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Name of the scholar – Dr Shoaib Alam

Name of the supervisor - Prof Mohammad Husain

Name of the Department- Biotechnology

Topic of research- "**Search for potential inhibitors against lung adenocarcinoma using structure based drug design approach**"

Findings

1. Tq and Qu showed appreciable binding affinities toward Bax (-6.2 and -7.1 kcal/mol, respectively) and Bcl2 (-5.6 and -6.4 kcal/mol, respectively) with well-organized conformational fitting compatibility
2. It was found that time-evaluation average RMSD values for Bax-Qu, Bax-Tq, Bcl2-Qu and Bcl2-Tq were found to be 0.25 nm, 0.20 nm, 0.37, and 0.32 nm respectively, confirming the stability of Bax and Bcl2 structures with thymoquinone and quercetin
3. The IC_{50} values of Tq and Qu alone in A549 cells were found to be 45.78±3.31 µM and 35.69±3.02µM, while that of Qu along with low dose Tq (10µM) the IC_{50} came out to be 22.49±2.76µM. Similarly, the corresponding IC_{50} values of Tq and Qu in H1299 cells were found to be 20.55±4.83µM and 35.09±0.21µM respectively; while that of Qu along with low dose Tq (10µM) the IC_{50} came out to be 25.90±3.21µM
4. In A549 cells, the total percent apoptosis values were 54%± 3.73(Tq), 37.6%±4.42 (Qu) and 60.8%±3.21 (Tq+Qu).
5. Further both the drugs (Tq and Qu) also led to an inhibition in overall cell migration against A549 cells, indicating some possible anti-metastatic role of such treatments

Summary of Abstract

Lung cancer mortality is projected to reach around 2.45 million worldwide by 2030. The treatments available for non-small cell lung cancer exert various side effects in patients, and the burden of treatment cost is high. Therefore, exploring the alternative system of medicines, including therapies based on natural compounds, has become inevitable in developing anticancer

therapeutics. Natural compounds have long been regarded as potential therapeutic alternatives to synthetic drugs because they are relatively safe, effective and affordable.. In various studies, increased Bcl2 expression was found in lung cancer tissues obtained from patients. Therefore, blocking Bcl2 expression could be a successful strategy to combat lung adenocarcinoma. Molecular docking followed by molecular dynamics (MD) simulation of Thymoquinone (Tq) and Quercetin (Qu) with Bax and Bcl2 were carried out to explore their interactions and stability under explicit solvent conditions. All-atom MD simulations showed that thymoquinone and quercetin induced minimal conformational alterations in Bax and Bcl2. The MD simulation results revealed the development of stable complexes. Further studies with these compounds were carried out using various *in-vitro* experimental approaches like MTT assay, apoptotic assay and Western blot. Studies showed that both thymoquinone as well as quercetin induced cytotoxicity/cell death in NSCLC (A549 and H1299) cells .The results show that though Tq and Qu show strong apoptotic induction via binding to Bax and Bcl-2 proteins to induce programmed cell death in NSCLC.