Identification of Biomolecular Drug Targets of Chemical Constituents of Curcuma longa (Turmeric)

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Indian medicinal plants are known to be beneficial in a multitude of diseases and disorders, their role has been documented in ancient Indian texts over the centuries. How do they work? Which molecule of the plant binds to which biological target and how does this elicit the known therapeutic response? The current work focuses on answering these questions by decoding this knowledge at a molecular level and thus, pushing the traditional medicinal utilization of Indian medicinal plants towards a more rational drug design approach. Firstly, a comprehensive database was created with 170 compounds found in Curcuma longa (Turmeric), which are known to elicit bioactivity to humans at the cellular level, but their targets remain elusive. These compounds were then used to predict bio-molecular targets using computational reverse screening methodologies based on shape screening, pharmacophore screening and molecular docking. This enabled the prediction of compounds exhibiting high affinity to therapeutically relevant protein targets. The compounds exhibiting stable binding to their respective targets were studied using unbiased molecular dynamics (MD). Subsequently, the study presented investigates the change in dynamical behavior upon ligand binding of some of these targets namely, quinone oxidoreductase, nuclear receptor ROR-alpha, and bile acid receptor known to be involved in cardiovascular, intellectual development, and liver diseases, respectively. The comparative trajectory analysis revealed that compounds cause change in dynamical behavior of these targets compared to targets without bound ligand. Further, the conformational variations have been analyzed to yield the effects of ligand binding. This study could prove to be valuable in a molecular understanding of plant-based medicine and in identifying new cures based on natural products.