Executive Summery

Tuberculosis is a transmittable disease triggered by Mycobacterium tuberculosis, a small, aerobic, nonmotile bacillus. TB is curable. However, the bugs that cause TB are strong and it can take a long time for them to die. Active TB (when there are symptoms) is treated with a combination of antibiotics for at least 6 months. Antibiotic resistance is a growing problem with increasing rates of multiple drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB).

The present study has utilized most advanced computer aided drug designing tools for finding out of more promising lead systems from phytochemical repository. The most fundamental goal in drug design is to predict whether a given molecule will bind to a target and if so, how strongly. Computational methods are an important part of the drug design process and is often referred as Computer-Aided Drug Design (CADD). It helps in identifying potent drug molecules and targets via bioinformatics tools, evaluate the target structures for possible active sites, generate active drug molecules and check for their dynamic and kinetic properties. Computational methods also help to predict the affinity of a compound before it is synthesized and hence only one compound needs to be synthesized, saving enormous time and cost. In practice, it still takes several iterations of design, synthesis, and testing before an optimal drug is discovered. Computational methods have accelerated discovery by reducing the number of iterations required and have often provided novel structures. . Docking studies, one of the techniques of drug design helps to know the affinity and efficacy of developed molecule and rank them according to their binding affinities. The molecules which are showing better activity can be modified and build to get good activity towards the target molecules, further optimize the molecules to improve binding characteristics.Docking is regularly used in different stages of drug design strategies, such as to facilitate design of potentially active leads.

Protein characterization studies revealed the significance of DprE1 (decaprenylphosphoryl-beta-d-ribose oxidase) as potential target enzyme. Primary and secondary structure analysis has carried out on twenty protein targets and found the efficiency of the crystal structure 4FEH for molecular docking studies. Molecular docking studies has revealed the leadlikeness of ellagic acid and quercertin , promising anti-inflammatory phytochemical compounds.

QSAR analysis on a set of DprE1 inhibitors revealed the significance of physicochemical properties such as A logP2, nBonds2, nHBint7, minHBd, maxHBint6, PubchemFP636 and PubChemFP527 and VCH-6 towards the target enzyme inhibition.

Since DprE1inhibition effect of ellagic acid and quercertin has revealed through molecular docking studies, the antibacterial effect of both the systems were analysed against Pseudomonas aeroginosa and Streptococcus pneumonia. The zone of inhibition was greater for ellagic acid than quercetin for both the cultures. The result obtained is compared with that of pomegranate leaf extract, Ellagic acid showed maximum zone of inhibition of 1.4 against Pseudomonas aeruginosa while the leaf extract has 1.4 cm maximum inhibition zone against Streptococcus pneumoniae.here the potential inhibitory nature of both the lead systems, ellagic acid and pomegranate leaf extract are highly significant.

Quercetin has also exhibited inhibitory nature against Pseudomonas aeroginosa and Streptococcus pneumonia. The presence and quantification of both the lead systems were done using HPLC analysis.

Through the present study, DprE1inhibitory effect of the candidates ellagic acid and quercertin has revealed through insilico analysis and their antibacterial effect has identified through invitro studies. Therefore the potential pharmacological effect of the corresponding systems can be considered for better treatment of tuberculosis like inflammatory disorders.