Gamma-glutamyl Transpeptidase Inhibition: Combating Multi-Drug Resistance

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Multi-drug resistance (MDR) is a condition enabling disease causing microorganisms to resist distinct antibiotics. At present, the only way to fight against this problem is to develop a new drug against that microorganism. Gamma glutamyl transpeptidase (GGT) is an enzyme that plays a key role in the gamma-glutamyl cycle, a pathway for the synthesis and degradation of glutathione and drug, and helps in the peptide and amino acid uptake as well. Thus, specifically inhibiting microbial GGT is seen as the solution against MDR. In the presented study, E.coli was taken as the model microorganism. Antibiotic profiling of the E.coli BL21 strain was done. The screening of the natural products was done by the in-silico study to find out drug accompanying specific microbial GGT inhibitor followed by the GGT assay to study the effect of the screened product over the enzyme. Minimum Inhibition Concentration (MIC) was determined and antibiotic profiling of the E.coli BL21 strain in presence of curcumin was done. To study the mechanism behind the link of GGT inhibition and MDR, glutathione export was observed. In-silico study indicated that Curcumin can be used as a specific microbial GGT inhibitor. It was observed that GGT inhibition action of curcumin was different from its anti-microbial action. According to antibiotic profiling, curcumin increases antibiotic sensitivity of the E.coli BL21 strain. Thus, the proposed idea is a novel way to combat MDR.

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