

A Commercial Extract of *Cyanotis arachnoidea* Roots as a Source of Unusual Ecdysteroid Derivatives with Insect Hormone Receptor Binding Activity

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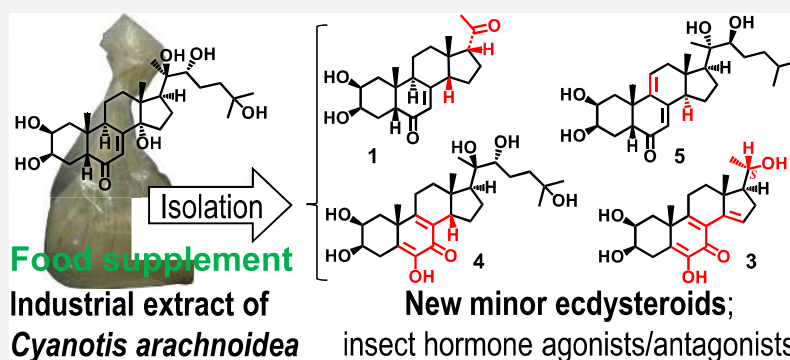
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ABSTRACT: Ecdysteroids act as molting hormones in insects and as nonhormonal anabolic agents and adaptogens in mammals. A wide range of ecdysteroid-containing herbal extracts are available worldwide as food supplements. The aim of this work was to study such an extract as a possible industrial source of new bioactive ecdysteroids. A large-scale chromatographic isolation was performed from an extract of *Cyanotis arachnoidea* roots. Ten ecdysteroids (1–10) including eight new compounds were isolated and characterized by extensive nuclear magnetic resonance studies. Highly unusual structures were identified, including a H-14 β (1, 2, 4, and 10) moiety, among which a 14 β (H)17 β (H) phytosteroid (1) is reported for the first time. Compounds with an intact side chain (4–10) and 11 other natural or semisynthetic ecdysteroids (11–21) were tested for insect ecdysteroid receptor (EcR) binding activity. Two new compounds, i.e., 14-deoxydacryhainansterone (5) and 22-oxodacryhainansterone (6), showed strong EcR binding activity (IC_{50} = 41.7 and 380 nM, respectively). Six compounds were identified as EcR agonists and another two as antagonists using a transgenic ecdysteroid reporter gene assay. The present results demonstrate that commercial *C. arachnoidea* extracts are rich in new, unusual bioactive ecdysteroids. Because of the lack of an authentic plant material, the truly biosynthetic or artifactual nature of these compounds cannot be confirmed.

Ecdysteroids represent a particularly versatile group of natural products due to their chemical variability and the broad range of bioactivities they can exert. They are best known as analogues of the insect-molting hormone 20-hydroxyecdysone (20E). Their polar, polyhydroxylated character hinders the absorption of typical phytoecdysteroids through the cuticle of insects; in contrast, they need to be consumed to function as insect hormones, which prevents their use as sprays in pest management. Nevertheless, these compounds serve as models for the rational design of synthetic analogues,^{1,2} rendering the study of their structure–activity relationships important. Ecdysteroids are also bioactive in mammals; some of their representatives, including 20E and its metabolite poststerone,^{3,4} act as nonhormonal, green anabolic agents and adaptogens and offer a wide range of metabolic benefits. As a result, their consumption is typically considered

“healthy”. This has led to the production and worldwide marketing of ecdysteroid-containing herbal extracts⁵ for various purposes, particularly as anabolic food supplements for athletes. A simple Internet search revealed that ecdysteroid-containing extracts typically prepared from the roots of *Cyanotis arachnoidea* C.B. Clarke (Commelinaceae) are available for online purchase up to a scale of several metric tons per month at highly competitive prices; depending on the

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