PROJECT

The genus *Helichrysum* (Asteraceae) consists of approximately 500 species worldwide, with 245 indigenous to South Africa. As a result of the large number of species, the chemistry and biological activity of several species have not yet been investigated. The aim of this project was to investigate the phytochemistry of three species and propose a synthetic route to one of the antibacterial compounds isolated.

An extensive literature review regarding the widespread traditional uses, biological activity and phytochemistry of the South African Helichrysum species is provided.

From *Helichrysum splendidum*, a plant used traditionally to treat rheumatism, two monomeric guaianolides and a dimeric guaianolide, helisplendidilactone, were isolated. The stereochemistry of these known compounds was confirmed and the NMR assignments for certain peaks of helisplendidilactone were corrected. An X-ray structure for helisplendidilactone was obtained for the first time.

The phytochemistry of *Helichrysum montanum* was investigated for the first time and novel diastereoisomers of known guaianolides were isolated. The phytochemistry of *H. splendidum* and *H. montanum* is remarkably similar and supports their morphological classification in the same taxonomic group. The chloroform:methanol extract of *H. montanum* yielded a novel dimeric guaianolide, helimontanilactone, which is related to helisplendidilactone, as well as three monomeric guaianolides (of which one is a novel diastereomer of a known compound). The extract also yielded spathulenol (a sesquiterpene), umbelliferone (a coumarin) and 4',5,7-trihydroxy-3,3',8-trimethoxyflavone (a flavonoid).

Thirty-five *Helichrysum* species were screened for antimicrobial activity against six micro-organisms and a preliminary cytotoxic assay, which included the use of "normal" and cancer cell lines, was performed. *Helichrysum excisum* was selected for further study based on the fact that it exhibited promising antimicrobial activity and relative low toxicity. Furthermore, with the exception of the essential oil, the phytochemistry of this species has not been investigated.

From the aerial parts of *H. excisum*, five flavonoids, identified as pinocembrin, gnaphaliin, lepidissipyrone, 5-hydroxy-7,8-dimethoxyflavone and isoscutellarein 7-O-β-glucoside were isolated. Four of these flavonoids have an unsubstituted B-ring, a phenomenon often observed in flavonoids isolated from *Helichrysum* species. The active antimicrobial component of *H. excisum* has been identified as lepidissipyrone.

Due to the interesting biological activities reported for phloroglucinol α-pyrones and the synthetic challenges associated with these molecules, lepidissipyrone was selected for a synthetic study. Both the flavanone and pyrone moieties present in lepidissipyrone have been successfully synthesised. A successful strategy towards the CH_2 linker between the two units has been illustrated. The strategy could be used to synthesise similar phloroglucinol pyrones.

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