometrically. Half maximal inhibitory concentrations (IC₅₀) were calculated for comparative efficacy, using ascorbic acid as a positive control. All tests were performed in triplicate to ensure reproducibility.

2.5. Cellular Studies on Oxidative Stress and Viability

Human epithelial cell lines exposed to hydrogen peroxide (H₂O₂)-induced oxidative stress served as biological models. Cells were pre-treated with varying concentrations of *Cymbopogon citratus* extracts before oxidative challenge. Intracellular reactive oxygen species (ROS) were quantified by fluorescence with the probe dichlorofluorescein diacetate (DCFDA). DNA integrity was assessed via comet assay to evaluate strand breaks. Cellular viability was monitored to exclude cytotoxic confounders.

2.6. Molecular Biomarker Analyses

Quantitative RT-PCR and Western blotting quantified the expression of antioxidant enzymes, primarily superoxide dismutase (SOD) and catalase (CAT), at transcriptional and protein levels, respectively. Apoptotic markers were also evaluated to elucidate the modulation of cell death pathways by treatments. Statistical analyses were conducted using one-way ANOVA and Tukey's post hoc test, with significance defined as $p < 0.05$.

3. Results

3.1. Phytochemical Composition of *Cymbopogon citratus* Extracts

The metabolomic profiling of methanolic and chloroformic extracts revealed a complex mixture of bioactive secondary metabolites. NMR spectroscopy and chromatographic analyses identified key classes including polyphenols, terpenoids, and flavonoids. The methanolic extract was particularly enriched in polar compounds such as glycosylated polyphenols and flavonoids. Conversely, the chloroformic extract contained a higher proportion of non-polar terpenoids. These compositional differences underpinned the observed variance in biological activities between the two extracts.

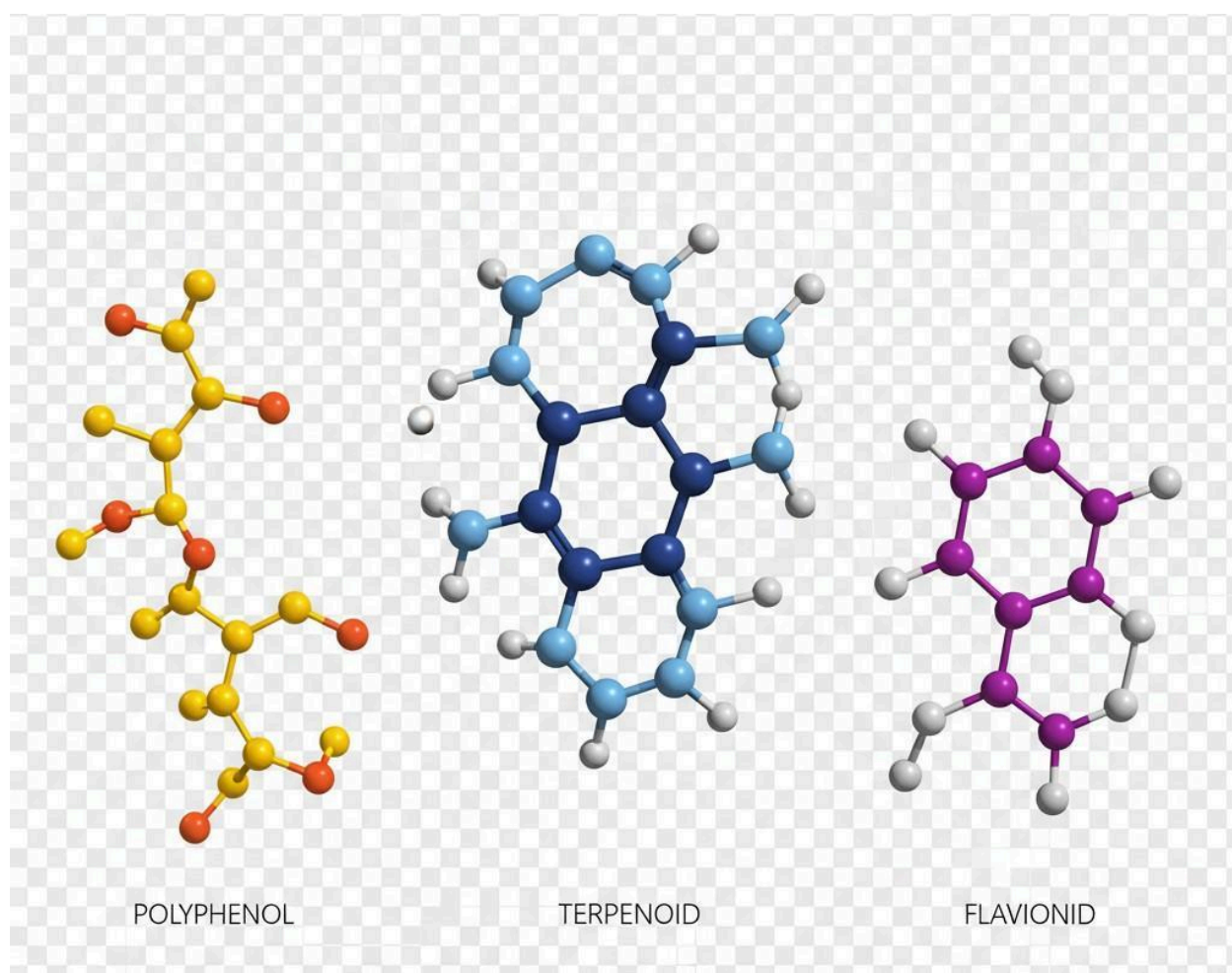


Figure X. Chemical structure of the main natural compounds of *Cymbopogon citratus*

3.2. In Vitro Antioxidant Activity

Assessment via DPPH and ABTS radical scavenging assays indicated superior antioxidant activity in the methanolic fraction. Dose-dependent increases in radical neutralization were recorded for both extracts; however, the IC₅₀ values demonstrated greater potency of the methanolic extract when compared to the chloroformic one. Ascorbic acid control exhibited the highest scavenging potency, serving as a benchmark.

3.3. Cellular Protection Against Oxidative Stress

In human epithelial cells challenged with H₂O₂ to induce oxidative stress, pretreatment with *Cymbopogon citratus* extracts significantly reduced intracellular ROS accumulation as revealed by DCFDA fluorescence. The methanolic extract conferred stronger cytoprotective effects, markedly decreasing DNA strand breaks as observed in comet assays. The chloroformic extract showed moderate, yet notable, protection. Cell viability assays confirmed the extracts' non-cytotoxic nature at effective concentrations.

3.4. Modulation of Antioxidant Enzymes and Apoptotic Markers

Quantitative molecular analyses revealed upregulation of key antioxidant enzymes SOD and CAT in cells treated with the methanolic extract. Western blot and RT-qPCR data confirmed increased protein and mRNA levels, indicating enhanced endogenous defense systems. Apoptotic markers were modulated consistent with early tumor suppressive activity, suggesting that *Cymbopogon citratus* extracts favorably influence cell fate under oxidative challenge. The chloroformic fraction induced similar effects but to a lesser degree.

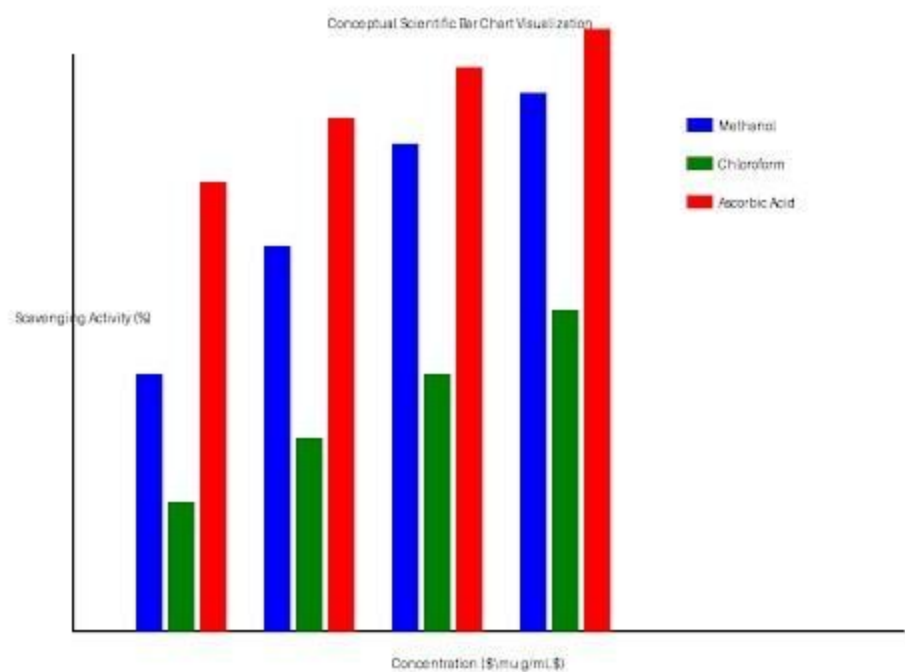


Figure X. Results of in vitro antioxidant activity (e.g., DPPH assay)

4. Discussion

The findings substantiate the therapeutic potential of *Cymbopogon citratus* secondary metabolites in mitigating oxidative stress—a critical factor in cancer initiation and progression. The methanolic extract's higher efficacy correlates with its abundance of polar antioxidant compounds, which effectively scavenge reactive oxygen species and prevent oxidative macromolecular damage. The moderate activity of the chloroformic extract suggests complementary roles of non-polar terpenoids, possibly through anti-inflammatory and signaling modulatory mechanisms.

This study highlights a coordinated biochemical framework, where polyphenols neutralize radicals and terpenoids modulate cellular signaling pathways regulating apoptosis and antioxidant enzyme expression. Such synergy underpins the chemopreventive properties of *Cymbopogon citratus*, advancing its candidacy as a phytotherapeutic agent in oncology.

The *in vitro* nature of this work invites cautious extrapolation to clinical contexts, emphasizing the need for further *in vivo* and pharmacokinetic studies to assess bioavailability and safety. Isolation of specific active compounds and mechanistic elucidation will potentiate the development of targeted phytomedicinal formulations.

CELLULAR PROTECTION: ANTIOXIDANT EFFECT OF CYMBOPOGON CITRATUS

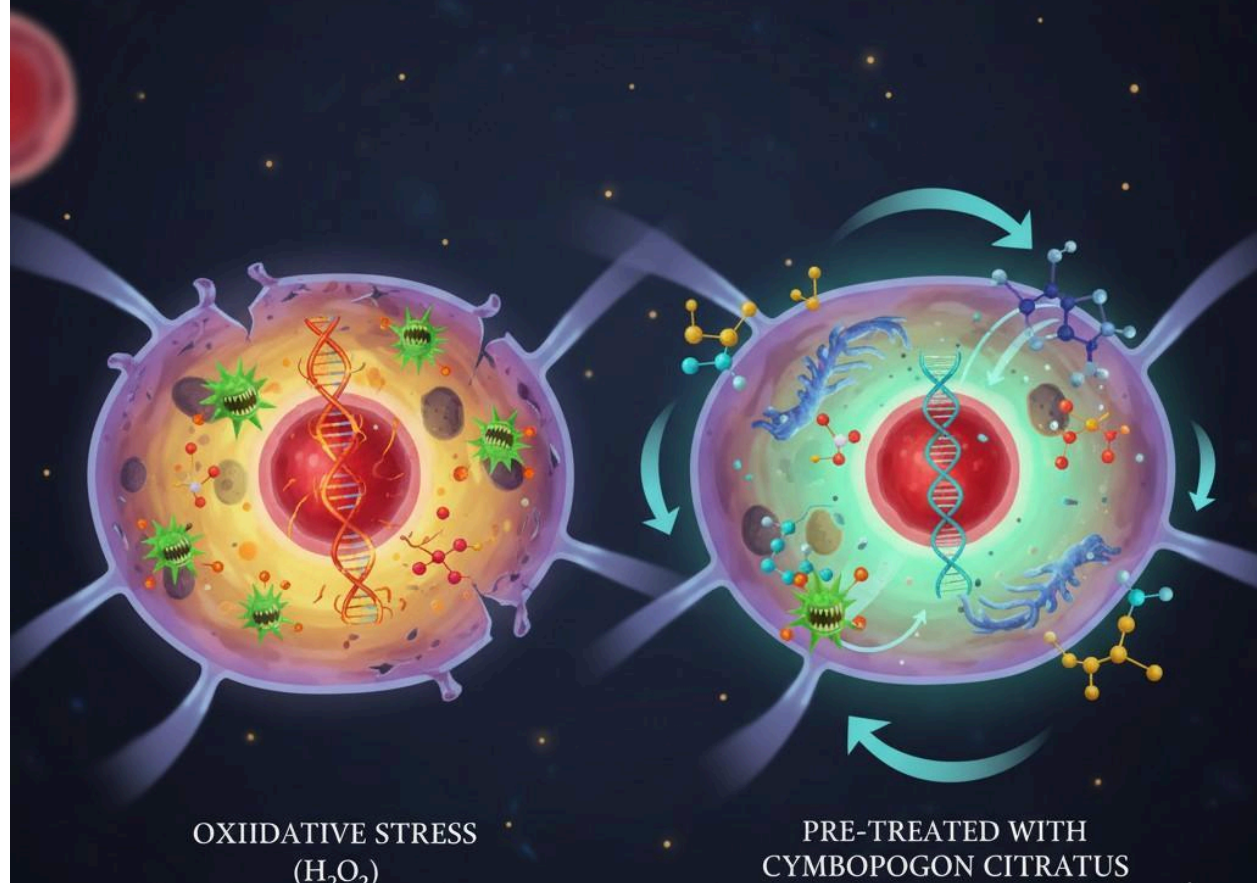


Figure X. Cellular impact of extracts on oxidative stress (e.g., cell diagram)

5. Conclusion

This study provides compelling evidence for the significant chemopreventive potential of *Cymbopogon citratus* leaf extracts through detailed phytochemical characterization coupled with robust functional assays. The diverse array of bioactive secondary metabolites identified, particularly polar polyphenols and terpenoids, play critical roles in mitigating oxidative stress and protecting cellular DNA from damage—key factors in tumor initiation prevention. The methanolic extract exhibited superior antioxidant and cytoprotective effects, underscoring the therapeutic promise of the polar fraction of these natural products.

From a pharmacological perspective, the enhancement of endogenous antioxidant defenses and modulation of apoptosis-related pathways establish a solid molecular foundation for the cancer-preventive properties of *Cymbopogon citratus* metabolites. These insights pave the way for the rational development of phytomedicinal formulations that harness the synergistic potential of multiple metabolite classes.

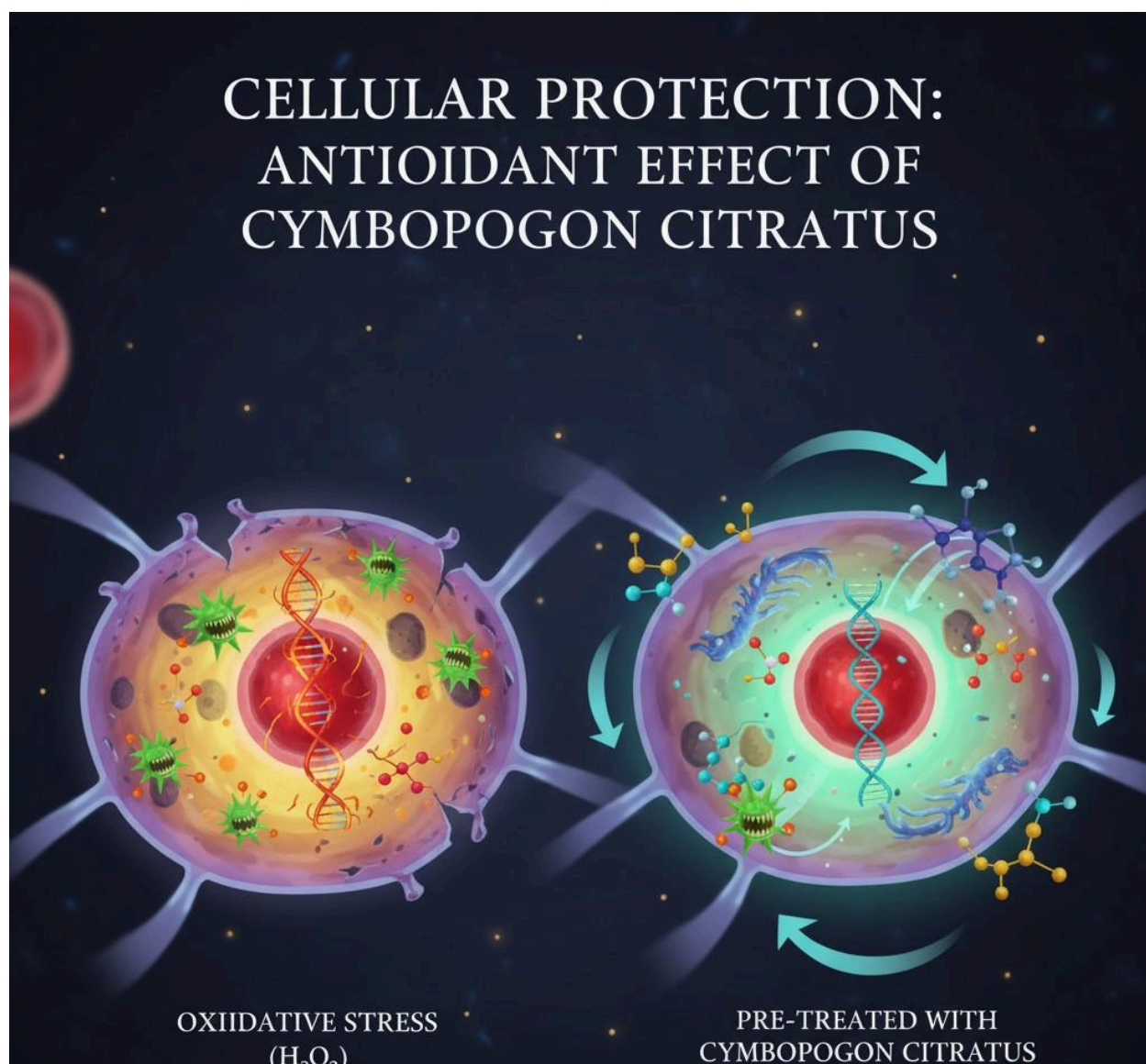


Figure X. Enzyme modulation and apoptosis

Moving forward, advancing these promising in vitro findings necessitates comprehensive in vivo studies and clinical trials to evaluate bioavailability, efficacy, and safety in physiological contexts. Further, isolating and characterizing individual active compounds will be critical for optimizing therapeutic formulations. Multidisciplinary approaches integrating metabolomics, pharmacokinetics, and toxicology are strongly recommended to fully elucidate the clinical utility of Cymbopogon citratus extracts as innovative agents in cancer chemoprevention.

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