

Introduction

Rhododendron arboreum Sm. is an evergreen small tree that belongs to the family Ericaceae, that has been traditionally used to treat various human ailments. This proposed study focused on exploring the phytochemical composition, antioxidant activity and anticancer potential of *R. arboreum*, particularly against gastric cancer.

Methodology

The qualitative and quantitative phytochemical analysis of *R. arboreum* leaves and flowers were conducted using standard methods. Functional groups were identified and characterized by FT-IR, NMR and GC-MS. Antioxidant capacity was evaluated using DPPH, ABTS, H₂O₂, LPO and FRAP assays. Cytotoxic effects on AGS gastric cancer cells were measured by MTT assay. *In vivo* analysis, the gastric cancer was induced in C57BL/6 mice with AGS cells, followed by oral treatment with *R. arboreum* extracts and standard drug for eight weeks. Post-treatment, histopathological and biochemical analyses were performed.

In silico studies, the SwissADME predicted the ADME properties and drug-likeness of active compounds. Network pharmacology identified target proteins linked to gastric cancer with PPI networks analysed via STRING and Cytoscape. Functional enrichment highlighted key pathways using DAVID and ShinyGO. Molecular docking and molecular dynamics simulations confirmed stable binding of bioactive compounds to cancer-related proteins, supporting their therapeutic potential.

Results

The proposed work involved a comprehensive analysis of aqueous, methanol, ethanol, acetone, chloroform and petroleum ether extracts of leaves and flowers showed the presence of diverse bioactive compounds. In quantitative analysis, the methanol extracts of both leaf and flower were significantly higher when compared to ethanol and acetone.

The antioxidant potential of the leaf extracts possessed stronger radical scavenging capabilities when compared to the flower extracts. For instance, the DPPH and ABTS test showed IC₅₀ values of 56.8±1.91 µg/mL and 60.7±2.13 µg/mL for leaves and 67.3±2.95 µg/mL and 65.9±1.97 µg/mL for flowers respectively. Similarly, In H₂O₂ and LPO assay, the leaf extracts exhibited higher inhibition rates when compared to the flower extracts. Whereas, the FRAP assay indicated that the flower extracts had superior reducing power, with activity increasing at higher concentrations than the leaf extracts.

In the cytotoxicity assay, the methanol extracts inflicted substantial damage to the AGS gastric cancer cell line. Whereas the anti-cancer potential of *R. arboreum* was evidenced by significant suppression of tumour growth in C57BL/6 mice model. In GC-MS spectrum revealed the presence of several bioactive compounds and cross-referencing with IMPPAT database identified ten compounds, which binds to 113 proteins, with 22 linked to gastric cancer via GeneCards. Cytoscape revealed a binary network with 10 nodes and 35 edges. ShinyGO identified 20 cancer-related enriched functions, including EGFR Tyrosine Kinase Inhibitor Resistance Among the identified compounds, quercetin showed the highest binding constant, with molecular dynamics confirming stable protein-ligand interactions over 100 ns.

Conclusion

This research highlights the significant phytochemical, antioxidant and anticancer properties of *Rhododendron arboreum* leaf and flower extracts. The *in vivo* results showing significant tumour suppression, alongside the identification of quercetin as a key bioactive compound providing a strong foundation for further investigation of *R. arboreum* as a source of novel anticancer agents for gastric cancer.

These findings pave the way for exploring the molecular mechanisms and potential as a plant -based therapeutic for gastric cancer. Future research will aim to strengthen the correlation between *in vitro* and *in vivo* results through detailed pharmacokinetic studies and exploring its efficacy against other cancer types to expand its translational applications.