ABSTRACT

Amyloidosis is a degenerative disease caused by the accumulation of abnormal protein fibrils due to the process of protein misfolding and aggregation. Anti-aggregation compounds play an important role in inhibiting fibril formation and have the potential to be developed as an alternative therapy. Mahogany beans (Swietenia sp.) are known to be a source of hydrophobic triterpenoids, and the fermentation process is reported to be able to increase its content and biological activity. This study aims to evaluate the anti-aggregation potential of fermented mahogany beans through in vitro and in silico approaches. Fermentation of mahogany beans increases the triterpenoid content by up to 300%, with a yield of ethyl acetate (EAF) fraction of 1.75% and phytochemical filtration results showing the dominance of triterpenoids. In vitro assays of anti-aggregation activity using thermal induction and DTT models showed that EAF provided a higher percentage of aggregation inhibition than quercetin as a positive control, which was confirmed through turbidimetry testing and Congo red staining. LC-MS analysis tentatively identified five dominant compounds, namely Swietemahonin F, Swietenine, Isorhamnetin 3,4′-diglucoside, Methyl angolensate, and Khayasin T. In silico studies using the bovine serum albumin (BSA) model showed that the compounds in EAF interacted stably in the hydrophobic region and occupied the main interaction clusters with better performance than quercetin control ligands. Simulations of molecular dynamics confirmed the increased stability of the active residue of the protein, with isorhamnetin 3,4′-diglucoside as the most potent compound. Follow-up studies on β-amyloid models showed the highest binding affinity (−6.6 kcal/mol) and high conformational stability, indicating a potential inhibition of the amyloidosis process. The results of this study show that fermented mahogany beans have the potential to be candidates for natural anti-amyloidosis agents.