

Microbial transformation of isosteviol lactone and evaluation of the transformation products on androgen response element.

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Abstract

Two filamentous fungi, *Cunninghamella bainieri* ATCC 9244 and *Aspergillus niger* BCRC 32720, were used to investigate the biotransformation of isosteviol lactone (4 α -carboxy-13 α -hydroxy-13,16- seco-ent-19-norbeyeran-16-oic acid 13,16-lactone) (2), which was derived by reacting isosteviol (ent-16-oxobeyeran-19-oic acid) (1) with m-chloroperbenzoic acid. Incubation of 2 with *C. bainieri* afforded metabolites 3- 6, which involved isomerization, hydroxylation, and ring cleavage reactions followed by oxidation and selective O-methylation. Incubation of 2 with *A. niger* afforded mono-, di-, and trihydroxylated metabolites 3, 4, and 7- 12. The structures of 3- 12 were elucidated on the basis of spectroscopic analyses, and structures 3, 4, and 6 were confirmed by X-ray crystallographic studies. Compounds 2- 6, 8- 10, and 12 were assayed as androgen agonists using an ARE (androgen response element)-mediated luciferase reporter gene assay. Compounds 3, 6, and 10 were significantly active, with 6 showing more activity than testosterone.