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Repurposing FDA-approved antimalarial drugs: Mefloquine as a promising multi-targeted therapeutic for non-small cell lung cancer

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Lung cancer, particularly non-small cell lung cancer (NSCLC), remains a major global health challenge, accounting for 85% of cases. Despite progress in immunotherapy targeting mutations like EGFR, MET, and RET, issues such as drug resistance, high treatment costs, and limited efficacy persist. Drug repurposing has emerged as a promising strategy to overcome these obstacles. This study investigates the potential of FDA-approved antimalarial drugs as multi-target therapies for NSCLC. Fourteen antimalarial drugs have been screened using molecular docking, leveraging their established safety profiles. Mefloquine (MQ), artesunate, artemether, and quinine show strong binding affinities for EGFR, MET, and RET targets, with MQ exhibiting the most significant interactions. Molecular dynamics (MD) simulations have confirmed MQ's stability and favorable binding to these targets, supported by RMSD, RMSF, and Rg analyses. *In vitro* tests using the Sulforhodamine B (SRB) assay demonstrate a dose-dependent inhibitory effect of MQ on A549 NSCLC cell proliferation, with notable reductions in cell viability at concentrations as low as 10 μM. The findings suggest MQ's potential as a cost-effective therapeutic candidate for NSCLC treatment, either alone or in combination with other therapies. Further research is needed to explore MQ's anticancer mechanisms and optimize its clinical use.

Keywords: Repurposing, Antimalarial, Mefloquine, Docking, Dynamic simulation, Anticancer