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Cytotoxic and allergenic sesquiterpene lactones from cushion bush (Leucophyta brownii Cass.)

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Cushion bush (Leucophyta brownii Cass., Asteraceae) has become a popular pot and outdoor container plant in some Nordic countries. Several cases of allergic contact dermatitis caused by cushion bush have been reported [1, 2]. Cushion bush is rich in sesquiterpene lactones containing an α,β-unsaturated γ-lactone moiety that are known for their anti-inflammatory and cytotoxic activity due to reactions with sulphydryl groups of functional proteins via a Michael-type reaction. This also makes this type of sesquiterpene lactones potential allergenic [1, 3]. Seven sesquiterpene lactones (1–7) containing an α,β-unsaturated γ-lactone moiety were isolated from cushion bush and identified by LC-MS and 1D and 2D NMR spectroscopy as described previously [3]. Compounds 1–7 were investigated for their cytotoxic activity towards human breast cancer (MCF-7) and colon cancer (HT-29) cells as well as their allergenicity. Compounds 2, 3, 5 and 6 reduced proliferation of HT-29 and MCF-7 cells with IC50 values < 10 µM, whereas compounds 1, 4 and 7 showed less cytotoxicity with an IC50 value of > 20 µM for both cell lines. Six of seven sesquiterpene lactones elicited positive reactions in 4 of 11 patients. The sesquiterpene lactones 3 and 5–7 were confirmed to be sensitizers, whereas leucophytalin A (4) and 4α-hydroxy-5αH,10αH-1,11(13)-guaiadin-8β,12-olide (1) were shown to be allergenic for the first time. No clear correlation between the cytotoxic activity and allergenicity of the tested compounds could be established. However, the present investigation confirmed a connection between type IV allergenicity and cytotoxicity of sesquiterpene lactones containing an α,β-unsaturated γ-lactone moiety.