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Review Article: Antioxidant Activity of *Ziziphus oenoplia* Leaves Extract in Rats

Krishnapal Nagda, Guide Dr. Jai Singh Vaghela

Abstract: ***This review evaluates the antioxidant activity of Z. oenoplia leaves extract by synthesizing findings from phytochemical analyses, in vitro assays, and in vivo studies in rat models. Phytochemical profiling reveals that the leaves are rich in polyphenolic compounds, particularly flavonoids, tannins, and phenols, which are key contributors to free radical scavenging activity. In vitro studies using methanol, aqueous, and ethyl acetate extracts demonstrate strong antioxidant activity across standard assays, including DPPH and hydrogen peroxide scavenging models. Evidence from in vivo research, notably in alloxan-induced diabetic rats, indicates that ethanolic and aqueous extracts exert significant hypoglycemic and hypolipidemic effects, indirectly reducing oxidative stress. Additional findings from studies on other plant parts, such as the roots, further support its protective role against oxidative and tissue injury. Collectively, these results suggest that Z. oenoplia leaves extract possesses both direct antioxidant activity through free radical neutralization and indirect benefits via metabolic regulation. However, the absence of studies in healthy animals using direct oxidative stress markers, such as superoxide dismutase (SOD), catalase (CAT), and malondialdehyde (MDA), highlights a critical gap. Future research should focus on establishing baseline antioxidant effects in normal physiology and elucidating molecular pathways to advance its therapeutic application.***

Keywords: Ziziphus oenoplia, antioxidant properties, phytochemical compounds, oxidative stress, metabolic regulation

1. Introduction

Antioxidants are natural or synthetic compounds that help protect the body's cells from oxidative stress, which is caused by free radicals. Free radicals are unstable molecules that can damage proteins, DNA, and cell membranes, contributing to aging and the development of diseases.

Types of Antioxidants

1. Enzymatic Antioxidants (produced by the body):

- Superoxide dismutase (SOD)
- Catalase
- Glutathione peroxidase

2. Non-Enzymatic Antioxidants (dietary sources):

- Vitamins: Vitamin C, Vitamin E, Vitamin A (as beta-carotene)
- Minerals: Selenium, Zinc, Copper
- Phytochemicals: Flavonoids, Polyphenols, Lycopene, Curcumin, Resveratrol

Sources of Antioxidants

- Fruits: Berries, grapes, oranges, pomegranates
- Vegetables: Spinach, kale, broccoli, carrots, tomatoes
- Nuts & Seeds: Almonds, walnuts, sunflower seeds
- Beverages: Green tea, coffee, red wine (in moderation)
- Herbs & Spices: Turmeric, ginger, cinnamon

2. Literature Review

Ziziphus oenoplia belongs to the family "Rhamnaceae". It is commonly known as Jackal Jujube or Small fruited jujube in English, Bahukantaka, Karkandhauh in Sanskrit, Shiakol in Bengali and pargi in Kannada. Ziziphus oenoplia mostly found in India, Pakistan, Bangladesh, Sri Lanka, Malaysia and Australia. It grows throughout India in dry forests and open bushy places along the roadside forests and thickets. The Roots, seeds and leaves are used in traditional & folklore Medicine. The pharmacological studies have shown that precatorius possesses a number of biological activities such as anti-bacterial, anti-cancer, anti-diabetic, anti-fertility, antimicrobial, antioxidant activity, anti-inflammatory, anti-arthritic, anti-seratonergic, nephroprotective etc.

Figure: Ziziphus oenoplia leaves

Pharmacological Profile and Bioactive Compounds

The foundation of Ziziphus oenoplia's medicinal potential lies in its rich composition of bioactive compounds. Scientific analysis has consistently shown that the leaves of this plant are a potent source of phytochemicals known for their health benefits (en. wikipedia. org). The antioxidant capacity of the plant is primarily attributed to its high concentration of polyphenols, particularly flavonoids and tannins (pmc. ncbi. nlm. nih. gov).

One study quantified the phytochemical content in a methanol extract of Z. oenoplia leaves, revealing significant amounts of beneficial compounds (pharmacologyonline. silae. it):

Total Phenol Content: 57.33 ± 3.18 mg gallic acid /g dried extract

Total Flavonoid Content: 116.19 ± 4.29 mg quercetin/g dried extract

Total Flavonols Content: 59.77 ± 0.15 mg quercetin /g dried extract

Total Condensed Tannins Content: 287.85 ± 0.54 mg catechin /g dried extract

Research indicates that flavonoids, in particular, may be the most crucial contributors to the antioxidant effects observed in the Ziziphus genus (pmc. ncbi. nlm. nih. gov). This rich chemical profile provides a strong basis for the extract's ability to neutralize harmful free radicals and protect cells from oxidative damage.

In Vitro Antioxidant Activity:

Establishing the Potential Numerous laboratory studies have firmly established the antioxidant capabilities of *Ziziphus oenoplia* leaves extracts. These in vitro assays are critical for confirming a substance's ability to combat oxidative stress before proceeding to animal or human trials.

Various solvents have been used to create extracts, with methanol, hot water, and ethyl acetate extracts all showing promising results. The methanol extract, in particular, often demonstrates superior performance, which is attributed to the high solubility of antioxidant phytochemicals in polar solvents (devagirijournals.com). These extracts have proven effective in several standard antioxidant tests, including the hydrogen peroxide scavenging assay and DPPH free radical scavenging model (pmc. ncbi. nlm. nih. gov). The mechanism in these tests is primarily based on the ability of the phenolic and flavonoid compounds within the extract to donate hydrogen atoms, thereby neutralizing unstable free radicals and stopping damaging chain reactions (devagirijournals.com).

These consistent in vitro results provide a strong scientific rationale for investigating the extract's effects in living organisms.

Analysis of In Vivo Studies in Rat Models

While direct research measuring standard antioxidant markers in healthy rats administered Z. oenoplia leaves extract is not widely available in the current literature, highly relevant findings come from studies using disease-specific rat models.

The most significant evidence is derived from a 2017 study by Mourya et al., which investigated the effects of ethanolic and aqueous extracts of *Ziziphus oenoplia* on alloxan-induced diabetic rats. This study is crucial because diabetes is a metabolic disorder characterized by chronic hyperglycemia, which leads to excessive production of reactive oxygen species and a state of severe oxidative stress.

3. Key Findings

Significant Hypoglycemic Effect: The leaves extracts were effective at lowering elevated blood sugar levels in the diabetic rats.

Potent Hypolipidemic Effect: The extracts also helped normalize blood lipid profiles, which are often disrupted in diabetes.

By mitigating hyperglycemia and hyperlipidemia, the extract directly addresses the root causes of oxidative stress in this disease model. This provides powerful indirect evidence of the extract's in vivo antioxidant activity. In essence, the extract helps protect the rats' bodies from the damage induced by the diabetic state.

Furthermore, other studies on rats using different parts of the plant lend support to its protective properties. For instance, root extracts of Z. oenoplia have demonstrated significant anti-ulcer and hepatoprotective (liver-protective) activities in rats, both of which involve protecting tissues from chemical and oxidative injury.

4. Summary

Ziziphus oenoplia (jackal jujube) leaves contain high levels of bioactive compounds, especially flavonoids, phenols, and tannins, which underpin their antioxidant potential. Laboratory studies (in vitro) consistently show strong free radical scavenging activity, particularly in methanolic extracts, due to the high solubility of antioxidant phytochemicals.

Animal studies (in vivo), though limited, provide important evidence. In diabetic rat models, leaves extract significantly reduced blood sugar and lipid levels, indirectly lowering oxidative stress. Additional studies with other plant parts suggest protective effects against ulcers and liver injury, both linked to oxidative damage.

The antioxidant action likely works through two mechanisms:

Direct - neutralizing free radicals via flavonoids and phenolic compounds.

Indirect - improving metabolic health, thereby reducing the production of harmful reactive oxygen species.

However, there is a research gap: no studies have yet measured direct antioxidant markers (e.g., SOD, CAT, MDA) in healthy rats treated with the extract. Future research should address this gap and explore molecular pathways to confirm its protective effects in broader disease models.

5. Conclusion and Future Research Directions

The available evidence strongly supports the conclusion that Ziziphus oenoplia leaves extract possesses significant antioxidant properties that are active in vivo. While its potential is firmly established through its rich phytochemical

content and consistent in vitro results, the primary in vivo evidence in rats comes from its proven ability to ameliorate the conditions of diabetes, a disease state defined by high oxidative stress.

The extract likely exerts its antioxidant effects in rats through a dual mechanism: direct neutralization of free radicals by its flavonoid and phenolic constituents, and an indirect effect by improving metabolic health, thereby reducing the systemic generation of reactive oxygen species.

A clear gap in the current research is the lack of studies focusing on healthy rats to measure direct antioxidant markers, such as the activity of endogenous enzymes like superoxide dismutase (SOD) and catalase (CAT), or levels of malondialdehyde (MDA), a marker of lipid peroxidation. Future research should aim to:

Quantify direct antioxidant effects in healthy rats to establish a baseline protective capacity.

Elucidate specific molecular pathways by measuring antioxidant enzyme levels in various tissues of rats treated with the extract.
Conduct further studies in other oxidative stress-related disease models to broaden the understanding of the extract's therapeutic applications.

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