Ind. J. Pharm. Edu. Res., 2026; 60(3):1152-1158.
https://www.ijper.org

Original Article

Xing Xia Di Tan Decoction Enhances Microwave Ablation and Chemotherapy in Lung Cancer: Molecular Insights from Network Pharmacology

Peixi Chen[1,#], Junming Huang[1,#,*], Shaoshan Du[1], Sili Deng[2]

[1]Department of Oncology, Panyu Hospital of Traditional Chinese Medicine, Panyu Hospital Guangzhou University of Chinese Medicine, Guangzhou, CHINA.
[2]Department of Traditional Chinese Medicine Nursing Clinic, Panyu Hospital of Traditional Chinese Medicine, Panyu Hospital GuangZhou University of Chinese Medicine, Guangzhou, CHINA.

ABSTRACT

Background/Aim: Non-small cell lung cancer (NSCLC) accounts for most lung cancer cases and remains a major health burden. Many elderly patients cannot tolerate targeted or immune therapies, or develop resistance, underscoring the need for alternative strategies. This study evaluated the synergistic effects of Xing Xia Di Tan Decoction (XXDTD), a Traditional Chinese Medicine (TCM) formula, with microwave ablation (MWA) and chemotherapy, and explored its molecular mechanisms. **Materials and Methods:** Network pharmacology was used to identify active compounds and potential targets of XXDTD, followed by pathway enrichment analysis. Experimental validation in A549 NSCLC cells included apoptosis detection (flow cytometry), BAX mitochondrial translocation (Western blot), RXRA expression (qPCR), and proliferation assays (CCK8). RXRA knockdown was performed using siRNA. **Results:** Network pharmacology identified RXRA, BAX, and CASP3 as key targets involved in apoptosis and chemoresistance pathways. XXDTD treatment increased apoptosis in a dose-dependent manner, promoted BAX mitochondrial translocation, and significantly upregulated RXRA expression. Silencing RXRA reversed XXDTD's inhibitory effects on cell proliferation and its synergy with cisplatin. The combination of XXDTD and cisplatin showed stronger antiproliferative activity compared with cisplatin alone. **Conclusion:** XXDTD enhances the efficacy of MWA and chemotherapy in NSCLC by activating BAX-mediated apoptosis and upregulating RXRA, thereby overcoming chemoresistance. These findings support the clinical potential of XXDTD as an adjunct therapy for elderly patients with advanced lung cancer.

Keywords: Lung cancer, Xing Xia Di Tan Decoction, Microwave ablation, Chemotherapy, Network pharmacology, RXRA, BAX.

Correspondence:
Dr. Junming Huang
Department of Oncology, Panyu Hospital of Traditional Chinese Medicine, Panyu Hospital Guangzhou University of Chinese Medicine, Guangzhou, CHINA.
Email: junminghuang1006@163.com

Received: 16-12-2025;
Revised: 25-02-2026;
Accepted: 06-04-2026.

INTRODUCTION

Lung cancer is the most common malignancy with the highest incidence and mortality rates worldwide. Non-Small Cell Lung Cancer (NSCLC) constitutes 80% to 85% of all lung cancer cases.[1,2] Despite recent advances in targeted therapy and Immune Checkpoint Inhibitors (ICIs) that have significantly improved patient survival rates, many elderly patients with advanced NSCLC are unable to tolerate these therapies due to their physical condition or adverse reactions, or they develop drug resistance, leading to treatment failure.[3-5] Therefore, exploring new and effective treatment strategies for elderly patients with advanced lung cancer is of great clinical significance.

Currently, the treatment of lung cancer involves a combination of surgical resection, radiotherapy, chemotherapy, molecular targeted therapy, immunotherapy, and Traditional Chinese Medicine (TCM).[6-10] TCM has demonstrated efficacy in inhibiting tumor progression, alleviating symptoms, and improving patients' quality of life.[11-13] Xing Xia Di Tan Decoction (XXDTD), a TCM formula derived from the extensive clinical experience of Professor Zhou Daihan, has shown promising results in the treatment of lung cancer. This formula is composed of multiple herbs, including *Aconiti Lateralis Praeparatus, Pinelliae Rhizoma Praeparatum, Gecko, Coicis Semen, Houttuyniae Herba, Herba Hieracii, Platycodonis Radix, Armeniacae Semen Amarum, Trichosanthis Fructus*, and *Fritillariae Cirrhosae Bulbus*. It follows the TCM principle of "treating phlegm" as the core, aiming to resolve phlegm and detoxify, disperse stasis and nodules, and strengthen the spleen and dry dampness. In clinical

DOI: 10.5530/ijper.20263058

practice, XXDTD has been used to treat patients with lung cancer, particularly those with phlegm-dampness and blood stasis syndrome, and has achieved positive therapeutic effects in improving symptoms, reducing tumor size, and enhancing patients' quality of life.

In recent years, Microwave Ablation (MWA) has emerged as a promising minimally invasive therapeutic technique for lung tumors.[14,15] It works by inducing cancer cell apoptosis through heat-induced Reactive Oxygen Species (ROS) upregulation and endoplasmic reticulum stress or mitochondrial apoptosis pathways.[16] Combining TCM with MWA may enhance therapeutic efficacy and reduce adverse effects.[17]

This study aims to investigate the clinical efficacy of XXDTD combined with MWA and chemotherapy in elderly patients with advanced lung cancer. We will also explore the underlying molecular mechanisms used *in vitro* experiments. Our findings may provide new insights into the treatment of advanced lung cancer in elderly patients and offer a theoretical basis for the clinical application of XXDTD.

MATERIALS AND METHODS

Network Pharmacology Analysis

Network Enrichment Analysis of Active Components in Traditional Chinese Medicine

The chemical components of each herb in the Xingxia Ditanchen Decoction were retrieved from the Herb Group Identification database (http://herb.ac.cn/).[18] Cytoscape software was used to construct a "Traditional Chinese Medicine - Component" network for each herb and its components. The cytoHubba plugin was employed to analyze the network, and the top twenty key components were selected based on Radiality as the main components of the prescription.

Active Components - Gene Network Analysis

For each component, the corresponding target genes were retrieved from the Herb Group Identification (http://herb.ac.cn/) database. Cytoscape was used to construct the network visualization of active components and potential targets. On the STRING platform, the species was limited to human (Homo sapiens), and the confidence threshold for protein-protein interactions was set to medium confidence (0.4), with other parameters set to default, to generate the target protein interaction network.[18]

Active Components - Gene Network Enrichment Analysis

Subsequently, the Network Analyzer tool was employed to analyze the topological characteristics of the gene network.[18] With the Radiality score as the screening criterion, the top twenty key nodes were selected to screen the core active components and key target genes.

Pathway Enrichment Analysis

The Database for Annotation, Visualization, and Integrated Discovery (DAVID) were employed for Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG).[18,19]

Experimental Validation

Cell Culture and Drug Preparation

Cell Line

The human non-small cell lung cancer cell line A549 was procured from the Chinese Academy of Sciences Cell Bank. Cells were cultured in RPMI-1640 medium supplemented with 10% Fetal Bovine Serum (FBS) and 1% penicillin-streptomycin and maintained at 37°C in a 5% CO_2 humidified incubator.

Drug Preparation

The herbal formulation (Rhizoma Arisaematis 15 g, Pinelliae Rhizoma Praeparatum 15 g, Gecko 5 g, Coix seed 30 g, Houttuynia cordata 30 g, Schizophylla 30 g, Prunella vulgaris 15 g, Platycodon radix 10 g, Prunus dulcis Batsch 10 g, whole Trichosanthis fructus 15 g, Panax notoginseng 5 g, Fritillaria zhejiang-fritillary 15 g) was decocted twice in distilled water (1 hr per cycle), filtered, and lyophilized. The resulting powder was dissolved in PBS to a stock concentration of 20 mg/mL, sterile-filtered (0.22 μm), and stored at –80°C. Quality control was performed via HPLC.

siRNA Transfection Protocol

Cells were seeded in a 24-well plate at a density of 250,000 cells per well in 500 μL of antibiotic-free RPMI-1640 medium with 10% FBS. After 24 hr, cells reached 30-50% confluency. For each well, 1.25 μL of *RXRA* siRNA (20 μM stock) was diluted in 100 μL of Opti-MEM culture medium (Invitrogen, 31985070) to achieve a final concentration of 50 nM. Lipofectamine 2000 (Invitrogen, 11668019) was diluted in 100 μL of Opti-MEM. The siRNA and Lipofectamine 2000 solutions were mixed and incubated at room temperature for 20 min. The mixture was then added dropwise to the cells. After 6 hr of incubation at 37°C in a 5% CO_2 incubator, the medium was replaced with fresh RPMI-1640 medium containing 10% FBS. Transfection efficiency was verified by qPCR after 48 hr. The siRNA sequences used in this study are listed below:

siRNA NC forward: 5'-UUCUCCGAACGUGUCACGU-3',

siRNA NC reverse: 5'-ACGUGACACGUUCGGAGAA-3';

RXRA siRNA 1 forward: 5'-AGUUAUCUUUGGAAAAAGGGG-3',

RXRA siRNA 1 reverse: 5'-CCUUUUUCCAAAGAUAACUCA-3';

RXRA siRNA 2 forward: 5'-UAGUAACAGAAAUAAGGAGGG-3',

RXRA siRNA 2 reverse: 5'-CUCCUUAUUUCUGUUACUACU-3';

RXRA siRNA 3 forward: 5'-UGAAGAAGAAGAGAUGUUCCA-3',

RXRA siRNA 3 reverse: 5'-GAACAUCUCUUCUUCUUCAAG-3';

Detection Methods

Flow Cytometry for Apoptosis Detection: Cells were harvested, washed with cold PBS, and resuspended in binding buffer. Annexin V-FITC and Propidium Iodide (PI) were added according to the manufacturer's instructions (KeyGen Biotech, KGA106). Samples were analyzed using a BD Calibur flow cytometer, and data were processed with CellQuest software.

Western Blot for *BAX* Mitochondrial Translocation: Mitochondrial and cytoplasmic fractions were isolated using a cell mitochondria isolation kit (Beyotime, C3601). Proteins were separated by SDS-PAGE, transferred to PVDF membranes, and probed with primary antibodies against *BAX* (Rabbit Anti-Mouse IgG, 1:1000, Abcam, ab32503) and COXIV (Rabbit Anti-Mouse IgG, 1:1000, Abcam, ab202554). Secondary antibodies were conjugated to horseradish peroxidase, and bands were visualized using an Electrochemiluminescence (ECL) detection system.

qPCR for *RXRA* Expression

Total RNA was extracted using Trizol reagent (Invitrogen, 15596026), and cDNA was synthesized with a PrimeScript II 1st Strand cDNA Synthesis Kit (TaKaRa, 6210A). qPCR was performed using TB Green® Premix Ex Taq™ (TaKaRa, RR420A) on an ABI VII a7 Real-Time PCR System. Primer sequences were as follows:

RXRA forward: 5'-GCCTACTGCAAGCACAAGTA-3',

RXRA reverse: 5'-GAAGGTGTCAATGGGTGTGT-3';

GAPDH forward: 5'-AACGGATTTGGTCGTATTGGG-3',

GAPDH reverse: 5'-CCTGGAAGATGGTGATGGGAT-3'.

CCK8 Assay for Cell Proliferation

Cells were seeded in 96-well plates and treated with various concentrations of XXDTD. After 24 hr, CCK8 solution (Beyotime, C0037) was added, and absorbance was measured at 450 nm after 4 hr of incubation. The proliferation rate was calculated using the formula: Proliferation rate = (mean OD value at other time points ÷ mean OD value at 0 hr - 1) × 100% (for the same sample).

RESULTS

Network Pharmacology Prediction

The network pharmacology analysis revealed key components and targets of XXDTD. The "Traditional Chinese Medicine - Component" network was constructed, and the top twenty key components were identified based on Radiality scores. The main active components included Quercetin, Beta-sitosterol, and others (Table 1, Figure 1A). The target genes for each component were retrieved, and the network visualization of active components and potential targets was constructed. The analysis revealed key targets including *RXRA, BAX, CASP3*, and others (Figure 1B). The core active components and key target genes were identified based on the Radiality score. GO and KEGG pathway enrichment analysis showed that the predicted targets are significantly involved in cell apoptosis (p=1.2E-8) and chemoresistance (p=4.5E-6) pathways. TCGA database analysis indicated that high expression of *RXRA* is associated with poor prognosis in patients with lung squamous cell carcinoma (HR=1.5, p=0.004; Figure 1C).

XXDTD Promotes Apoptosis in A549 Cells

Flow cytometry results showed that XXDTD significantly increased the apoptosis rate of A549 cells in a dose-dependent manner. The apoptosis rate in the XXDTD 20 mg/mL group was significantly higher than that in the control group (p<0.001; Figures 1D-I). The XXDTD treatment group showed a significant increase in early apoptotic cells and late apoptotic cells compared to the control group.

XXDTD Facilitates *BAX* Translocation to Mitochondria

Western blot analysis demonstrated that XXDTD treatment increased the level of *BAX* protein in the mitochondrial fraction of A549 cells. The results indicated that XXDTD promotes the translocation of *BAX* to mitochondria. The *BAX* protein level in the mitochondrial fraction of the XXDTD group was significantly higher than that in the control group (Figure 2A).

Table 1: Major Bioactive Components of Xingxia Tanqin Decoction.

ID	Ingredient Name	CAS ID	PubChem ID
HBIN041495	Quercetin	117-39-5	5280343
HBIN018278	Beta-sitosterol	83-46-5	222284
HBIN044730	Stearic acid	57-11-4	5281
HBIN038680	Palmitic acid	67701-02-4	985
HBIN044918	Stigmasterol	83-48-7	5280794
HBIN025965	Ethylpalmitate	628-97-7	12366
HBIN038026	Oleic acid	112-80-1	445639
HBIN044152	Sitogluside	474-58-8	5742590

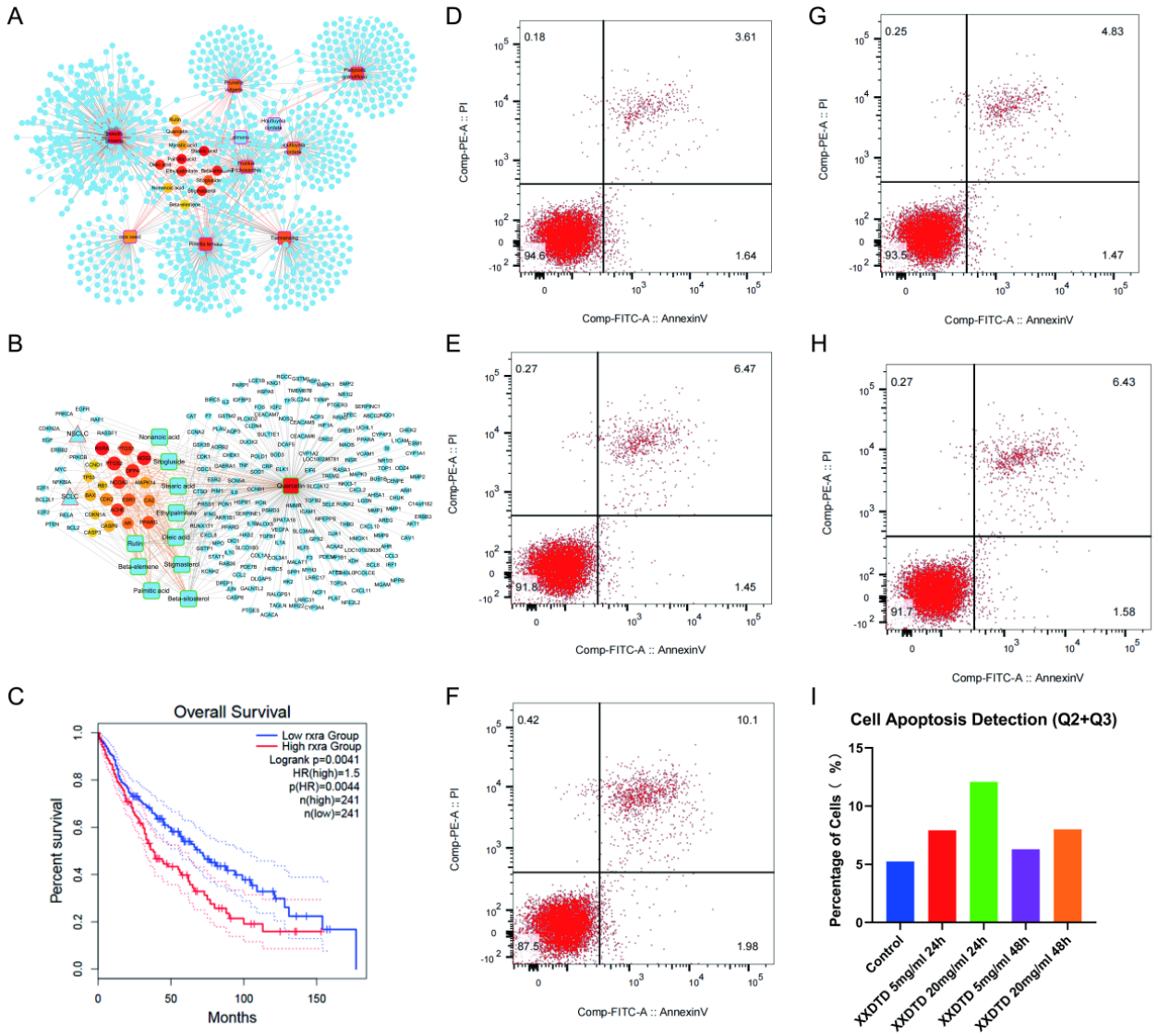

Figure 1: Integrated pharmacological analysis and experimental validation of the anti-lung cancer mechanism of Xingxia Tanqin Decoction (XXDTD). (A) Compound interaction network of XXDTD. The network illustrates interactions among herbal compounds, with node size representing the Radiality score of each component. (B) Compound-target network and Protein-Protein Interactions (PPI). Active compounds (green squares) and their corresponding target genes (blue circles) are displayed, with key targets (e.g., RXRA, BAX, CASP3) highlighted in orange. Node size corresponds to the Radiality score. Networks (A) and (B) were constructed using Cytoscape. (C) Prognostic value of RXRA in lung squamous cell carcinoma. Kaplan–Meier survival curve based on TCGA data shows that high RXRA expression is significantly associated with worse overall survival (HR = 1.5, p = 0.004). (D–I) XXDTD induces apoptosis in A549 cells in a dose- and time-dependent manner. (D–H) Flow cytometry plots of A549 cells under different treatment conditions: (D) Control; (E) XXDTD (5 mg/mL, 24 hr); (F) XXDTD (20 mg/mL, 24 hr); (G) XXDTD (5 mg/mL, 48 hr); (H) XXDTD (20 mg/mL, 48 hr). Quadrant definitions: viable cells (Annexin V^-/PI^-, Q3), early apoptotic cells (Annexin V^+/PI^-, Q4), late apoptotic cells (Annexin V^+/PI^+, Q2), necrotic cells (Annexin V^-/PI^+, Q1). (I) Bar chart summarizing total apoptosis rates (Q2 + Q4) across treatment groups.

XXDTD Upregulates *RXRA* Expression

qPCR results showed that XXDTD treatment significantly upregulated the expression of *RXRA* mRNA in A549 cells. The expression level of *RXRA* in the XXDTD group was 2.3 times higher than that in the control group ($p<0.01$; Figure 2B). The upregulation of *RXRA* expression suggests that XXDTD may enhance the chemosensitivity of lung cancer cells.

RXRA siRNA Reverses the Chemotherapeutic Effects of XXDTD

qPCR verified the transfection efficiency of *RXRA* siRNA. The results showed that *RXRA* siRNA significantly reduced the expression of *RXRA* in A549 cells. Among the three RXRA siRNAs, RXRA siRNA3 showed the highest transfection efficiency, significantly reducing RXRA expression and reversing the inhibitory effect of XXDTD on cell proliferation. Therefore, RXRA siRNA3 was selected for subsequent experiments (Figure 3A).

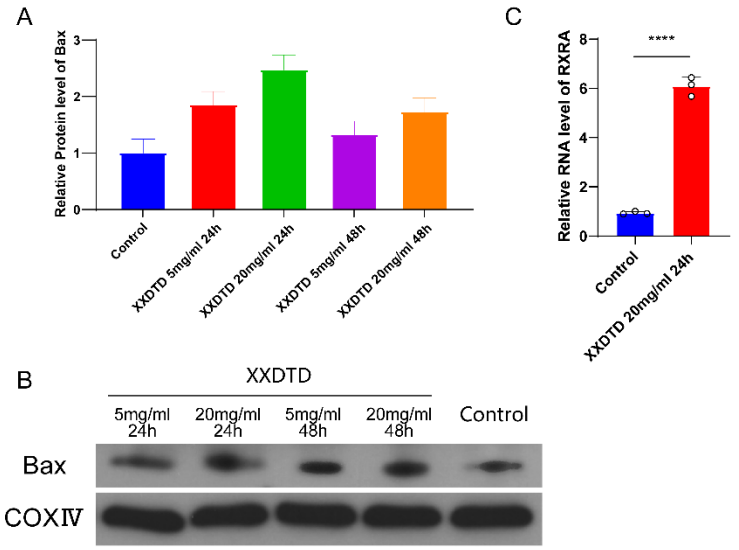

Figure 2: Effects of XXDTD on *BAX* Mitochondrial Translocation and *RXRA* Expression. (A) Quantification of *BAX* protein levels in the mitochondrial fraction of A549 cells treated with XXDTD at different concentrations and time points. Results are expressed as fold changes relative to the control group (Mean ± SD, *n*=3). (B) Representative Western blot images showing *BAX* and COXIV (mitochondrial marker) protein levels in A549 cells treated with XXDTD at various concentrations and time points. (C) *RXRA* mRNA expression levels in A549 cells treated with XXDTD (20 mg/mL, 24 hr) measured by qPCR. Results are expressed as fold changes relative to the control group (Mean ± SD, *n*=3, ***p*<0.01).

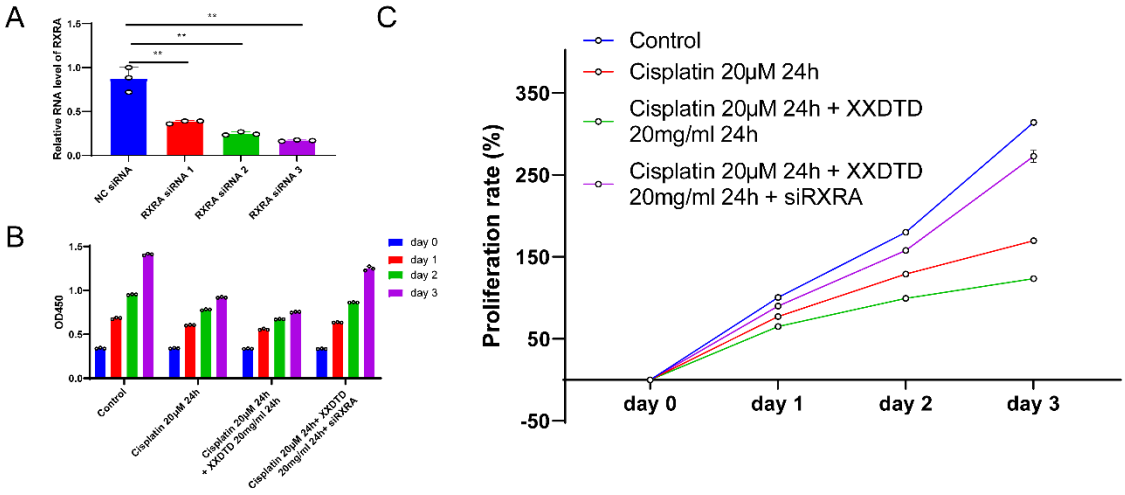

Figure 3: siRNA Screening and Cell Proliferation Assay. (A) qPCR results showing the screening of three *RXRA* siRNAs in A549 cells. *RXRA* siRNA3 demonstrated the highest knockdown efficiency, leading to its selection for subsequent experiments (mean ± SD, *n*=3, ***p*<0.01). (B) CCK8 assay results showing the OD450 values of A549 cells in different treatment groups: control group, cisplatin (20 μM), cisplatin + XXDTD (20 mg/mL), and cisplatin + XXDTD + *RXRA* siRNA. (C) Proliferation rates of A549 cells calculated from OD450 values, illustrating the inhibitory effect of XXDTD on cell proliferation and its reversal by *RXRA* siRNA (Mean ± SD, *n*=3, ***p*<0.01).

XXDTD Inhibits A549 Cell Proliferation and Synergizes with Cisplatin

CCK8 assay results showed that XXDTD treatment significantly inhibited the proliferation of A549 cells. The proliferation rate of cells in the XXDTD group was lower than that in the control group. Additionally, the combination of XXDTD and cisplatin further reduced the proliferation rate of cells compared to cisplatin alone, indicating a synergistic effect between XXDTD and cisplatin (Figures 3B-C).

DISCUSSION

This study provides the first comprehensive insight into the dual role of XXDTD in potentiating both microwave ablation and chemotherapy through distinct yet synergistic mechanisms. By promoting *BAX* mitochondrial translocation, XXDTD synergizes

with microwave ablation-induced heat stress to enhance apoptotic cell death. Additionally, XXDTD upregulates *RXRA*, a nuclear receptor with transcriptional activity, to reverse cisplatin resistance by activating downstream pathways like HtrA1.[20]

Our results confirm that XXDTD significantly increases apoptosis in A549 cells in a dose-dependent manner and promotes the translocation of *BAX* to the mitochondrial membrane. This *BAX* translocation is pivotal for mitochondrial apoptotic pathways, and when combined with the heat stress from microwave ablation, leads to a synergistic enhancement of apoptosis.[21,22] This is supported by previous research showing that hyperthermia can sensitize cancer cells to apoptosis through the upregulation of heat shock proteins and the amplification of mitochondrial apoptotic signals.[23,24] Furthermore, XXDTD markedly upregulates *RXRA* expression in A549 cells. *RXRA*, as a nuclear receptor, plays a crucial role in transcriptional regulation.[25] The upregulation of *RXRA* by XXDTD is linked to the activation of downstream tumor-suppressive pathways. Specifically, *RXRA* enhances the transcription of HtrA1, which is known to be involved in the sensitization of cancer cells to chemotherapeutic agents like cisplatin.[20] This finding aligns with the study by Wang *et al.*, which demonstrated that *RXRA* activation can restore cisplatin sensitivity in non-small cell lung cancer cells.[20]

The study also highlights the innovative mechanism by which XXDTD induces *BAX* mitochondrial translocation to synergize with microwave ablation. This mechanism is consistent with the study by Kong et al., which showed that hyperthermia can promote the translocation of *BAX* to the mitochondria and enhance apoptosis.[26] Our results further elaborate on how XXDTD can be used in combination with microwave ablation to improve therapeutic outcomes.

RXRA exhibits a "double-edged sword" characteristic.[27,28] While this study shows that *RXRA* upregulation promotes apoptosis, it also indicates that *RXRA* might suppress the immune response. This discrepancy may be attributed to the context-dependent role of *RXRA*, suggesting that its effects could vary with dosage and cellular environment. Therefore, optimizing the dosage of XXDTD to achieve the desired therapeutic effect while minimizing potential adverse effects is essential.

CONCLUSION

Finally, this research provides a molecular basis for the combined use of XXDTD with microwave ablation and chemotherapy, offering a new treatment strategy for elderly patients with advanced lung cancer who may have limited tolerance for conventional therapies. The TCGA database analysis indicates that high expression of *RXRA* is associated with poor prognosis in patients with lung squamous cell carcinoma (Figure 3). This implies that targeting *RXRA* may improve survival outcomes, offering a promising direction for future clinical research. However, studying has several limitations. Crucially, while we identified RXRA as a prognostic biomarker, its potential role as a predictive biomarker for treatment response, particularly concerning the XXDTD-based combination therapy, was not explored. We did not investigate whether *RXRA* expression levels could be used to identify patient subgroups most likely to benefit from this specific therapeutic strategy, which is essential for translating this finding into precise clinical applications and improving treatment accuracy. Furthermore, the study is limited by the absence of *in vivo* experiments to further validate the findings. Future research should incorporate animal models to evaluate XXDTD's therapeutic applicability across diverse populations (e.g., different age groups, NSCLC subtypes) in combination with microwave ablation and chemotherapy. Additionally, more in-depth studies are needed to explore the specific molecular mechanisms underlying the effects of XXDTD, particularly regarding the interaction between XXDTD and *RXRA*. Importantly, future work must also rigorously evaluate the clinical utility of RXRA, specifically its ability to predict response to the XXDTD combination therapy in prospective clinical cohorts.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

TCM: Traditional Chinese Medicine; **XXDTD:** Xing Xia Di Tan Decoction; **NSCLC:** Non-Small Cell Lung Cancer; **ICIs:** Immune Checkpoint Inhibitors; **MWA:** Microwave Ablation; **ROS:** Reactive Oxygen Species; **HPLC:** High Performance Liquid Chromatography; **siRNA:** Small Interfering RNA; **qPCR:** Quantitative Polymerase Chain Reaction; **PBS:** Phosphate Buffered Saline; **FBS:** Fetal Bovine Serum; **RPMI:** Roswell Park Memorial Institute; **TCGA:** The Cancer Genome Atlas; **RXRA:** Retinoid X Receptor Alpha; **BAX:** BCL2 Associated X Protein; **GO:** Gene Ontology; **KEGG:** Kyoto Encyclopedia of Genes and Genomes; **ECL:** Electrochemiluminescence; **COX:** Cytochrome C Oxidase; **HR:** Hazard Ratio.

FUNDING

This study was funded by the Panyu District Science and Technology Program [Grant No. 2022-Z04-089].

SUMMARY

Lung cancer is a major global health concern, with Non-Small Cell Lung Cancer (NSCLC) comprising 80–85% of all cases. Despite recent therapeutic advances, many elderly patients with advanced NSCLC cannot tolerate these treatments or develop resistance, necessitating novel strategies. This study investigates the synergistic effects of Xing Xia Di Tan Decoction (XXDTD), a Traditional Chinese Medicine (TCM) formula, in enhancing microwave ablation (MWA) and chemotherapy. Using network

pharmacology and experimental validation, we show that XXDTD promotes *BAX* mitochondrial translocation and upregulates *RXRA* expression, thereby overcoming chemoresistance. Our findings provide a molecular basis for the clinical use of XXDTD in elderly lung cancer patients, offering a promising new treatment strategy.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018; 68(6): 394-424. doi: 10.3322/caac.21492, PMID 30207593.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al.* Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021; 71(3): 209-49. doi: 10.3322/caac.21660, PMID 33538338.
3. Wang M, Herbst RS, Boshoff C. Toward personalized treatment approaches for non-small-cell lung cancer. Nat Med. 2021; 27(8): 1345-56. doi: 10.1038/s41591-021-01450-2, PMID 34385702.
4. Leader AM, Grout JA, Maier BB, Nabet BY, Park MD, Tabachnikova A, *et al.* Single-cell analysis of human non-small cell lung cancer lesions refines tumor classification and patient stratification. Cancer Cell. 2021; 39(12): 1594-1609.e12. doi: 10.1016/j.ccell.2021.10.009, PMID 34767762.
5. Memon D, Schoenfeld AJ, Ye D, Fromm G, Rizvi H, Zhang X, *et al.* Clinical and molecular features of acquired resistance to immunotherapy in non-small cell lung cancer. Cancer Cell. 2024; 42(2): 209-224.e9. doi: 10.1016/j.ccell.2023.12.013, PMID 38215748.
6. Li Y, Yan B, He S. Advances and challenges in the treatment of lung cancer. Biomed Pharmacother. 2023; 169: 115891. doi: 10.1016/j.biopha.2023.115891, PMID 37979378.
7. Chocarro L, Arasanz H, Fernández-Rubio L, Blanco E, Echaide M, Bocanegra A, *et al.* CAR-T cells for the treatment of lung cancer. Life (Basel). 2022; 12(4): 561. doi: 10.3390/life12040561, PMID 35455052.
8. Radovic M, Kanesvaran R, Rittmeyer A, Früh M, Minervini F, Glatzer M, *et al.* Multidisciplinary treatment of lung cancer in older patients: a review. J Geriatr Oncol. 2019; 10(3): 405-10. doi: 10.1016/j.jgo.2018.09.005, PMID 30292418.
9. Hoy H, Lynch T, Beck M. Surgical treatment of lung cancer. Crit Care Nurs Clin North Am. 2019; 31(3): 303-13. doi: 10.1016/j.cnc.2019.05.002, PMID 31351552.
10. Hori A, Dejima I, Hori S, Oka S, Nakamura T, Ueda S. Transarterial treatment of lung cancer. Life (Basel). 2022; 12(7): 1078. doi: 10.3390/life12071078, PMID 35888165.
11. Su XL, Wang JW, Che H, Wang CF, Jiang H, Lei X, *et al.* Clinical application and mechanism of traditional Chinese medicine in treatment of lung cancer. Chin Med J (Engl). 2020; 133(24): 2987-97. doi: 10.1097/CM9.0000000000001141, PMID 33065603.
12. Zhang W, Tian W, Wang Y, Jin X, Guo H, Wang Y, *et al.* Explore the mechanism and substance basis of Mahuang FuziXixin Decoction for the treatment of lung cancer based on network pharmacology and molecular docking. Comput Biol Med. 2022; 151(A) A(2022): . doi: 10.1016/j.compbiomed.2022.106293, PMID 36399857.
13. He Z, Wang Y, Han L, Hu Y, Cong X. The mechanism and application of traditional Chinese medicine extracts in the treatment of lung cancer and other lung-related diseases. Front Pharmacol. 2023; 14: 1330518. doi: 10.3389/fphar.2023.1330518, PMID 38125887.
14. Sebek J, Taeprasartsit P, Wibowo H, Beard WL, Bortel R, Prakash P. Microwave ablation of lung tumors: A probabilistic approach for simulation-based treatment planning. Med Phys. 2021; 48(7): 3991-4003. doi: 10.1002/mp.14923, PMID 33964020.
15. Shen X, Chen T, Liu N, Yang B, Feng G, Yu P, *et al.* MRI-guided microwave ablation and albumin-bound paclitaxel for lung tumors: initial experience. Front Bioeng Biotechnol. 2022; 10: 1011753. doi: 10.3389/fbioe.2022.1011753, PMID 36406211.
16. Shu M, Wang J, Xu Z, Lu T, He Y, Li R, *et al.* Targeting nanoplatform synergistic glutathione depletion-enhanced chemodynamic, microwave dynamic, and selective-microwave thermal to treat lung cancer bone metastasis. Bioact Mater. 2024; 39: 544-61. doi: 10.1016/j.bioactmat.2024.04.016, PMID 38883314.
17. Hu X, Zhang ZY, Wu LW, Zeng LH, Chen H, Zhu HJ, *et al.* A natural anthraquinone derivative shikonin synergizes with AZD9291 against wtEGFR NSCLC cells through reactive oxygen species-mediated endoplasmic reticulum stress. Phytomedicine. 2020; 68: 153189. doi: 10.1016/j.phymed.2020.153189, PMID 32070867.
18. Chen Y, Li K, Zhao H, Hao Z, Yang Y, Gao M, *et al.* Integrated lipidomics and network pharmacology analysis to reveal the mechanisms of berberine in the treatment of hyperlipidemia. J Transl Med. 2022; 20(1): 412. doi: 10.1186/s12967-022-03623-0, PMID 36076294.
19. Chi Q, Teng H, Zhao Y, Wang X, Zhang J, Shen H, *et al.* Design and synthesis of 3,4-seco-lupane triterpene-tryptamine derivatives and revealing their anti-bladder cancer mechanisms by combining TCGA and transcriptomic approaches. Sci Rep. 2025; 15(1): 19723. doi: 10.1038/s41598-025-04855-y, PMID 40473811.
20. Wang W, Zhao M, Cui L, Ren Y, Zhang J, Chen J, *et al.* Characterization of a novel HDAC/RXR/HtrA1 signaling axis as a novel target to overcome cisplatin resistance in human non-small cell lung cancer. Mol Cancer. 2020; 19(1): 134. doi: 10.1186/s12943-020-01256-9, PMID 32878625.
21. Smaili SS, Hsu YT, Sanders KM, Russell JT, Youle RJ. Bax translocation to mitochondria subsequent to a rapid loss of mitochondrial membrane potential. Cell Death Differ. 2001; 8(9): 909-20. doi: 10.1038/sj.cdd.4400889, PMID 11526446.
22. Charan RA, Johnson BN, Zaganelli S, Nardozzi JD, LaVoie MJ. Inhibition of apoptotic Bax translocation to the mitochondria is a central function of parkin. Cell Death Dis. 2014; 5(7): e1313. doi: 10.1038/cddis.2014.278, PMID 24991765.
23. Ahmed K, Tabuchi Y, Kondo T. Hyperthermia: an effective strategy to induce apoptosis in cancer cells. Apoptosis. 2015; 20(11): 1411-9. doi: 10.1007/s10495-015-1168-3, PMID 26354715.
24. Jo Y, Han YI, Lee E, Seo J, Oh G, Sung H, *et al.* The combination of tumor treating fields and hyperthermia has synergistic therapeutic effects in glioblastoma cells by downregulating STAT3. Am J Cancer Res. 2022; 12(3): 1423-32. PMID 35411245.
25. Chen Y, Zhang Z, Pan F, Li P, Yao W, Chen Y, *et al.* Pericytes recruited by CCL28 promote vascular normalization after anti-angiogenesis therapy through RA/RXRA/ANGPT1 pathway in lung adenocarcinoma. J Exp Clin Cancer Res. 2024; 43(1): 210. doi: 10.1186/s13046-024-03135-3, PMID 39075504.
26. Kong SP, Zhang X, Tan QW. Effects of electroacupuncture at "Jiaji" (EX-B 2) on myocardial apoptosis and the expression of Bcl-2 and Bax in rats with ischemia-reperfusion injury. Zhongguo Zhen Jiu. 2013; 33(6): 529-32. PMID 23967644.
27. Wang L, Zheng Y, Gao X, Liu Y, You X. Retinoid X receptor ligand regulates RXRalpha/Nur77-dependent apoptosis via modulating its nuclear export and mitochondrial targeting. Int J Clin Exp Pathol. 2017; 10(11): 10770-80. PMID 31966420.
28. Zhang XK, Su Y, Chen L, Chen F, Liu J, Zhou H. Regulation of the nongenomic actions of retinoid X receptor-α by targeting the coregulator-binding sites. Acta Pharmacol Sin. 2015; 36(1): 102-12. doi: 10.1038/aps.2014.109, PMID 25434990.

Cite this article: Chen P, Huang J, Du S, Deng S. Xing Xia Di Tan Decoction Enhances Microwave Ablation and Chemotherapy in Lung Cancer: Molecular Insights from Network Pharmacology. Indian J of Pharmaceutical Education and Research. 2026;60(3):1152-8.