# *Garcinia Mangostana:* A potent inhibitor of renin for management of dyslipidemia

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Inhibiting renin appears to be appropriate for the management of dyslipidemia because of the high specificity and unique role of this enzyme in the renin–angiotensin cascade. Renin exclusively catalyzes the reaction that produces angiotensin I from angiotensinogen. In clinical trials several type I (peptide-like) renin inhibitors reduced high blood pressure in patients with similar pharmacological efficacy as compared to ACE inhibitors. All potent renin inhibitors investigated to date, however, show insufficient oral bioavailability or short duration of action requiring high oral dosing, and therefore are unlikely to be useful as therapeutic agents. The concerted effort using molecular modelling techniques, crystallographic structure elucidation and biological assays have led to the design of novel, highly potent and selective non-peptide, natural product inhibitors of human renin. These small-molecule inhibitors have favorable physicochemical properties, such as remarkably good water solubility and low lipophilicity as compared to type-I inhibitors, and are resistant to rapid biodegradation by peptidases in the intestinal tract, blood circulation and liver. Crystal structure analysis of renin–inhibitor complexes combined with computational methods was employed in the medicinal-chemistry optimization process. Structure analysis revealed that the natural product inhibitor from *Garcinia Mangostana* binds as predicted, to the active site pocket. The molecular dynamic simulation further proved that the binding of the inhibitor to the active site gorge stabilized the protein and the active site amino acid residues during a 10000 ns simulation time as compared to that of Aliskiren (Control).

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