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# Exploring the Anticancer Potential of Justicia tranquebarensis L.f: Mechanisms of Action, Phytochemicals, and Therapeutic Implications in Oncology and Radiotherapy

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**ABSTRACT**

*Justicia tranquebarensis* L.f., a tropical medicinal plant from the Acanthaceae family, has been traditionally used for its anti-inflammatory, antimicrobial, and analgesic properties. Recent studies highlight its potential as a source of bioactive compounds including flavonoids, alkaloids, terpenoids, saponins, and tannins with notable anticancer activities. Preclinical evidence demonstrates that these phytochemicals can induce apoptosis via intrinsic and extrinsic pathways, arrest the cell cycle at critical checkpoints, and inhibit metastasis by modulating matrix metalloproteinases (MMPs), vascular endothelial growth factor (VEGF), and related signaling pathways. In vitro and in vivo studies show that quercetin, kaempferol, trigonelline, and eugenol exert cytotoxic effects on multiple cancer cell lines and reduce tumor progression in animal models. Additionally, these compounds exhibit synergistic effects with conventional chemotherapeutic agents, enhancing their efficacy by overcoming drug resistance, increasing oxidative stress in tumor cells, and modulating drug efflux mechanisms. *J. tranquebarensis* compounds also provide protective effects during radiotherapy, mitigating radiation-induced oxidative damage, inflammation, and tissue injury in healthy cells. Despite promising preclinical findings, clinical validation remains limited, emphasizing the need for standardized extracts, optimized dosing, and rigorous pharmacokinetic and safety studies. Overall, *J. tranquebarensis* presents a multi-targeted therapeutic potential as an adjunct in cancer treatment, supporting conventional chemotherapy and radiotherapy while offering protective benefits to normal tissues. Future research should focus on mechanism-based clinical trials to fully realize its application in integrative oncology

**Keywords:** Justicia tranquebarensis; Anticancer; Phytochemicals; Apoptosis; Chemotherapy; Radiotherapy

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## INTRODUCTION

*Justicia tranquebarensis* L.f., a tropical medicinal plant belonging to the Acanthaceae family, is widely distributed in the coastal and sandy regions of India. Traditionally, it has been used in folk and Ayurvedic medicine for its anti-inflammatory, antimicrobial, and analgesic properties [1–2]. Recent studies have highlighted its potential as a natural source of bioactive compounds, including flavonoids, alkaloids, terpenoids, saponins, and tannins, which exhibit antioxidant, cytotoxic, and anticancer activities [3–5]. Cancer continues to be a major global health challenge, with conventional therapies such as chemotherapy and radiotherapy often associated with adverse effects, drug resistance, and limited selectivity toward cancer cells [6–7]. Consequently, there is growing interest in complementary and alternative approaches that utilize natural products to enhance treatment efficacy and reduce toxicity [8–9]. Plant-derived bioactive compounds can modulate key molecular pathways involved in cancer progression, including apoptosis, cell cycle regulation, angiogenesis, and metastasis [10–11].

Preclinical studies suggest that compounds isolated from *J. tranquebarensis,* such as quercetin, kaempferol, and eugenol, can induce apoptosis through both intrinsic and extrinsic pathways, inhibit tumor cell proliferation, and reduce metastasis by modulating matrix metalloproteinases (MMPs) and vascular endothelial growth factor (VEGF) signaling [12–14]. Additionally, these compounds may synergize with conventional chemotherapeutics and radiotherapy, enhancing cytotoxicity while protecting normal tissues from oxidative stress and inflammation [15–16]. Despite these promising results, clinical evidence for *J. tranquebarensis* in oncology is limited, underscoring the need for rigorous trials to evaluate safety, efficacy, and pharmacokinetics in humans [17–18].

This review aims to provide a comprehensive overview of *J. tranquebarensis*, focusing on its phytochemical constituents, molecular mechanisms of anticancer action, and potential as an adjunctive therapy in cancer treatment. By integrating preclinical findings, we highlight the prospects of this plant for mechanism-based anticancer therapies and its future translational potential in clinical oncology [12–14].

## Phytochemical Profile of *Justicia tranquebarensis*

*Justicia tranquebarensis* is a rich source of bioactive phytochemicals, which are believed to contribute to its traditional and modern therapeutic uses. The plant contains diverse classes of secondary metabolites, including flavonoids, alkaloids, terpenoids, saponins, and tannins, which have demonstrated antioxidant, anti-inflammatory, and anticancer properties in preclinical studies [19–22].

Flavonoids, such as quercetin and kaempferol, are among the most studied compounds in *J. tranquebarensis*, exhibiting strong antioxidant activity and the ability to induce apoptosis in cancer cells [23,24]. Alkaloids, including trigonelline and nicotine, have been reported to exert cytotoxic effects and modulate cellular signaling pathways [25]. Terpenoids such as eugenol and β-caryophyllene demonstrate anti-inflammatory and anticancer potential, partly by regulating oxidative stress and angiogenesis-related pathways [26,27]. Saponins and tannins also contribute to anticancer activity by promoting apoptosis and immune modulation [28,29].

The extraction of these phytochemicals is typically carried out using polar and non-polar solvents such as ethanol, methanol, and water, followed by chromatographic techniques like high-performance liquid chromatography (HPLC), thin-layer chromatography (TLC), and gas chromatography-mass spectrometry (GC-MS) for identification and quantification [30,31]. Standardized extracts of *J. tranquebarensis* have shown consistent bioactivity across studies, highlighting the importance of controlling extraction methods and seasonal variations to maximize therapeutic potential [32] [Table 1].

## Mechanisms of Anticancer Activity

The anticancer activity of *Justicia tranquebarensis* is mediated through multiple molecular mechanisms. Its bioactive compounds, particularly flavonoids (quercetin, kaempferol), terpenoids (eugenol), and alkaloids (trigonelline), modulate key cellular pathways involved in tumor progression, including apoptosis, cell cycle regulation, and metastasis [33–36].

### *Induction of Apoptosis*

Apoptosis, or programmed cell death, is essential for eliminating damaged or transformed cells. Compounds from *J. tranquebarensis* trigger apoptosis via both intrinsic (mitochondrial) and extrinsic (death receptor) pathways. Quercetin promotes mitochondrial membrane depolarization and activates caspase-3, whereas kaempferol enhances p53 expression and increases the Bax/Bcl-2 ratio, resulting in apoptosis [33–34]. Trigonelline activates caspase-3 and -8 cascades, and eugenol modulates Fas/FasL death receptor signaling to induce cell death [35–36].

### *Cell Cycle Arrest*

*Cell cycle arrest* is a critical mechanism for inhibiting tumor cell proliferation. Bioactive compounds from *J. tranquebarensis* inhibit cyclin-dependent kinases (CDKs) and upregulate checkpoint proteins. Quercetin induces G2/M phase arrest, kaempferol inhibits cyclin D1/CDK4 leading to G1 phase arrest, and trigonelline upregulates p21 to maintain G0/G1 phase arrest [33–34]. This halts uncontrolled proliferation and limits tumor growth.

### *Inhibition of Metastasis*

Metastasis contributes significantly to cancer-related mortality. Compounds from *J. tranquebarensis* inhibit invasion, migration, and angiogenesis. Kaempferol suppresses matrix metalloproteinases (MMPs) and VEGF signaling, quercetin modulates E-cadherin and tissue inhibitors of metalloproteinases (TIMPs), and eugenol inhibits VEGF and FGF pathways, collectively reducing tumour invasiveness [35–36] [Table 2].

## Therapeutic Implications in Oncology and Radiotherapy

The bioactive compounds of *Justicia tranquebarensis* not only demonstrate direct anticancer activity but also have significant implications in enhancing conventional cancer therapies. Their effects have been investigated in both chemotherapy and radiotherapy, highlighting potential synergy and protection of normal tissues.

## Synergistic Effects with Chemotherapy

Chemotherapy often faces challenges such as drug resistance, systemic toxicity, and limited selectivity. Preclinical studies suggest that compounds from *J. tranquebarensis* can enhance the cytotoxicity of conventional chemotherapeutics by modulating molecular pathways associated with apoptosis, drug efflux, and oxidative stress [37–39]. For example, kaempferol has been shown to increase doxorubicin-induced apoptosis by elevating oxidative stress, quercetin inhibits P-glycoprotein-mediated drug resistance to enhance paclitaxel efficacy, and eugenol sensitizes cancer cells to 5-fluorouracil while reducing metastasis [37–39] [Table 3].

## Adjunctive Role in Radiotherapy

Radiotherapy is a cornerstone of cancer treatment, but its efficacy

**Table 1:** Key Bioactive Compounds of *Justicia tranquebarensis.*

| Compound Class | Example Compounds | Pharmacological Activities |
|---|---|---|
| Flavonoids | Quercetin, Kaempferol | Antioxidant, anticancer, anti-inflammatory |
| Alkaloids | Trigonelline, Nicotine | Cytotoxic, antimicrobial, anticancer |
| Terpenoids | Eugenol, β-Caryophyllene | Anti-inflammatory, anticancer, antioxidant |
| Saponins | Various glycosides | Anticancer, anti-inflammatory, immunomodulatory |
| Tannins | Polyphenols | Antioxidant, anticancer, antimicrobial |

**Table 2:** Summary Table: Mechanisms of Action.

| Compound/Class | Target Pathway | Mechanism of Action | Effect |
|---|---|---|---|
| Quercetin (Flavonoid) | Mitochondrial pathway | Mitochondrial membrane depolarization, caspase-3 activation | Induces apoptosis |
| Kaempferol (Flavonoid) | p53 pathway, Cyclin/CDK | Enhances p53, alters Bax/Bcl-2 ratio, inhibits cyclin D1/CDK4 | Apoptosis induction, G1 phase arrest |
| Trigonelline (Alkaloid) | Caspase pathway, CDK inhibition | Activates caspase-3/8, upregulates p21 | Apoptosis and G0/G1 arrest |
| Eugenol (Terpenoid) | Fas/FasL, VEGF/FGF | Modulates death receptor signaling, inhibits angiogenesis | Apoptosis and anti-metastasis |
| Quercetin & Kaempferol | TIMPs, E-cadherin, MMPs | Downregulates MMPs, upregulates TIMPs | Reduced cell invasion and migration |

**Table 3:** Synergistic Effects with Chemotherapeutic Agents.

| Compound/Class | Chemotherapeutic Agent | Synergistic Mechanism | Observed Effect |
|---|---|---|---|
| Kaempferol (Flavonoid) | Doxorubicin | Enhances oxidative stress and apoptosis | Increased cytotoxicity |
| Quercetin (Flavonoid) | Paclitaxel | Inhibits P-glycoprotein-mediated drug efflux | Improved drug sensitivity |
| Eugenol (Terpenoid) | 5-Fluorouracil | Modulates metastasis pathways | Reduced invasion and metastasis |

**Table 4:** Protective Effects in Radiotherapy.

| Compound/Class | Radiation-Induced Side Effect | Mechanism | Observed Effect |
|---|---|---|---|
| Quercetin (Flavonoid) | Skin erythema, mucositis | Antioxidant, anti-inflammatory | Reduced tissue damage |
| Kaempferol (Flavonoid) | Fatigue, immune suppression | Immune modulation, oxidative stress reduction | Improved systemic tolerance |
| Eugenol (Terpenoid) | Oral ulcers, inflammation | Inhibition of pro-inflammatory cytokines | Reduced mucositis and ulceration |

**Table 5:** Future Perspectives and Clinical Considerations.

| Aspect | Consideration | Importance |
|---|---|---|
| Dosage and Administration | Determine optimal dose and route (oral, topical, etc.) | Ensures maximum efficacy and minimal side effects |
| Safety and Toxicity | Assess long-term safety, potential interactions with chemo/radiotherapy | Crucial for patient safety and clinical acceptance |
| Efficacy in Humans | Evaluate anticancer effects in clinical settings | Validates preclinical results and therapeutic potential |
| Standardization | Ensure consistent bioactive compound concentrations | Enables reproducible pharmacological activity |
| Regulatory Approval | Submit data for approval to FDA/EMA | Necessary for legal clinical use and market authorization |

may be limited by tumor resistance and collateral damage to healthy tissues. Compounds from *J. tranquebarensis* can potentiate radiotherapy by enhancing tumor cell apoptosis and protecting normal cells from radiation-induced oxidative damage [40–42]. Quercetin reduces DNA damage in healthy tissues while enhancing tumor radiosensitivity, kaempferol promotes pro-apoptotic signaling, and eugenol mitigates radiation-induced inflammation and tissue injury [40–42] [Table 4].

## Future Perspectives and Clinical Implications

Despite promising preclinical evidence, the clinical translation of *Justicia tranquebarensis* in oncology remains limited. Further research is needed to establish its efficacy, safety, and pharmacokinetics in humans [43–46]. The bioactive compounds, particularly flavonoids, alkaloids, and terpenoids, have demonstrated potential as adjuncts to conventional therapies, but well-designed clinical trials are essential to confirm these effects.

## Clinical Trials and Human Studies

Clinical studies should focus on determining optimal dosage, administration routes, and potential side effects when *J. tranquebarensis* is used alone or in combination with standard cancer therapies. Pharmacokinetic studies will provide insights into absorption, distribution, metabolism, and excretion of bioactive compounds, ensuring maximum therapeutic efficacy while minimizing toxicity [43–44].

## Standardisation of Extracts

Variation in bioactive compound content due to geographic location, seasonal changes, and extraction methods poses challenges for clinical application. Standardization using techniques such as high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS) is necessary to ensure consistent pharmacological activity and reproducible therapeutic outcomes [45].

## Safety and Regulatory Considerations

Before clinical use, safety evaluations must consider potential drug interactions, long-term toxicity, and compliance with regulatory guidelines such as those from the FDA or EMA. Preclinical studies suggest a favourable safety profile, but rigorous testing is required to prevent adverse effects and establish regulatory approval for clinical applications [46] [Table 5].

# CONCLUSION

*Justicia tranquebarensis* L.f. demonstrates considerable potential as a natural anticancer agent due to its rich composition of bioactive compounds, including flavonoids, alkaloids, terpenoids, saponins, and tannins. Preclinical studies indicate that these compounds

induce apoptosis, arrest the cell cycle, inhibit metastasis, and exhibit synergistic effects with conventional chemotherapy and radiotherapy.

The therapeutic potential of *J. tranquebarensis* extends beyond direct cytotoxicity; its bioactive constituents can enhance treatment efficacy while protecting normal tissues from oxidative stress and radiation-induced toxicity. Standardization of extracts, mechanistic understanding, and carefully designed clinical trials are crucial for translating these findings into safe and effective cancer therapies.

Overall, *J. tranquebarensis* represents a promising candidate for integration into modern oncology as an adjunctive natural therapy, offering a multi-targeted approach to enhance treatment outcomes and reduce adverse effects. Future research should focus on clinical validation, safety evaluation, and mechanism-based combination therapies to realize its full therapeutic potential in cancer care.

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