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**Letters to Editor**

# Thymoquinone and chemoresistance in non-small cell lung cancer: Preclinical promise or therapeutic potential?

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## To the Editor

Non-small cell lung cancer (NSCLC) accounts for approximately 85% of lung cancer cases and remains a major cause of cancer-related mortality worldwide. Despite advances in targeted therapies and immunotherapies, resistance to platinum-based chemotherapy, particularly cisplatin continues to undermine treatment success [1]. The quest for agents capable of modulating chemoresistance has drawn increasing attention to phytochemicals, among which thymoquinone (TQ), the principal bioactive component of *Nigella sativa L.* (black cumin), has demonstrated notable antitumor properties in preclinical research [2].

Emerging evidence suggests that TQ exhibits cytotoxic effects against various NSCLC cell lines, including A549 and H460, primarily through the induction of apoptosis, suppression of proliferation, and inhibition of metastatic potential [3-5]. Notably, Jafri et al. demonstrated that TQ synergistically enhanced the effects of cisplatin in H460 xenograft models, leading to significant tumor growth inhibition compared to either agent alone [6]. More recently, Gurbilek et al. reported that TQ sensitized H460 cells to both cisplatin and ionizing radiation by modulating PPAR-γ and NF-κB signaling, two pathways implicated in chemoresistance and inflammation-driven tumor progression [5].

Beyond its interaction with cisplatin, TQ has shown promise in targeting molecular pathways associated with therapy resistance. For instance, Gomathinayagam et al. discussed how TQ targets multiple oncogenic signaling pathways such as PI3K/Akt/mTOR, STAT3, and Bcl-2 which are implicated in promoting cell survival, proliferation, and resistance to chemotherapy in various cancer models [7]. In another recent study, Zhang et al. observed that TQ disrupted cancer stem cell (CSC) characteristics by promoting YAP degradation, thereby impeding self-renewal and tumorigenic potential [8]. Given that CSCs play a pivotal role in recurrence and resistance, these findings highlight a plausible mechanism by which TQ may mitigate therapeutic failure [8].

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Despite the preclinical promise, the therapeutic potential of TQ has yet to be confirmed through well-designed clinical investigations. TQ's poor water solubility, low bioavailability, and absence of standardized dosing have limited its transition from bench to bedside. Nonetheless, advances in drug delivery including nanoemulsion and liposomal formulations are being actively explored to improve pharmacokinetic performance and therapeutic index [9]. Furthermore, the absence of major adverse effects in animal models supports its potential as a safe adjuvant to conventional chemotherapy.

In conclusion, TQ, derived from black cumin, represents a compelling candidate for overcoming chemoresistance in NSCLC, particularly when used in combination with cisplatin. While the existing body of evidence supports its mechanistic plausibility and antitumor synergy, clinical trials are essential to confirm efficacy, optimize formulation, and establish safety in human populations. We advocate for rigorous translational research to clarify whether TQ's preclinical promise can be realized as therapeutic potential.

## Authors' contributions

Study design, Project administration, and Supervision: MAB, SHA. Data collection, Writing original draft, and Critical revisions: MAB, NK, SHA. All authors read and approved the final version of manuscript.

## Conflict of interest

No potential conflict of interest was reported by the authors.

## Ethical declarations

Not applicable.

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