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Inhibition Kinetics and Theoretical Studies on Zanthoxylum chalybeum Engl. Dual Inhibitors of α-Glucosidase and α-Amylase

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A systematic analysis involving phytochemical isolation, bioassays and in silico procedures of the metabolites from the root bark of Zanthoxylum chalybeum established four amides, chaylbemide A (1), chalybemide B (2), and chalybemide C (3), fagaramide (4); four benzophenanthridine alkaloids skimmianine (5), norchelerythrine (6), 6-acetonyldihydrochelerythrine (7) and 6-hydroxy-N-methyl decarine (8); and three lignans, ailanthoidol (9), 2,3-epoxy-6,7-methylenedioxy coniferyl alcohol (10), sesamine (11). These compounds showed relative potentail towards moderating the activities α-amylase and α-glycosidase as an effort to validate the plants application in the management of diabetes. Preliminarily ccompounds 1–8 displayed inhibitory activities against both α-amylase and α-glycosidase in the range of IC50 = 43.22–49.36 μM which showed no significant ($p > 0.05$) difference to the positive control acarbose (IC50 = 42.67; 44.88 μM). Based on Linewaever-Burk and Dixon plot, the alkaloids (5, 6, 7 and 8) showed mixed inhibition against both α-glucosidase and α-amylase with comparable Ki to the reference acarbose ($p > 0.05$) on amylase but significantly higher activity than acarbose on α-glucosidase. One phenolic (10) showed a competitive mode of inhibition both on amylase and glucosidase with comparable ($p > 0.05$) to the activity of acarbose. The other compounds (1, 2, 3, 4, 9 and 10) displayed varied modes of inhibition between noncompetitive and uncompetitive with moderate inhibition constants. Using Molecualar Operating Environment (MOE) software, the compounds predicted binding affinities in the range of −9.4 to −13.8 and −8.0 to −12.6 relative to the acarbose affinities at −17.6 and −20.5 kcal/mol on α-amylase and α-glucosidase residue, respectively. Such binding energies were associated with H-bonding, π-H, and ionic interactions on variable amino acid residues on both the enzymes. The study thus lends credence to the application of extracts of Z. chalybeum in the management of postprandial hyperglycemia.

Biography

Dr. Charles O. Ochieng is a member of the Kenya Chemical Society and works at Maseno University as a lecturer of organic Chemistry and researcher of Natural Product Chemistry. Charles, started his career in natural product research after graduating with PhD degree in Chemistry from Maseno University cosponsored by DAAD in-country scholarship and TWAS-sandwich programme to Central Drug Research Institute in Lucknow, India. He has been published as author and co-author of over 20 papers in peer-reviewed journals and supervised five postgraduate students.