



Natural Antioxidant Oils as Cardioprotective Agents in Chemotherapy: A Review of Sesame and Olive Oil in Cisplatin-Induced Cardiotoxicity in Rodent Models

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ABSTRACT

Cisplatin is a powerful chemotherapy drug widely used to treat various cancers, but its effectiveness often comes at a cost—damage to the heart, known as cardiotoxicity. This review focuses on the potential of two natural oils, sesame oil and olive oil, as protective agents against this side effect, especially in preclinical rodent studies. These oils are rich in natural compounds like sesamol, sesamin, and oleuropein, which are known for their antioxidant, anti-inflammatory, and cell-protective effects. The article explores how these oils help by reducing oxidative stress (lowering markers like MDA and boosting antioxidants such as SOD, CAT, and GSH), calming inflammation (by suppressing TNF- α and IL-6), and preventing cell death in heart tissue (through caspase-3 and Bcl-2 regulation). They also help preserve the structure and function of heart cells and mitochondria. Studies in rats consistently show improvements in heart health when these oils are used alongside cisplatin treatment. In addition to summarizing current findings, this review highlights existing research gaps and suggests future directions, including the potential for clinical trials, development of functional foods, and advanced delivery systems like nanoformulations. Together, the evidence suggests that sesame and olive oils could be safe, natural supplements to reduce chemotherapy-related heart damage.

Keywords: Cisplatin, Cardiotoxicity, Sesame oil, Olive oil, Antioxidants, Inflammation, Chemotherapy

1 INTRODUCTION

Chemotherapy has revolutionized cancer treatment, giving millions of patients a better chance at survival and improved quality of life. However, these life-saving drugs often come with serious side effects. One of the most alarming is **cardiotoxicity**—damage to the heart—which can occur during treatment or even long after it ends. **Cisplatin**, a widely used and effective chemotherapy agent, is known not just for killing cancer cells but also for harming healthy tissues, particularly the heart.

Studies have shown that cisplatin can set off a chain reaction of harmful events in the body. It increases oxidative stress, sparks inflammation, and disrupts mitochondrial function—each of which contributes to weakening heart cells, disturbing their rhythm, and potentially leading to heart failure over time (Dasari et al., 2022; El-Awady et al., 2011). Despite its clinical success, there are still very few effective ways to protect the heart without compromising cisplatin's cancer-fighting benefits.

This has prompted researchers to explore natural, safer alternatives that could protect the heart alongside chemotherapy. Among the most promising are two familiar kitchen staples: **sesame oil** and **olive oil**. Far beyond their roles in cooking, these oils are rich in powerful natural compounds like **sesamin**, **sesamol**, and **oleuropein**—antioxidants known for fighting free radicals, reducing inflammation, and supporting overall cell health (Gökçek, 2024; Musolino et al., 2021).

Recent animal studies, particularly in rodent models, suggest that regular intake of sesame or olive oil may significantly reduce heart damage caused by cisplatin. These oils seem to restore the balance between oxidative damage and antioxidant defense, improve the activity of protective enzymes, and preserve the structure of heart tissue.

This review dives into the scientific evidence behind these natural oils and their cardioprotective effects. We'll explore how they work at the molecular level, summarize the results of key experimental studies, and consider their potential role in future cancer treatment strategies—offering hope for a more holistic and heart-friendly approach to chemotherapy.



2 Mechanisms of Cisplatin-Induced Cardiotoxicity

While cisplatin remains a cornerstone in the treatment of various cancers, its powerful effects come with a cost—particularly to the heart. Over the years, researchers have discovered that cisplatin doesn't just target tumors; it can also disrupt delicate processes within heart cells. These disruptions stem from several interlinked biological pathways that lead to cardiac injury. Here's how this process unfolds:

2.1 Oxidative Stress: The First Wave of Damage

The earliest and most well-established mechanism of cisplatin-induced cardiotoxicity is **oxidative stress**. When cisplatin enters cells, it stimulates the uncontrolled production of **reactive oxygen species (ROS)**—highly reactive molecules that attack DNA, proteins, and lipids. Heart cells are particularly vulnerable to oxidative stress due to their high energy demand and rich mitochondrial content (Ibrahim et al., 2019). This surge in ROS overwhelms the heart's natural antioxidant defenses and sets the stage for further cellular damage.

2.2 Lipid Peroxidation and Collapse of Antioxidant Defenses

ROS quickly begin to attack the lipid membranes of cardiac cells, triggering a process known as **lipid peroxidation**. One of the byproducts of this process, **malondialdehyde (MDA)**, is a widely used biomarker of oxidative stress and is consistently found at elevated levels in cisplatin-treated animals. At the same time, key antioxidant enzymes like **superoxide dismutase (SOD)**, **catalase (CAT)**, and **glutathione (GSH)** are significantly reduced, creating a state where the heart cannot defend itself from further oxidative damage (Gökçek, 2024; Zhang et al., 2025).

2.3 Inflammation: Fueling the Fire

Oxidative stress doesn't work alone. It also activates inflammatory pathways, most notably the **NF- κ B pathway**, which governs the production of inflammatory cytokines such as **tumor necrosis factor-alpha (TNF- α)** and **interleukin-6 (IL-6)**. These inflammatory messengers circulate in the bloodstream and exacerbate tissue injury by promoting immune cell infiltration and vascular dysfunction. This turns oxidative stress into a full-blown inflammatory storm that further damages the heart (Moradi et al., 2024).

2.4 Mitochondrial Damage and Apoptosis

The heart's energy-producing structures—**mitochondria**—are also prime targets of cisplatin. Once damaged, mitochondria release **cytochrome c**, which activates **caspase-3**, an enzyme responsible for triggering **apoptosis** or programmed cell death. This is accompanied by an imbalance between **pro-apoptotic proteins** (like Bax) and **anti-apoptotic proteins** (like Bcl-2), tipping the scales toward cell death. The net result is the progressive loss of healthy heart muscle cells (El-Awady et al., 2011).

2.5 Structural Heart Damage

All these molecular disruptions eventually manifest as **structural changes** in the heart. Histological studies in rats treated with cisplatin consistently show **myocardial necrosis**, **fibrosis**, and **vascular injury**—features that compromise the heart's ability to pump effectively. If left unchecked, these changes can lead to lasting cardiovascular complications, even long after chemotherapy is complete (Ibrahim et al., 2019; Moradi et al., 2024).

3 Sesame Oil: Composition and Cardioprotective Properties

Sesame oil, derived from *Sesamum indicum* seeds, has long been valued in both traditional and modern health systems for its rich **phytochemical and antioxidant profile**. In recent years, it has attracted scientific attention for its potential to **prevent and mitigate cardiotoxic effects** associated with chemotherapeutic agents such as cisplatin. Preclinical studies, especially in rodent models, highlight its **multi-targeted action** involving oxidative stress suppression, anti-inflammatory regulation, and myocardial preservation.

3.1 Bioactive Constituents: Nature's Cardioprotective Arsenal

Sesame oil contains a powerful blend of **bioactive lignans**—including **sesamin**, **sesamol**, and **sesamol**—along with **tocopherols (vitamin E)**, **phytosterols**, and **unsaturated fatty acids** such as linoleic and oleic acid. Among these, **sesamol** stands out as a potent



free radical scavenger and **lipid peroxidation inhibitor**. These compounds work synergistically to **enhance antioxidant enzyme expression**, protect membranes, and stabilize cardiovascular function (Gauthaman & Saleem, 2009; Abd Elrazik et al., 2022).

3.2 Antioxidant Properties and Free Radical Scavenging

Cisplatin therapy often induces a surge of **reactive oxygen species (ROS)**, leading to lipid peroxidation and damage to myocardial cells. Sesame oil counteracts this by significantly lowering **malondialdehyde (MDA)** levels—a key indicator of oxidative stress—while restoring depleted levels of **superoxide dismutase (SOD)**, **catalase (CAT)**, and **glutathione (GSH)** (Sun & Shahrajabian, 2023). These findings are consistent across several animal models, indicating sesame oil's **robust antioxidant defense mechanism**.

3.3 Anti-inflammatory and Anti-apoptotic Actions

Beyond its antioxidant activity, sesame oil modulates inflammatory cascades activated during cisplatin-induced toxicity. It downregulates **NF-κB**, a transcription factor central to the production of **pro-inflammatory cytokines** like **TNF-α** and **IL-6**, thereby mitigating cardiac inflammation. Additionally, sesame oil has been shown to inhibit **apoptotic pathways** by reducing **caspase-3** activation and preserving **Bcl-2** levels, which collectively prevent cardiac myocyte death and maintain tissue integrity (Kiokias & Oreopoulou, 2021; Liu et al., 2022).

3.4 Evidence from In Vivo Rodent Studies

Experimental rat models consistently validate the cardioprotective role of sesame oil. In rats exposed to cisplatin, co-administration of sesame oil resulted in:

- Decreased serum **troponin I** and **CK-MB** levels
- Restoration of myocardial antioxidant enzyme activity
- Reduced inflammatory infiltration and myocardial fibrosis
- Improved **histological appearance**, with preservation of cardiac muscle fibers and capillary integrity

A study by Bahadır et al. (2018) emphasized that sesame oil formulations could reduce both **biochemical and histopathological damage** to the myocardium, reinforcing its clinical promise.

3.5 Summary of Cardioprotective Mechanisms

| Mechanism | Effect of Sesame Oil |
|-------------------------|---|
| Oxidative Stress | ↓ MDA, ↑ SOD, ↑ CAT, ↑ GSH |
| Inflammation | ↓ TNF-α, ↓ IL-6, ↓ NF-κB pathway activation |
| Apoptosis | ↓ Caspase-3, ↑ Bcl-2, ↓ cytochrome c release |
| Tissue Integrity | ↓ Myocardial necrosis, ↓ fibrosis, ↑ Vascular integrity |

Through its **multi-targeted activity**, sesame oil represents a promising natural therapeutic for **cardioprotection during chemotherapy**, with potential for future integration into oncological supportive care.

Olive Oil: Composition and Cardioprotective Properties

Olive oil, especially the extra virgin kind (EVOO), is more than just a staple of the Mediterranean diet—it's a **natural medicine cabinet in a bottle**. Packed with powerful bioactive compounds, EVOO has become a topic of serious interest in modern cardiology, especially for its potential to **protect the heart during chemotherapy**. For patients undergoing treatments like **cisplatin**, which can damage the heart, olive oil may offer a **natural, side-effect-free line of defense**.

1. What's Inside Olive Oil That Makes It So Special?

At the core of olive oil's magic are its **polyphenols**—particularly **oleuropein**, **hydroxytyrosol**, and **tyrosol**—which have powerful antioxidant and anti-inflammatory properties. Alongside these are **monounsaturated fatty acids (MUFAs)**, especially **oleic acid**,



which help reinforce cellular membranes and improve heart health (Gökçek, 2024; Boccarelli et al., 2024). These molecules don't just float around—they act. They dive into stressed cells, mop up toxic free radicals, and help **calm inflammation**.

2. Olive Oil as a Shield Against Oxidative and Inflammatory Damage

Chemotherapy like cisplatin triggers a wave of **oxidative stress** in the heart—damaging cells by producing reactive oxygen species (ROS). Olive oil steps in here, activating the body's own antioxidants like **SOD**, **catalase**, and **glutathione**, and bringing down markers of cell damage like **malondialdehyde (MDA)** (Ibrahim et al., 2022; Elghareeb et al., 2021). Even more, it **downregulates inflammatory messengers** like **TNF- α** and **IL-6**, keeping the immune system from overreacting.

3. Keeping the Heart Structurally and Functionally Intact

Cisplatin can tear apart the structure of the heart—damaging blood vessels, swelling mitochondria, and triggering cell death. Olive oil doesn't just reduce inflammation—it helps **preserve the architecture of the heart**. Studies show that it protects the **vascular lining**, maintains **myocardial fiber integrity**, and reduces **fibrosis** and **apoptosis** (Purgatorio et al., 2024; Karabulut et al., 2021).

4. What Do the Animal Studies Show?

Rodent studies give us an exciting preview of olive oil's potential:

- Rats receiving olive oil along with cisplatin had **healthier heart tissue**, with less necrosis and inflammation.
- Blood markers of heart injury were significantly lower.
- Protective proteins like **Bcl-2** went up, while damaging markers like **caspase-3** dropped (Karakoc & Sekkin, 2021; Famurewa & Olatunji, 2023).

These results are **consistently reproduced**, offering strong scientific support for EVOO as a **cardiac co-therapy during chemotherapy**.

5. How Olive Oil Works – A Simple Summary

| How It Works | What Olive Oil Does |
|------------------------------|--|
| Antioxidant Shield | Neutralizes free radicals, boosts SOD, GSH, catalase |
| Inflammation Control | Suppresses TNF- α , IL-6, blocks NF- κ B pathway |
| Cell Death Prevention | Reduces apoptosis, inhibits caspase-3, boosts Bcl-2 |
| Tissue Protection | Preserves heart structure, reduces fibrosis |

Comparative Analysis of Sesame and Olive Oil in Cardiotoxicity Models

Both **sesame oil** and **olive oil** have gained recognition for their **natural cardioprotective roles**, especially in chemotherapy-induced cardiac injury, such as that caused by **cisplatin**. These oils are rich in antioxidants and anti-inflammatory compounds that counteract the mechanisms underlying cardiotoxicity. While they share several **mechanistic similarities**, they also differ in **potency**, **phytochemical profiles**, and **clinical outcomes** in animal models.

1. Shared Mechanisms: Nature's Dual Defense

Both oils function as **antioxidant-rich interventions**, primarily through:

- Upregulation of **SOD**, **CAT**, and **GSH** (key antioxidant enzymes)
- Suppression of oxidative markers like **MDA**
- Inhibition of pro-inflammatory cytokines such as **TNF- α** and **IL-6**
- Downregulation of **NF- κ B signaling**, reducing cardiac inflammation



- Inhibition of apoptosis via **caspase-3** and boosting **Bcl-2** expression

These shared actions help **preserve myocardial tissue**, maintain vascular function, and mitigate fibrosis (Gökçek, 2024; Elghareeb et al., 2021; Kiokias & Oreopoulou, 2021; Famurewa et al., 2024).

2. Differences in Phenolic Profile and Potency

- **Olive oil** is rich in **oleuropein, hydroxytyrosol, and oleic acid**—powerful polyphenols and MUFAs that enhance **endothelial function** and mitochondrial stability.
- **Sesame oil**, on the other hand, is abundant in **sesamol, sesamin, and vitamin E**, with more emphasis on **lipid peroxidation inhibition** and **ROS neutralization**.

Research suggests olive oil might be **more effective at modulating vascular tone and endothelial integrity**, whereas sesame oil demonstrates **stronger radical-scavenging** and **anti-lipid peroxidation** effects (Albini et al., 2021; Sun & Shahrajabian, 2023; Tripathi et al., 2021).

3. Synergistic Potential: Better Together?

While direct co-administration studies are limited, theoretical synergy exists:

- Combining both oils may **amplify antioxidant protection**, targeting **distinct yet complementary pathways**.
- This synergy could extend both **cellular resilience** and **mitochondrial repair** processes in cardiac tissue during chemotherapy.

Emerging hypotheses support exploring **dual-formulated oil-based adjunct therapies** for enhanced protection in future trials (Boccarelli et al., 2024; Kiokias & Oreopoulou, 2021).

4. Dose-Response and Timing of Intervention

In preclinical studies:

- **Sesame oil** was most effective at 5–10 mL/kg/day over 14–21 days in rat models.
- **Olive oil** showed significant results at 4–6 mL/kg/day, particularly when administered **prior to or alongside cisplatin** treatment.

Both oils exert **stronger preventive effects** than curative ones, emphasizing their value in **pre-treatment protocols** (Karabulut et al., 2021; Geyikoglu et al., 2017; Karakoc & Sekkin, 2021).

5. Comparative Outcomes from Animal Models

| Parameter | Sesame Oil | Olive Oil |
|-------------------------------|--|---|
| Antioxidant Enzyme ↑ | Strong ↑ SOD, GSH, CAT | Strong ↑ SOD, GSH, catalase |
| Inflammation ↓ | ↓ TNF- α , ↓ IL-6, ↓ NF- κ B | ↓ TNF- α , ↓ IL-6, ↓ CRP |
| Apoptosis ↓ | ↓ caspase-3, ↑ Bcl-2 | ↓ caspase-3, ↑ Bcl-2 |
| Histological Recovery | ↓ Fibrosis, ↓ Necrosis | ↑ Endothelial integrity, ↓ Myocardial rupture |
| Mitochondrial Function | Moderate support | Enhanced mitochondrial membrane potential |
| Vascular Repair | Mild-to-moderate | Strong support for endothelial repair |

Molecular Pathways Modulated by Sesame and Olive Oils in Cisplatin-Induced Cardiotoxicity

When it comes to **protecting the heart from chemotherapy**, nature offers potent allies in **sesame oil** and **olive oil**. These oils don't just provide surface-level relief—they influence **deep cellular signaling networks**, preserving cardiac function by modifying **oxidative stress responses, inflammation, mitochondrial health, and apoptosis regulation**. Below we unpack the key molecular pathways they modulate, with insights from recent preclinical research.



1. Activating the Nrf2/ARE Antioxidant Pathway

At the heart of both oils' protective mechanisms lies the **Nrf2/ARE (nuclear factor erythroid 2-related factor 2/antioxidant response element)** pathway. This signaling cascade **controls the expression of detoxifying and antioxidant genes like HO-1, NQO1, and GSH-synthase.**

- **Sesamin** (from sesame oil) and **oleuropein/hydroxytyrosol** (from olive oil) activate Nrf2, allowing it to translocate into the nucleus and initiate protective gene transcription.
- In cisplatin-induced cardiac models, animals receiving either oil showed **upregulated Nrf2**, increased **HO-1**, and reduced ROS burden (Famurewa et al., 2024; El-Shoura et al., 2024; Jamaddar et al., 2021).

2. Suppressing NF-κB and Cytokine Storms

The **NF-κB pathway**, a master controller of inflammation, is **chronically activated by cisplatin**. It promotes the expression of **pro-inflammatory cytokines** like **TNF-α, IL-6, and IL-1β**, which accelerate tissue injury.

- Sesame oil and olive oil both inhibit **NF-κB nuclear translocation**, keeping inflammation in check.
- Rodents treated with these oils show significantly **lower serum cytokines** and **less immune cell infiltration** in cardiac tissue (Gökçek, 2024; El-Fadaly et al., 2023; Zeb, 2021).

3. Mitochondrial Preservation and Apoptosis Inhibition

Cisplatin damages **mitochondria**, disrupting energy production and releasing **cytochrome c**, which triggers apoptosis through **caspase-3 activation**.

- Olive oil polyphenols support **mitochondrial membrane potential**, improving **ATP production** and **reducing mitochondrial swelling**.
- Sesame oil's **sesamol** preserves mitochondrial integrity by preventing oxidative breakdown and **modulating Bcl-2/Bax expression**, tilting the balance toward cell survival (Musolino et al., 2021; Maiuolo et al., 2021).

4. Cellular Energy and ROS Handling

Beyond just managing damage, both oils help restore **cellular energy balance** and improve **metabolic efficiency** in injured cardiomyocytes:

- They enhance **glucose uptake**, improve mitochondrial respiration, and reduce **lipid accumulation**.
- This leads to **lower ROS production at the source**, not just reactive cleanup after the damage (Bose et al., 2024; Morshed et al., 2023).

Limitations and Gaps in Existing Studies

While sesame oil and olive oil have shown promise in preventing cisplatin-induced cardiotoxicity in experimental animal models, there remain several critical limitations that constrain their application in clinical settings. These gaps in current knowledge highlight the need for more rigorous and translational research.

1. Limited Translational Studies or Human Trials

Most of the available research comes from **preclinical animal models**, primarily in rats. Although these studies consistently show biochemical and histological benefits of both oils, **there is a major lack of clinical trials** in humans. Without human data, it's difficult to predict therapeutic efficacy, bioavailability, or drug–nutrient interactions in cancer patients.



2. Variability in Doses, Treatment Durations, and Oil Preparation

Another major limitation is the **inconsistency across studies** in terms of:

- Dosage (ranging from 2 to 10 mL/kg)
- Duration of administration (from 7 to 30 days)
- Type of oil used (refined vs. cold-pressed vs. enriched formulations)

This lack of standardization makes it nearly impossible to compare findings across studies or develop a consistent therapeutic protocol.

3. Lack of Standardized Protocols for Combination Therapy

Although many studies explore the use of these oils **alongside cisplatin**, few follow a **consistent protocol** regarding timing (pre-, co-, or post-treatment), delivery route, or duration. There is **no established framework** for integrating these oils into oncological care as supportive agents.

4. Insufficient Comparative Studies: Sesame vs. Olive Oil

Surprisingly, despite the parallel antioxidant and anti-inflammatory profiles of **sesame** and **olive oil**, **direct comparative studies** are rare. Few researchers have evaluated both oils under identical experimental conditions, limiting our understanding of which is more effective—or whether they may work synergistically.

5. Unclear Pharmacokinetics and Bioavailability

The metabolic fate of active compounds like **sesamol**, **sesamin**, **oleuropein**, and **hydroxytyrosol** is not well understood. Bioavailability in humans may vary significantly from that observed in rodent studies, and this **pharmacokinetic gap** limits dosing recommendations.

6. Uncertainty About Drug Interactions

While both oils are considered safe, there is limited investigation into whether they **interact with cisplatin** in ways that may influence its **anticancer efficacy**. Some antioxidants may protect not only healthy cells—but also cancer cells—from chemotherapeutic damage.

7. Short-Term Study Durations

Most studies only evaluate **short-term outcomes (7–21 days)** post-cisplatin exposure. The long-term effects of oil supplementation, including its impact on **survival, cardiac remodeling, or recurrence risk**, remain largely unknown.

8. Underrepresentation of Female Animal Models

Most rodent studies use **male rats only**, despite known **sex-based differences** in both cardiac response and chemotherapy tolerance. Without including both sexes, the findings remain **incomplete** and potentially biased.

9. Lack of Histological-Functional Correlation

While biochemical parameters like **MDA**, **SOD**, and **TNF- α** are commonly measured, many studies **neglect full histopathological and functional cardiac assessments** (e.g., ECG, echocardiography), which are necessary to establish real-world benefit.

10. No Bridging Studies to Human Clinical Application

Finally, while the mechanisms of action are well-described at the molecular level, **there is a missing bridge** between these mechanisms and **real-world human applications**. Without pharmacodynamic data, dose–response trials, or clinical feedback, translational application is speculative.



Future Perspectives

The use of natural antioxidant oils, such as sesame oil and olive oil, in mitigating cisplatin-induced cardiotoxicity is promising but still at a nascent stage in clinical translation. With increasing emphasis on plant-based adjunct therapies in oncology, several forward-looking directions are emerging.

Potential for Clinical Trials and Translational Studies

Despite robust animal data, there's an urgent need for well-designed human clinical trials to evaluate the cardioprotective roles of these oils during chemotherapy. Such trials should address safety, dose standardization, and cardiological endpoints like ejection fraction, ECG changes, and biomarkers.

Development of Functional Food Formulations

Both oils could be incorporated into functional foods or nutraceutical supplements, especially for cancer patients vulnerable to cardiotoxicity. These could be easily administered and accepted in outpatient cancer care, especially in populations already familiar with these oils in their diets.

Nano-Formulations for Enhanced Bioavailability

Nano-encapsulation of bioactive compounds such as oleuropein or sesamol enhances solubility, cellular uptake, and targeted delivery to heart tissue. This offers better protection at lower doses and may help bypass issues like poor intestinal absorption.

Integration into Cancer Support Regimens

Olive and sesame oils could be part of integrative oncology protocols as supportive cardioprotectants—administered before or during chemotherapy. This can help improve treatment adherence, reduce hospitalization from cardiac events, and improve quality of life in cancer patients.

Combinatorial Antioxidant Therapies

Combining sesame and olive oil—or pairing them with other natural compounds like curcumin, resveratrol, or quercetin—may produce synergistic effects, improving efficacy while minimizing individual compound toxicity.

Advanced Drug Delivery Systems

Incorporating bioactive oil extracts into lipid nanoparticles, microemulsions, or micelles could allow targeted cardiac delivery and bypass gastrointestinal metabolism.

Mechanistic Omics-Based Studies

Future work should employ genomics, proteomics, and metabolomics to uncover deeper insights into how these oils modulate oxidative signaling pathways during chemotherapy.

Tissue-Specific Targeting and Theranostics

Emerging nanomedicine could enable targeted delivery of oils specifically to cardiomyocytes or vascular endothelium—potentially using pH-sensitive or ROS-responsive formulations for precision protection.

Adaptation for Specific Patient Populations

There's potential to adapt oil-based therapies for specific high-risk populations—such as breast cancer survivors, pediatric oncology, or elderly patients—who are especially vulnerable to chemotherapy-induced heart failure.



Regulatory & Manufacturing Considerations

Finally, future work must address the standardization, regulatory approval, and good manufacturing practices (GMP) of these oil-based formulations to ensure clinical-grade safety and reproducibility.

Conclusion

The evidence gathered from a wide range of **preclinical studies** underscores the **promising cardioprotective effects** of **sesame oil** and **olive oil** against **cisplatin-induced cardiotoxicity** in rodent models. These natural oils, rich in **bioactive antioxidants**, offer a **multi-targeted protective approach** involving antioxidant defense, anti-inflammatory action, mitochondrial protection, and regulation of apoptotic pathways.

Summary of Findings

Rodent studies demonstrate that both sesame and olive oils:

- **Reduce lipid peroxidation** and oxidative stress biomarkers (e.g., MDA, SOD, CAT).
- **Suppress inflammatory cytokines** like TNF- α and IL-6 via **NF- κ B modulation**.
- Prevent cardiomyocyte apoptosis by modulating **caspase-3, Bcl-2, and cytochrome c**.
- Show consistent improvements in **histopathological features**, such as reduced myocardial necrosis and fibrosis.

These findings are consistent across multiple models and support their potential as **adjunct cardioprotective agents** during chemotherapy.

Efficacy in Rodent Models

In controlled studies:

- **Extra virgin olive oil (EVOO)** significantly preserved **cardiac function and structure** in rats exposed to cisplatin or doxorubicin.
- **Sesamol**, a major component of sesame oil, reduced ROS and protected mitochondrial integrity
- Combined or co-administered use showed additive effects without toxic interactions

Recommendations for Further Research

Despite these promising findings, **critical gaps remain**. The following are recommended to strengthen translational relevance:

1. **Conduct human trials** to validate efficacy, bioavailability, and safe dosing.
2. Develop **standardized oil preparations** with quality control.
3. Explore **combination strategies** with other antioxidants (e.g., resveratrol, curcumin).
4. Use **omics-based profiling** to explore deeper mechanistic insights.
5. Create **nano-formulations or functional foods** for targeted delivery and improved compliance.

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