Promising Ursolic Acid as a Novel Antituberculosis Agent: Current Progress and Challenges

ABSTRACT

Tuberculosis (TB) stands as the second most prevalent cause of global human mortality from infectious diseases. In 2022, the World Health Organization documented an estimated number of global TB cases reaching 7.5 million, which causes death for 1.13 million patients. The continuous growth of drug-resistant TB cases due to various mutations in the Mycobacterium tuberculosis (MTB) strain, raises the urgency of the exploration of novel anti-TB treatments. Ursolic acid (UA) is a natural pentacyclic triterpene found in various plants that has shown potential as a novel anti-TB agent. This review aims to provide an overview of the therapeutic prospects of UA against MTB, with a particular emphasis on in silico, in vitro, and in vivo studies. Various mechanisms of action of UA against MTB are briefly recapped from in silico studies, such as enoyl acyl carrier protein reductase inhibitors, FadA5 (AcetylCoA acetyltransferase) inhibitors, tuberculosinyl adenosine transferase inhibitors, and small heat shock protein 16.3 inhibitor. The potential of UA to overcome drug resistance and its synergistic effects with existing antituberculosis drugs are briefly explained from in vitro studies using a variety of methods, such as Microplate Alamar Blue Assay, Mycobacteria Growth Indicator Tube 960 and Resazurin Assays, morphological change evaluation using transmission electron microscopy, and in vivo studies using BALB/C infected with multi drug resistant clinical isolates. Besides its promising mechanism as an antituberculosis drug, its complex chemical composition, limited availability and supply, and lack of intellectual property are also reviewed as those are the most frequently occurring challenges that need to be addressed for the successful development of UA as novel anti-TB agent.