# BACK TO MY ROOTS: NEW THERAPEUTIC AGENTS FOR THE TREATMENT OF TYPE-2 DIABETES FROM AN ANCIENT HERBAL REMEDY

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The synthesis of a new class of zwitterionic glycosidase inhibitors from a natural plant source will be described. These compounds comprise a sulfonium ion with an internal sulfate counterion. Modification of the parent natural compound, salacinol, has yielded a variety of analogues as candidate inhibitors, some of which have subsequently been isolated from the plant source. Synthetic studies towards the stereochemical structure elucidation of another compound, kotalanol, from the same plant source will also be described. Structure activity relationships *in vitro* with recombinant human maltase glucoamylase, a critical enzyme involved in the post-amylase breakdown of carbohydrates in the small intestine, provide insight into the requirements of an effective inhibitor. These predictions have been subsequently verified by X-ray crystallography of the enzyme-inhibitor complexes. In addition, the latter studies confirm the original hypothesis that these inhibitors interact with the enzyme active site through stabilizing electrostatic interactions with the catalytically-active carboxylate residue. Finally, i*n vivo* studies in rats with selected compounds show control of plasma glucose and insulin levels, thus providing lead candidates for the control of Type 2 diabetes.