REVIEW ARTICLE
Dulcie A. Mulholland et al.
The chemistry and biological activity of the Hyacinthaceae
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The Hyacinthaceae (sensu APGII), with approximately 900 species in about 70 genera, can be divided into three main subfamilies, the Hyacinthoideae, the Urgineoideae and the Ornithogaloideae, with a small fourth subfamily the Ozirioideae, restricted to South America. The plants included in this family have long been used in traditional medicine for a wide range of medicinal applications. This, together with some significant toxicity to livestock has led to the chemical composition of many of the species being investigated. The compounds found are, for the most part, subfamily-restricted, with homoisoflavonones and spirocyclic nortriterpenoids characterising the Hyacinthoideae, bufadienolides characterising the Urgineoideae, and cardenolides and steroidial glycosides characterising the Ornithogaloideae. The phytochemical profiles of 38 genera of the Hyacinthaceae will be discussed as well as any biological activity associated with both crude extracts and compounds isolated. The Hyacinthaceae of southern Africa were last reviewed in 2000 (T. S. Pohl, N. R. Crouch and D. A. Mulholland, Curr. Org. Chem., 2000, 4, 1287–1324; ref. 1); the current contribution considers the family at a global level.

1 The Hyacinthoideae
2 The Urgineoideae
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This review reflects a [bracketed]† family and subfamily taxonomic arrangement for the Hyacinthaceae sensu APGII. A subsequent arrangement (APGIII)† based on further molecular analyses is not here adopted, where the Hyacinthaceae was hypothetically included in an expanded circumscription of the Asparagaceae. In that the group of plants here dealt with are monophyletic,† the systematic approach adopted for delimiting and naming family, subfamily or tribal level classifications ultimately has little bearing in relation to this review. We have adopted largely the phylogenies and generic concepts of Speta,† Pfosser and Speta, and subsequent workers (Martinez-Azorín et al.)† who have considered molecular, morphological and biogeographic characters in their circumscriptions. Ali Syed et al.† have provided an excellent overview of alternative and often controversial systematic arrangements, of primary and secondary centres of geographic diversity, and the distribution of subfamilies and tribes at a global level. It should be noted that such is the state of flux of generic circumscription in the Hyacinthaceae that when providing a subfamilial classification for this unit (Asparagaceae subfamily Scilloideae sensu APGIII) Chase et al.† did not list genera names, which they otherwise offered with most other expanded Asparagalean families they treated. Given the past nomenclatural instability of the Hyacinthaceae, the names of plants under which the original phytochemical and pharmacological work was conducted often differs radically from the names accepted currently. For this reason we here provide both current and reported names, with species authors, to make clear this link. The literally reported (and sometimes incorrectly spelt) taxon names and species authors (if given) are provided in parentheses. The subfamilies are discussed in turn, starting with the Hyacinthoideae as most work has been conducted on this, the largest, subfamily. The Urgineoideae and finally the Ornithogaloideae follow. No reported investigations into the Ozirioideae appear in the literature. Within each subfamily, those species receiving a substantial amount of attention will be discussed first, followed by the genera grouped by region (Europe and the Mediterranean, Middle and Far East and North Africa, southern Africa and finally, in the case of the Urgineoideae, India).
Plants have been considered on a regional basis as in many cases the secondary metabolites found reflect a strong geographic pattern. Any early work on a genus is discussed before later work.

1 The Hyacinthoideae

The subfamily Hyacinthoideae comprises more than 400 species in thirty-eight genera. The Hyacinthoideae are distributed in sub-Saharan Africa, India, Madagascar, eastern Asia, the Mediterranean region and Eurasia. Sub-Saharan Africa appears to be the centre of origin for the subfamily, with a secondary centre of diversification and radiation being the Mediterranean region. Twenty genera of the Hyacinthoideae have been investigated, with the bulbs receiving most attention. The exception is Hyacinthus orientalis L., the flowers of which have been extensively examined. Homoisoflavonones and spirocyclic nortriterpenoids are widespread throughout the subfamily with chalcones, xanthones, flavonoids, alkaloids, stilbenoids, chromones, norliglans and benzopyranones also being reported.

Dulcie Mulholland leads the Natural Products Research Group and is Head of the Department of Chemistry at the University of Surrey. She undertook her PhD at the University of Natal, Durban, South Africa, under the supervision of David Taylor on the Chemistry of the Meliaceae. For the last 20 years she has collaborated with Neil Crouch investigating the phytochemistry of the Hyacinthaceae of southern Africa.

Sianne Schwikkard obtained her PhD from the University of KwaZulu-Natal, South Africa in 1998 (under the supervision of Professor Dulcie Mulholland). This was followed by post-doctoral studies at Virginia Tech with Professor David Kingston and further post-doctoral studies at the Rand Academic University with Professor Fanie du Toit. After spending 18 months working for Sasol Ltd, Sianne relocated to the United Kingdom and following a post-doctoral position, under Professor Keith Jones at Kingston University, has continued to teach in a part-time capacity at Kingston University in addition to her position as a part-time research associate at the University of Surrey.

Neil Crouch PhD (Natal) has worked as an ethnobotanist for the South African National Biodiversity Institute (SANBI) for nearly 20 years, largely on Zulu traditional medicine. He networks SANBI in natural products, pharmacological, horticultural, conservation, and Indigenous Knowledge Systems cataloguing programmes and is accordingly involved in state-sponsored bioprospecting consortia that develop new drugs for malaria and tuberculosis. As an Honorary Professor in the School of Chemistry and Physics at the University of KwaZulu-Natal, he explores his strong interest in the chemistry, traditional use and biosystematics of the Hyacinthaceae, a plant family with a major centre of diversity in southern Africa.

Abegaz et al.9 and du Toit et al.10 have reviewed the phytochemistry, biological activity, biosynthesis and synthesis of the homoisoflavonones. The homoisoflavonones can be divided into five categories, the 3-benzyl-4-chromanones 1, the 3-hydroxy-3-benzyl-4-chromanones 2, the 3-benzylidene-4-chromanones (E or Z) 3, the 3-benzyl-chrom-2-en-4-ones 4 and the scillascillins 5. The spirocyclic nortriterpenoids are generally of the lanosterol-type, showing a wide range of substitution patterns. The genera receiving the most attention, Eucomis L’Hér., Muscari Mill. and Ledebouria Roth. will be discussed first, followed by the lesser-studied Eurasian and Mediterranean genera Leopoldia Parl., Scilla L., Barnardia Lindl., Othocallis Salisb., Oncostema Raf., Hyacinthus L., Bellevalia Lapeyr., Autonoe (Webb & Berthel.) Speta and Hyacinthoides Medik. Lastly, the southern African genera Drimiopsis Lindl. & Paxton, Resnova van der Merwe, Veltheimia Gled., Merwilla Speta, Lachenalia J Jacq. ex Murray,
The genus *Eucomis* is widespread throughout eastern and southern Africa. It is used by traditional healers to treat a wide range of complaints, including rheumatism, as an anti-inflammatory and as a treatment for mental disease. Homoisoflavones and triterpenoid glycosides have been isolated from the bulbs of many of the species investigated, with the homoisoflavones usually accumulating in the waxy layer between the storage leaves of the bulb and the terpenoids in the bulb tissue. Early work on *Eucomis bicolor* Baker resulted in the isolation of the yellow crystalline needles of eucomin and the colourless hexagonal plates of eucomol. The configuration at C-3 of eucomol 7 was determined by CD experiments and confirmed by X-ray analysis of the p-bromophenacyl derivative. Four additional homoisoflavonoids have been isolated from the bulbs of *E. bicolor*, [8–11] followed a number of years later by the identification of seven triterpenoid oligosaccharides [12–18]. Scillasaraponin A 12 has a modified spirocyclic side chain at C-17 and C-23 and has been found to inhibit cyclic AMP phosphodiesterase (IC50 = 11.5 x 10–5 M). Compounds 13, 14 and 16 were found to be toxic to HeLa cells at concentrations of both 50 μg ml–1 and 5 μg ml–1. A later investigation of *E. bicolor* resulted in the isolation of twelve compounds from the dichloromethane extract and ten from the methanol extract. The dichloromethane extract yielded the seven known compounds (7, 10, 19, 20, 21, 22 and 23) and five novel triterpenoids (24 [the aglycone of 25], 26, 27, 28 and 29) and the methanol extract was found to contain the known homoisoflavonoid 30 as well as nine novel lanosterol glycosides (31–39).

There is a large range of complaints, including rheumatism, as an anti-inflammatory and as a treatment for mental disease. Homoisoflavones and triterpenoid glycosides have been isolated from the bulbs of many of the species investigated, with the homoisoflavones usually accumulating in the waxy layer between the storage leaves of the bulb and the terpenoids in the bulb tissue. Early work on *Eucomis bicolor* Baker resulted in the isolation of the yellow crystalline needles of eucomin and the colourless hexagonal plates of eucomol 7. The configuration at C-3 of eucomol 7 was determined by CD experiments and confirmed by X-ray analysis of the p-bromophenacyl derivative. Four additional homoisoflavonoids have been isolated from the bulbs of *E. bicolor*, [8–11] followed a number of years later by the identification of seven triterpenoid oligosaccharides [12–18]. Scillasaraponin A 12 has a modified spirocyclic side chain at C-17 and C-23 and has been found to inhibit cyclic AMP phosphodiesterase (IC50 = 11.5 x 10–5 M). Compounds 13, 14 and 16 were found to be toxic to HeLa cells at concentrations of both 50 μg ml–1 and 5 μg ml–1. A later investigation of *E. bicolor* resulted in the isolation of twelve compounds from the dichloromethane extract and ten from the methanol extract. The dichloromethane extract yielded the seven known compounds (7, 10, 19, 20, 21, 22 and 23) and five novel triterpenoids (24 [the aglycone of 25], 26, 27, 28 and 29) and the methanol extract was found to contain the known homoisoflavonoid 30 as well as nine novel lanosterol glycosides (31–39).
inhibitory activity of the leaf, root and bulb extracts, showed that the leaf extract inhibited COX-1 to a greater extent while the root and bulb extract showed greater inhibition of COX-2 (COX-2/COX-1 of 0.7 and 0.8 respectively for the root and bulb extracts).

There has been some interest in the biological effects of plant lectins obtained from the bulbs of *E. autumnalis*. These non-enzymatic proteins can bind, with high specificity and reversibility, mono- and oligosaccharides. Cyclooxygenase is a membrane-bound glycoprotein and as such could be affected by plant lectins. The partially purified lectin-like protein extract of *E. autumnalis* was found to have very good cyclooxygenase inhibitory activity (COX-1 inhibition of 88%) as well as good activity against the Gram-positive bacterium *Bacillus subtilis* (MIC of 0.2 mg ml<sup>-1</sup>)

The leaves of young plants showed greater COX-1 inhibitory activity than those of older plants, where the greatest activity was associated with bulbs and roots.

Six homoisosflavanones (19, 40, 47–50)<sup>14,36</sup> and the optically active 2-hydroxy-2-[(4-hydroxyphenyl)methyl]butanedioic acid 51 have been isolated from the bulbs of *Eucomis comosa* (Houtt.) H. R. Wehrh. (as *Eucomis punctata* L’Herit). The bulb wax of *Eucomis comosa* yielded the chroman-4-one 52 while an examination of the methanol extract of the fresh, air-dried bulbs gave five homoisosflavanones (47, 48, 50 and both the E and Z form of 6).<sup>39</sup> The same study included
Eucomis pallidiora Baker subsp. pole-evansii (N.E.Br.) Reyneke ex J.C.Manning and Eucomis schijffi Reynneke. The bulbs of Eucomis pallidiora subsp. pole-evansii contained the homoiso flavonone 53 and the spirocyclic nortriterpenoid 20 while Eucomis schijffi yielded two compounds, the spirocyclic nortriterpenoid 54 and scillascillin 55. Eucomis montana Comp-ton was investigated and the bulbs were found to contain eleven homoiso flavonones (6, 7, 9, 10, 30, 50, 56, 57, 58, 59 and 60). No inhibitory activity against cyclooxygenase enzymes (COX-1 and COX-2) was found for compounds 48, 53 and 55 isolated from E. comosa, E. pallidihora and E. schijffi respectively. Some antibacterial activity has been observed for homoiso flavonones isolated from E. comosa (MIC of 0.52 mM for compound 6 (E isomer) and 0.24 mM for compound 47) and E. schijffi (MIC of 0.50 mM for compound 55). The dichloromethane and methanol extracts of the whole plant of Eucomis vandermerwei I.Verd. yielded four known homoiso flavonones (6, 7, 10 and 56). Similarly, the whole plant of Eucomis zambesiaca Baker was investigated and this resulted in the isolation and identification of five homoiso flavonones (6, 19, 40, 61 and 62) and three nortriterpenoids (20, 21 and 63).

The bulbs of Muscari racemosum Mill. were found to contain homoiso flavonones of the 3-benzylidene-4-chromanone-type (64–66). Long-range coupling between C-2 and C-9, was indicative of Z geometry. These homoiso flavonones have been investigated with respect to their effect on lipid peroxidation in vitro. Strong anti-oxidant activity was noted (IC50 = 0.94–7.98 μM) and this led to an investigation into their antimutagenic/anticarcinogenic activity. It has been suggested that polyphenolics may be cancer preventative due to their antioxidant properties and a mixture of these three homoiso flavonones was found to contain significant antimutagenic activity. 

Estrogenic activity was found in an ether extract of the bulbs. The extract induced proliferation of MCF7 cells in a dose dependent manner at concentrations up to 5 μg ml⁻¹. This concentration produced the greatest effect of 181% of the control.
A wide range of compounds has been isolated from the bulbs of *Muscari armeniacum* Leichtlin ex Baker. These include flavonoids (67–69), homoisoavanones, with an unusual 3',4',5-trisubstitution pattern in the B ring (30, 62, 70–80), spirocyclic nortriterpenoid glycosides (81–87), and polyhydroxylated pyrrolizidine alkaloids (88–92). The alkaloids were assessed for their action against glycosidases. Compound 88 was found to be a potent inhibitor of rat intestine lactase (IC₅₀ = 4.4 μM) as well as a moderate inhibitor of α-L-fucosidase (IC₅₀ = 46 μM) and amyloglucosidase (IC₅₀ = 25 μM). Inverting the hydroxyl group at C-1 to give compound 89, enhanced the amyloglucosidase inhibition (IC₅₀ = 8.6 μM) but resulted in the loss of the α-L-fucosidase inhibition. Compounds 90 and 91 were less active. Three ribosome-inactivating proteins have been isolated from the bulbs of *M. armeniacum*. It has been proposed that this type of activity is linked to an anti-viral response. The petals of *M. armeniacum* have yielded four anthocyanins, the new muscarinin A 93 and the known 3-O-β-D-glucopyanoside of delphinidin, petunidin and malvidin (94–96). The principle water soluble polysaccharide in the bulbs of *M. armeniacum* (as *Muscari szovitsianum*) was found to be a neutral glucofructan, with glucose and fructose residues in the ratio 26:1.

Phytochemical investigations into the bulbs of *Muscari botryoides* (L.) Mill. confirmed a close taxonomic relationship with *Muscari armeniacum*. Similar homoisoavanones (19, 30, 58, 60, 77, 79, 97, 98) were isolated as well as similar spirocyclic nortriterpenoid glycosides (86, 87, 99, 100, 101, 102, 103). *Muscari neglectum* Guss. ex Ten. was found to contain a similar spread of homoisoavanones in the bulbs (30, 62, 80, 104–107) as well as an interesting scillascillin-type homoisoavanone with an unusual oxygenation pattern in the B ring (55). Ethanol extracts of the bulbs and leaves of *Muscari neglectum* have been tested for antifungal activity against the wood rots *Postia placenta* and *Trametes versicolor*. Significant reduction in wood weight loss was observed for Turkish oriental beech and Scots pine (weight loss dropped from 35–42% in the untreated wood to 5.4–18.3% in the treated wood).
An aqueous ethanol extract of the bulbs of *Ledebouria socialis* (Baker) Jessop (as *Scilla socialis* Baker) was found to contain eleven hyacinthacines (108–118) as well as two pyrrolidines (119–120) and three piperidines (121–123). Hyacinthacines appear to be restricted to the Hyacinthoideae. These compounds have been found in *Othocallis siberica* (Haw.) Speta (as *Scilla sibirica*), *Oncostema peruviana* (L.) Speta (as *Scilla peruviana*), *Hyacinthoides non-scripta* (L.) Chouard ex Rothm., *Hyacinthoides hispanica* (Mill.) Rothm. (as *Scilla campanulata*), and *Muscari armeniacum*. The hyacinthacines are characterised as 7α-R-hydro-1,2-dihydroxy-3-hydroxymethylpyrrolizidines and in general appear to be weak to moderate inhibitors of glycosidases. The dichloromethane and methanol extracts of the bulbs of *Ledebouria socialis* have yielded five compounds, the scillascillin-type homoisoavanones 124 and 125, phytol, stigmasterol and the polyhydroxylated difuran derivative, polybotrin 126. The different types of compounds isolated reflect the different solvents used for extraction, with the more polar extracts yielding the more polar polyhydroxy alkaloids and the less polar extracts the homoisoavanones and sterols.

Early work by Gunn *et al.* on some southern African *Ledebouria* species, examined the cardiac effect of *Ledebouria cooperi* (Hook.f.) Jessop (as *Scilla cooperi* Hook and as *Scilla rogersii* Baker) and *Ledebouria ovatifolia* (Baker) Jessop (as *Scilla lanceaefolia* Baker). Both species produced a similar action to digitalis when applied to isolated frog and cat hearts as well as in situ frog, cat and dog hearts. The extracts obtained were, however, insufficient in quantity to determine minimum lethal doses and the active components were not identified.

The chemical constituents of a further six southern African *Ledebouria* species have been investigated. Two samples of the bulbs of *Ledebouria zebrina* (Baker) S.Venter (as *Scilla zebrina* Baker), collected from two different regions in South Africa (Durban and Blyde River, Mpumalanga) have been investigated and the chemical differences noted. Both contained homoisoavanones (Durban bulbs compounds 127 and 128 and the Blyde River bulbs compounds 127, 129, 130). In addition to the homoisoavanones, the Blyde River bulbs also contained spirocyclic nortriterpenoids (131, 21), while the Durban bulbs produced a chalcone 132. The bulbs of *Ledebouria cooperi*...
yielded the homoisoflavanones 59 and 62 as well as the eucosterol-type spirocyclic nortriterpenoid 133 and malic acid. Ledebouria ovatifolia bulbs were found to contain the chalcones 132 and 134 as well as the homoisoflavanone 30. A. L. ovatifolia is used by the Zulu to treat gastro-enteritis, influenza and backache. In addition, it has been found to be toxic to sheep. Extracts of the bulbs were found to have good antibacterial activity against Gram-positive bacteria (MIC of 0.8-12.5 mg ml\(^{-1}\)), but poor anti-inflammatory and poor antihelmintic activity. A later investigation of the dichloromethane, ethyl acetate and methanol extracts of the bulbs led to the isolation of twenty-nine compounds, including xanthones (135-138), homoisoflavanones (7, 10, 30, 50, 74, 75, 139-148), triterpenoids (133, 149-150), chalcones (132, 151) and simple aromatic compounds (152-154), including polybotrin 126. Sixteen of the above compounds isolated from L. ovatifolia were assessed for anti-inflammatory activity, in particular the selective inhibition of the COX-2 enzyme. Compounds 75, 137 and 146 were found to significantly inhibit COX-1 and COX-2 (percentage activity relative to the non-inhibitor control of 54-56% for COX-1 and 0% for COX-2), while compound 145 showed good selectivity for the inhibition of COX-2 over COX-1 (IC\(_{50}\) for COX-2 of 2.87 \(\mu\)M, with no statistically significant inhibition for COX-1 up to a concentration of 20 \(\mu\)M). During the same study, the norlignan hinokiresinol 155, previously isolated from Drimiopsis burkei Baker, was synthesised and tested for selective COX-2 inhibitory activity. Significant selective inhibition against COX-2 was observed (percentage activity relative to the non-inhibitor control of 93.8% for COX-1 and 0% for COX-2). Ledebouria leptophylla (Baker) S.Venter (as Ledebouria graminifolia (Baker) Jessop), sourced in Botswana, is used traditionally to treat gastro-enteritis, backache and coughs as well as a treatment for skin irritations and for dressing wounds. A phytochemical investigation of the bulbs found seven 3-benzyl-4-chromanones (30, 62, 128, 156-159), two 3-benzyl-3-hydroxy-4-chromanones (7, 57), two scillascillin-type homoisoflavonones (160-161) and two xanthones (136 and 162). Cultivated and wild-sourced bulbs contained the same compounds. There was initial concern about the presence of the xanthones and speculation as to whether they may have come from a fungal or lichen contamination of the wild bulbs. The fact that the cultured bulbs contained the same xanthones confirmed that they were secondary metabolites of L. leptophylla.

Within South Africa Ledebouria revoluta (L.f.) Jessop is extremely widespread. It is used by the Sotho to drive away lightening and with the exception of pregnant women, to treat lumbago. The Kwenaland Tswana use it to treat wounds and skin conditions. The bulbs were found to contain homoisoflavonones (30, 59, 61 and 157). Ledebouria floribunda (Baker) Jessop is used by traditional healers in the Eastern Cape of South Africa to treat skin disorders, tuberculosis, urinary tract infections and gastro-enteritis. Three homoisoflavonanes, with unusual substituents at C-6, -7 and -8 (163-165) have been isolated from the bulbs as well as two 7-O-diglycosides (166-167) and five additional homoisoflavonanes (10, 30, 50, 62, 168). These latter seven homoisoflavonanes have shown good antioxidant activity against the DPPH radical (IC\(_{50}\) of 31-273 \(\mu\)g ml\(^{-1}\)) and in the \(\beta\)-carotene/
linoleic acid system (antioxidant activity of up to 79% after 120 min) as did 164 and 165 against the DPPH radical (IC$_{50}$ of 23.2 and 28.7 $\mu$g ml$^{-1}$ respectively).

*Leopoldia comosa* (L.) Parl. is found largely in the Mediterranean region and the bulbs have been used as a food source for generations. Evidence for the ancient use of this plant includes the discovery of traces of this species in a Neanderthal grave in Iraq. The bulbs (as *Muscari comosum* Mill.) were examined for antioxidant activity as part of a study on non-cultivated vegetables commonly consumed by Albanians living in southern Italy. Twenty-seven plant species were investigated, with two showing high activity, one of which was *L. comosa* (inhibitory activity on a DPPH assay of 85%). A further study also found good antioxidant activity as well as hypoglycemic activity via the inhibition of carbohydrate digestive enzymes. Extracts of *L. comosa* (as *Muscari comosum* Mill.) have resulted in the isolation of nineteen nortriterpenoids of the lanosterol-type as well as homoisosflavanones.

Initial work on the bulbs was complicated by the presence of complex glycosides. Acid catalysed methanolysis of the glycoside mixture resulted in the identification of the aglycones. Eucosterol 20 was found to be the major component, with compounds 21, 54, 169, 170, and 171 (23$R$) present in smaller amounts. Extensive work on the bulbs by Adinolfi et al. resulted in the isolation of the free aglycones present in the bulbs (20, 21, 22, 54, 169–175) as well as the full structural elucidation of the glycosides (86, 87, 102, 103, and 176). All the nortriterpenes isolated from *Leopoldia comosa* mentioned so far have $S$ configuration at C-23, three compounds with $R$ configuration have also been identified, 177, 178 (23$R$ 20) and 179 (23$R$ 170).

Two classes of homoisosflavanones have been isolated from the bulbs of *L. comosa*, the 3-benzyl-4-chromones (30, 58, 59, 61, 62, 80, 97, 180–181) and the scillascillin type (55, 104–107 and 182). The absolute configuration at C-3 of these
homoisoflavanones was determined using circular dichroism and found to be $R$ in all cases.\textsuperscript{98} For the scillascillin type, this was further confirmed by X-ray analysis.\textsuperscript{98} The crude extract of the bulbs has been subjected to anti-inflammatory bioassay-directed fractionation using a croton oil-induced mouse ear dermatitis test. The homoisoflavanone rich fraction was found to have high activity and further fractionation resulted in the isolation of \textsuperscript{30, 59, 61, 80} compounds \textsuperscript{97}, all of which showed activity, with compound \textsuperscript{30} being the most active at 41\% inhibition (100 $\mu$g ear$^{-1}$).\textsuperscript{100} Two flavonoids have been isolated from the flowers of \textit{L. comosa}, 3-glucoarabinosyl- and 3-rhamnoarabinosyl-3,4,5-trihydroxy-7-alkoxy flavone.\textsuperscript{101}

\textit{Leopoldia comosa} is used in the Basilicata region of southern Italy to treat toothache and headache.\textsuperscript{102} One third of the plants used for medicinal purposes in southern Italy are used to treat skin and soft tissue infections. As \textit{Staphyloccocus aureus} is a common cause of such infections, the effect of a number of Italian plants, including the bulbs of \textit{Leopoldia comosa}, on the inhibition of the \textit{S. aureus} biofilms has been studied. Significant dose-dependent biofilm inhibition ($IC_{50}$ = 16 $\mu$g ml$^{-1}$) was noted for \textit{L. comosa}.\textsuperscript{103}

Investigations into the chemistry of the bulbs of \textit{Scilla luciliae} (Boiss.) Speta (as \textit{Chionodoxa gigantea} Whittall and as \textit{Chionodoxa luciliae} Boiss.) has yielded a large number of lanosterol-type spirocyclic nortriterpenoids, many of which have been tested for biological activity. Compounds \textsuperscript{183}–\textsuperscript{186},\textsuperscript{104} \textsuperscript{187}–\textsuperscript{188} and \textsuperscript{187}–\textsuperscript{188}\textsuperscript{105} \textsuperscript{187}–\textsuperscript{190}\textsuperscript{107} \textsuperscript{197}–\textsuperscript{190} and \textsuperscript{197}–\textsuperscript{190}\textsuperscript{108}Compounds \textsuperscript{189} and \textsuperscript{190} and \textsuperscript{190}–\textsuperscript{197} and \textsuperscript{197}–\textsuperscript{190}\textsuperscript{109} compounds \textsuperscript{198}–\textsuperscript{204},\textsuperscript{108} \textsuperscript{205}–\textsuperscript{207}\textsuperscript{109} \textsuperscript{208}–\textsuperscript{209}\textsuperscript{109} have been isolated from the bulbs of this species (as \textit{C. luciliae}). Compounds \textsuperscript{183}–\textsuperscript{186} all showed some inhibitory activity on cyclic AMP phosphodiesterase, with compound \textsuperscript{183} giving the best results ($IC_{50}$ = 11.2 $\times$ 10$^{-3}$ M).\textsuperscript{104} Cytotoxicity against HeLa cells was assessed for \textsuperscript{13}, \textsuperscript{184}, \textsuperscript{187}, \textsuperscript{188}, \textsuperscript{189}, and \textsuperscript{190} with the 15-deoxoeucosterol oligosaccharides (\textsuperscript{13}, \textsuperscript{187} and \textsuperscript{190}) showing good activity down to 5 $\mu$g ml$^{-1}$.\textsuperscript{11} Compounds \textsuperscript{198}–\textsuperscript{204} as well as \textsuperscript{183} and \textsuperscript{185} were tested for activity against HSC-2 human oral squamous carcinoma cells. Compounds \textsuperscript{183}, \textsuperscript{185}, \textsuperscript{200}, \textsuperscript{201} and \textsuperscript{204} all gave good results with LD$_{50}$ values in the range 10–23 $\mu$g ml$^{-1}$ (etoposide LD$_{50}$ = 24 $\mu$g ml$^{-1}$, for etoposide resistant HSC cells). It was noted that the 23$R$ isomer of \textsuperscript{185}, compound \textsuperscript{186} did not show any activity.\textsuperscript{108} Compounds \textsuperscript{208} and \textsuperscript{209} showed only weak activity in the same assay (LD$_{50}$ of 254 and 238 $\mu$g ml$^{-1}$ respectively).\textsuperscript{108} In addition to the spirocyclic nortriterpenoids, the bulbs of \textit{Scilla luciliae} (as \textit{Chionodoxa luciliae}) have been found to contain the homoisoflavanones \textsuperscript{210}–\textsuperscript{222}\textsuperscript{109}.

The bulbs and aerial parts of \textit{Scilla bifolia} L. have been studied using HPLC and mass spectrometry. Eighteen polyphenols were identified from extracts of the bulbs and aerial parts (caftaric acid, isoquercitin, routine, myricetol, ideein, quercetol, patuletin, gentisic acid, caffeic acid, chlorogenic acid, p-coumaric acid, ferulic acid, hyperoside, quercitrin, rutin, kaempferol, apigenin and sinapic acid).\textsuperscript{110}

The methanol and aqueous ethanol extracts of the bulbs of \textit{Autonoe madeirensis} (Menezes) Speta (as \textit{Scilla maderensis} Menezes), a species endemic to the Portuguese archipelago of Madeira, was found to produce cardiac action on a frog heart and although TLC showed compounds with $R_{f}$ values and colours very similar to the bufadienolides proscillaridin A \textsuperscript{223} and scillaren A \textsuperscript{224}, typical of the Urgineoideae, the presence of these compounds was not conclusively established.\textsuperscript{111}
Barnardia japonica (Thunb.) Schult. & Schult.f. (as Scilla scilloides [Lind.] Druce) has been used for a long time by traditional Chinese healers to treat abscesses and to promote circulation. This plant also grows extensively in the wild in Japan and Korea and has been used by traditional healers of the latter country. The root extract has been evaluated for its potential as an anti-inflammatory and as an antioxidant. The root extract of *B. japonica* (as *Scilla scilloides*) was found to inhibit the growth of *Staphylococcus aureus*, *Salmonella enteritidis*, *Escherichia coli* and *Candida parapsilosis* down to a concentration of 0.1% of the extract. Anti-oxidant activity was evaluated by looking at the inhibition of hyaluronidase, an enzyme that initiates the degradation of hyaluronic acid, associated with inflammation. Examination was noted at concentrations of root extract of 0.1 (14.8% inhibition) and 1% (48.2% inhibition), but not below. Anti-oxidant activity was assessed by monitoring the oxidation of linoleic acid and good activity was found (anti-oxidative index of 33.2 at a concentration of 1%).

Extensive phytochemical investigations of the bulbs of *B. japonica* (as *Scilla scilloides*) resulted in the isolation of spirocyclic nortriterpenes (21, 22, 131, 225, 226 and 227), and the related oligoglycosides (187, 228–239 and 241–247) and homoisoflavonones (42, 55 and 248). Nishida et al. reported the isolation of sixteen compounds from the methanol extract of the bulbs, including three nortriterpenes (21, 22, and 225), a lignan 249, a xanthone 137, two homostilbenes (250 and 251) and nine homoisoflavonones (49, 55, C-3 epimer compound of 62, 182, 252, 253, and 254–156). The configuration at C-3 for 253, 254 and the epimer of compound 62 was unusually found to be S by circular dichroism. Scillascilloside E-3 239 and scillascilloside E-1 237 have shown potent cytotoxicity against a range of human cancer cells [ED_{50} 1.5–3.0 nM and 1.6–5.9 nM respectively] Patents have been filed covering the use of *B. japonica* (as *Scilla scilloides*) bulb extracts for the treatment of fungal infections and as a treatment for cancer. A later investigation into the methanol extract of the bulbs resulted in the isolation of two norlanostane-type triterpenoid glycosides (257 and 258), a phenylpropanoid glycoside 259 and two alkaloids (260 and 261). The aqueous methanol extract of the bulbs of *B. japonica* (as *Scilla japonica*) produced some cardiac action on an isolated toad heart muscle, although the active components responsible were not identified.

*Othocallis siberica* (as *Scilla sibirica* Haw.) is native to southwestern Russia, the Caucasus and Turkey. The bulbs were found to contain 0.04% glycosides and 0.15% alkaloids, with the alkaloid fraction being able to stop the function of an isolated frog heart. The glycoside fraction showed a strong hypertensive action and was a stimulant to respiration. The hot water extract of the bulbs produced an acylated glucomannan with D-mannose, D-glucose and an acyl group in a ratio of 7.7 : 1 : 2.4. As part of their investigations into potential glycencide inhibitors, Yamashita et al. examined the ethanol extract of the bulbs of *O. siberica* (as *Scilla sibirica*). They isolated...
and identified five pyrrolidines (262–266), two pyrrolidine glycosides (267–268), six piperidines (269–274), one piperidine glycoside (275) and eight pyrrolizidines (276–283). These alkaloids were tested for their inhibitory activity against various glycosidases. Compound 262 was found to be a potent inhibitor of bacterial (Caldocellum sacchrolyticum) β-glucosidase and mammalian β-galactosidase (IC50 = 3.2 µg ml⁻¹ and 4.4 µg ml⁻¹ respectively). The loss of the hydroxy group at C-6, to give compound 263, significantly lowered the activity. Moderate or no activity was found for all other compounds isolated. The bulbs of Oncostema peruviana (as Scilla peruviana) were found to contain rearranged lanosterol glycosides (scillasaponin B 284, peruvianoside A 285, peruvianoside B 286, and compounds 187–188 and 287–288) as well as a range of polyhydroxylated pyrrolidines (289–291) and pyrrolizidines (292–295). Moderate inhibitory activity against cyclic AMP...
phosphodiesterase was noted for peruvianoside A 285 (IC\textsubscript{50} = 23.5 \times 10^{-5} \text{ M}) and scillasaponin B 286 (IC\textsubscript{50} = 14.0 \times 10^{-5} \text{ M}),\textsuperscript{16,126} while compound 187, a 15-deoxoeucosterol oligosaccharide, was found to be toxic to HeLa cells at a concentration of 5 \text{ \mu g ml}^{-1}.\textsuperscript{17} The pyrrolidine 291 was found to be a potent inhibitor of bacterial \(\beta\)-glucosidase (IC\textsubscript{50} = 80 \text{ nM}), compounds 292 and 293 showed significant inhibition of yeast \(\alpha\)-glucosidase (IC\textsubscript{50} = 6.6 and 6.3 \text{ \mu M} respectively) with compound 293 also showing good inhibition of bacterial \(\beta\)-glucosidase (IC\textsubscript{50} = 5.1 \text{ \mu M}).\textsuperscript{110}
Phytochemical work on the Hyacinthaceae has primarily focused on the bulbs. The exception to this has been the genus Hyacinthus, where most of the work has been done on the flowers. Hyacinthus orientalis is used as an ornamental plant and can have blue, pink, yellow or white flowers. The blue flowers of H. orientalis have been found to contain a range of acylated anthocyanins (296–302). The anthocyanin content was also studied in the blue flowers produced in vitro. The same anthocyanins were produced with some small changes in the percentage composition of the different compounds. A later investigation of the blue flowers of H. orientalis revealed a further seven anthocyanins (317–323) in addition to those isolated previously. Differences in essential oil content between wild H. orientalis flowers and those generated in vitro have been studied. Four common components were found, 1-hepten-3-ol, benzyl alcohol, phenethyl alcohol and cinnamyl alcohol. The main components in the wild flowers were phenethyl alcohol (55% at stage 3 and 48% at stage 4) and cinnamyl alcohol (23% at stage 3 and 29% at stage 4) while the in vitro generated flowers produced 75% phenethyl alcohol as the major component. The bulbs of H. orientalis were found to be rich in polyhydroxy alkaloids. α-Homonojirimycin 324 was the major component with the compounds 325–334 being found in smaller amounts. Compound 332 was found to be a good inhibitor of bacterial β-glucosidase (IC50 = 3.8 μM), mammalian β-galactosidases (IC50 = 4.0 μM and 4.4 μM) and mammalian trehalases (5.0 μM and 2.0 μM), while compound 333 inhibited rice α-glucosidase (IC50 = 2.2 μM) and rat intestinal maltase (IC50 = 2.5 μM) and compound 334 inhibited α-L-fucosidase (IC50 = 50 μM). The methanol extract of the bulbs of Bellevalia paradoxa (Fisch. & C.A.Mey.) Boiss. (as Muscari paradoxum (Fisch. et C.A. Mey.) K.Koch) yielded eight 27-norlanostane glycosides (335–342) and seven tetranorlanosterol glycosides (25, 343–348). All were tested...
for cytotoxicity against HSC-2 human oral squamous cell carcinoma. Compounds 25 and 343–344 showed no activity while compounds 345–348 gave IC50 values of 6.3–59 μg ml⁻¹, with the standard etoposide giving an IC50 of 24 μg ml⁻¹. Compounds 335, 336, 338, 340 and 341, all 23S isomers, showed good activity relative to etoposide, but the corresponding 23R isomers showed no activity up to a dose of 100 μg ml⁻¹. The methanol extract of the bulbs of *Bellevalia romana* (L.) Sweet produced oligoglycosides of the eucosterol-type, four new compounds bellevaliosides A–D, 2-(4-maderensis Menezes), have produced as slightly unusual phytochemical profile. An investigation of the ethanol extract of the bulbs resulted in the isolation of a range of 2-hydroxy di- and tricarboxylic acids and esters, cis- and trans-hydroxycinnamate esters and a flavone diglucoside 359. A later study of the bulbs found 245-ethyl-5α-cholesta-7,22E-dien-3-ol-β-galactopyranoside 360 to be present. Dias et al. isolated the pyrimidine derivative 2-(4’-aminobenzylamine)pyrimidine and found it to be an α-adrenoreceptor antagonist.144

Work on the bulbs of *Hyacinthoides hispanica* (as *Scilla campanulata*) has focused on the isolation and structure determination of a mannose-specific lectin. Crystals have been grown and the structure determined by X-ray diffraction studies.145–149 In addition to the mannose-binding lectin, a fetuin-binding lectin has been isolated and identified.150 Polyhydroxylated alkaloids have been isolated from the ethanol extract of the bulbs of *H. hispanica* (as *Scilla campanulata*) and tested for glycosidase inhibitory activity. Compounds 361–368 were identified with compound 364 showing good inhibition of *Caldocellum saccharolyticum* β-glucosidase (IC50 = 3.8 μM) and bovine liver β-galactosidase (IC50 = 4.4 μM). Compound 366 was more active than compound 364 against *Caldocellum saccharolyticum* β-glucosidase (IC50 = 0.34 μM), but less so of bovine liver β-galactosidase (IC50 = 24 μM).151

*Hyacinthoides non-scripta* (bluebells) has long been known to be toxic to livestock. Horses suffer from abdominal pain and dysentery while cattle suffer from lethargy and dullness after consuming the plants. The toxic principles are the polyhydroxy pyrrolidine and pyrrolizidine alkaloids, common to many Hyacinthoideae.151,152 Alkaloids 361–367, also found in *Hyacinthoides hispanica* (as *Scilla campanulata*), have been isolated from the leaves, stalks and immature fruits of the bluebells.151,152 A glucosamannan has been isolated from the seeds of *H. non-scripta*. It is a linear polymer with α-glucopyranose and β-mannopyranose residues occurring in the ratio of 1 : 1.3.153 Southern African genera that have received the attention of phytochemists are *Drimiopsis*, *Resnova*, *Veltheimia*, *Mervilla*, *Lachenalia*, *Pseudoprospero*, *Schizocarpus* and *Spetaea*. The range of compounds isolated is typical of the subfamily Hyacinthoideae,
including homoisoflavanones, spirocyclic nortriterpenoids and xanthones, as well as some more unusual alkaloids. Three species of *Drimiopsis* have been studied, *Drimiopsis maculata* Lindl. & Paxton, *Drimiopsis burkei* and *Drimiopsis barteri* Baker. *Drimiopsis maculata* is a southern African species used by traditional healers for treating a variety of complaints, including stomach complaints in children and the relief of constipation. It has not been found to be toxic to livestock. 

The bulbs of this plant have yielded scillascillin-type homoisoflavanones (compound 106, previously isolated from *Muscari botryoides* and compound 182, previously isolated from *M. botryoides* and *M. armeniacum*), 154 xanthones (drimiopsins A–E, 163, 369, 138, and 370–372), three homoisoflavanones (30, 59, 373) and a norlignan 374. 155 *Drimiopsis burkei* is widespread throughout Botswana and Zimbabwe, occurring southward towards the Eastern Cape Province of South Africa. 69 In Botswana it is known as *thejane* and is used to treat stomach complaints. 155 A sample of this plant collected in KwaZulu-Natal, South Africa was found to contain the norlignan hinokiresinol 155 and a homoisoflavanone 375, while a sample collected in Mochudi, Botswana was found to contain the scillascillin-type homoisoflavanones (248 and 376), xanthones (137, 138, 369, 377–378), the norlignan hinokiresinol 155 and the homoisoflavanones (E-eucomin 6, 104, 128 and 379–382). 155 *Drimiopsis barteri* is the only genus member to occur in Cameroon, where it is used to treat fever. 156 The bulbs have been found to contain the unusual isoquinoline alkaloids (383 and 384) as well as the more expected scillascillin-type homoisoflavanones (161, 376, 385–387), 3-benzyl-4-chromanones (61, 214 and 388) and Z-eucomin 6. While the configuration at C-3 was not specified, the data compared favourably to known compounds of this type and would appear to be R. 155, 156 The homoisoflavanones 144, 373, 375, 387 and 389–391, were tested against the Gram-positive, methicillin-resistant *Staphylococcus aureus*. Compound 391 was found to have significant inhibitory activity with an MIC value of 0.47 mM. Compounds 389 and 375 showed some activity, but the quantities available were insufficient for conclusive testing. 41 The homoisoflavanone 389, showed significant vasodilating effects when tested on rat aortic rings (inhibition of the contraction elicited in aorta rings by high K+ gave pIC50 of 5.31 M). This result would serve to validate the use of these bulbs for the treatment of conditions involving vasoconstriction. 157 *Resnova humifusa* (Baker) U.Müll.-Doblies & D.Müll.-Doblies, a South African species, earlier placed in *Drimiopsis* by Jessop 40 was found to contain nine homoisoflavanones (7, 10, 30, 56–60, 392). The same study reported seven
to be common with those found in the South African species *Eucomis montana* (7, 10, 30, 56, 58, 59, 60), which in addition contained compound 8. A later study on the methanol extract of the bulbs of this plant resulted in the isolation of four homoioflavanones (50, 58, 59, 61), a chalcone 132 and a tetrahydropyran derivative 393.42

*Veltheimia bracteata* Harv. ex Baker is indigenous to South Africa. The petroleum ether and diethyl ether extracts of bulbs (as *Veltheimia viridifolia* Jacq.) grown from seeds in Berlin have yielded two homoioflavanones (394 and muscomin, 97) as well as a spirocyclic nortriterpenoid 133 and its pentaglycoside 395 from the petrol and chloroform extracts respectively.159 The homoioflavanone 394, was found to exhibit good inhibitory activity against phosphodiesterase (PDE).158 Compound 394 was found to inhibit the two PDE-isoenzymes by 70% and 75% at a concentration of 100 μmol l⁻¹.158 *Veltheimia capensis* (L.) DC., native to the Western Cape, South Africa, has been found to contain an indolizidine alkaloid, steviamine 396. This alkaloid is also present in *Stevia rebaudiana* Bertoni (Asteraceae), but such alkaloids have not yet been isolated from any other Hyacinthaceae taxa.160

*Merwilla plumbea* (Lindl.) Speta is widely used by southern African traditional healers. The Zulu use it as a purgative and to facilitate full term labour. The Sotho eat the cooked bulbs as an aperient, use bulb decoctions in enemas to treat internal tumours and for the treatment of lung disease in cattle. Powdered bulbs are rubbed on sprains and fractures by the Southern Sotho, while the Tswana believe that bulbs rubbed on the body will make them resistant to witchcraft. The Swati use a lotion prepared from the bulbs to treat veldsores and boils.161,162

Concern for the sustainability of *Merwilla plumbea* has led Neube et al. to include the bulbs of this plant in a study to compare the antibacterial, anticandidal and cyclooxygenase inhibitory activity of the leaves and the, more commonly harvested, bulbs of some popular medicinal plants, harvested during different seasons in the year. Antimicrobial activities between the leaves and bulbs of *Merwilla plumbea* were found to be comparable over all four seasons and as such they concluded that the leaves could be used in many cases as a substitute for the bulbs. Likewise both the leaves and bulbs produced good cyclooxygenase inhibitory activity throughout the year.163,164 A further study found that in vitro propagation of these plants could, under the right conditions, result in an increase in the flavonoid and galloamnin levels found in the shoots, which would allow for the successful mass propagation of these plants containing elevated levels of the potentially medicinally active components.159,165 A phytochemical investigation of the bulbs (as *Scilla natalensis* Planch.) found two homoioflavanones 62 and 72, seven known eucosterol-type spirocyclic nortriterpenoids and the new spirocyclic nortriterpenoids 397, 398 and 399.166 An extract of the lectin-like proteins from the bulbs of *M. plumbea* (as *Merwilla natalensis* Planch.) have been found to exhibit moderate inhibitory activity (47%) against cyclooxygenase (COX-1).167 In a separate study, the homoioflavanones 62 and 400 have been isolated from *M. plumbea* (as *Scilla natalensis* Planch.).168 In addition *M. plumbea* (as *S. natalensis*) has been shown to have good in vitro activity against the parasite *Schistosoma haematobium* (LC = 0.4 mg ml⁻¹).166 Three homoioflavanones (7, 62, 401) have been isolated from *Merwilla dracomontana* (Hilliard & B.L. Burtt) Speta (as *Scilla dracomontana* Hilliard and Burtt).169 A southern African member of the genus *Merwilla*, under its basionym *Scilla kraussii* Baker, was found to contain the homoioflavanone, 80.162

*Lachenalia* is the largest endemic genus of the Hyacinthaceae in southern Africa. Surprisingly, very little phytochemical work has been done on the genus.165 A study of the leaves of *Lachenalia unifolia* Jacq. has yielded flavone sulphates (luteolin-3'-sulphate and -7,3'-disulphate, tricetin-3'-sulphate and -7,3'-disulphate, diasmetin-3'-sulphate and -7,3'-disulphate)168 while the bulbs of *L. rubida* Jacq., collected from the Western Cape, South Africa, were found to contain the homoioflavanones 402 and 403.165 The bulbs of *Pseudoprospero firmifolium* (Baker) Speta have been found to contain five 3-hydroxy-3-benzyl-4-chromanone type...
homoisofavanones, all as racemic mixtures (404−408) as well as the spiropcyclic nortriterpenoid, 15-deoxoeucosterol.67 A subsequent study on the bulbs of *Pseudoprospero firmifolium* subsp. *natalensis* J.C. Manning confirmed the previous findings for the typical subspecies but, in addition, found the homoisofavanone 59 in the dichloromethane extract.68

*Schizocarphus nervosus* (Buch.) van der Merwe is widespread in southern Africa. Although toxic to livestock,1 it plays an important role in traditional medicine within the region. The bulbs are used by the Zulu to treat dysentery and nervous conditions in children as well as treat rheumatic fever.168 In Botswana the bulbs are used to enhance fertility and to treat infections.169 The methanol extract of the bulbs of *S. nervosus* (as *Scilla nervosa* (Buch.) Jessop) has been tested for anti-inflammatory and anti-microbial activity. The crude methanol extract displayed a strong, but short-acting effect on a croton-oil induced contact dermatitis in a mouse ear (66% reduction of oedema after 3 h) and the nonpolar components were active against *Staphylococcus aureus* (IC50 = 1.8 μg ml−1), *Klebsiella pneumonia* (IC50 = 2.0 μg ml−1) and *Candida albicans* (IC50 = 1.0 μg ml−1). Little discrimination was noted between the Gram-positive and Gram-negative bacteria, but some specificity for the yeast was observed.169 Five homoisofavanones (49 and 409–412) and two stilbenoids (413, 414) have been isolated from the bulbs.168 A further thirteen homoisofavanones (41, 49 and 415–425) and three stilbenes (414 and 426–427) have been isolated from the bulbs of *S. nervosus* (as *Scilla nervosa* (Buch.) Jessop subsp. *rigidifolia*).176,177 Compound 419 was found to be highly active against colon cancer (HT-29 cell line ED50 = 0.88 μg ml−1) and breast cancer (MDA-MB-435 cell line ED50 = 0.42 μg ml−1).178 The yellow inter-bulb scale deposits of this subspecies were likewise investigated and eight homoisofavanones, two of which were novel (428–429).172 There has been some evidence presented to indicate that the bulbs may cause damage to liver cells.173 A homoisofavanone 400 has been isolated from *Spetaea lachenaliflora* Wetschnig & Pfosser (as *Scilla plumbea* Lindl.). This is a little known species, neither toxic nor known to be used by traditional healers.65

2 The Urgineoideae

The subfamily Urgineoideae, with more than 100 species,7 has received considerable taxonomic attention in recent years, with widely differing opinions subsequently offered on generic circumscriptions. Speta recognised eleven genera,174 several of which have been studied from both a phytochemical and a pharmacological perspective. More than any other compound type, the bufadienolides characterise the Urgineoideae. Bufadienolides are C-24 steroids possessing an α-pyrene group (doubly unsaturated six-membered lactone ring) at position 17β. The presence of these highly toxic cardioactive steroids has led to these plants being used by man in antiquity, with the ancient Egyptians reportedly using preparations to treat heart disease.175 Research into this subfamily was further stimulated by the sometimes fatal toxicity associated with various species, both to stock176–178 and to humans.179,180 The systematic position of the sea onion, *Charydbis maritima* (L.) Speta, has long been debated.181 The ancient Greeks referred to the plant as skilla, the Romans as scilla and for much of the early research on this plant, the names *Urginea maritima* or *Scilla maritima* were applied. Subsequent work by Pfosser and Speta182 provided evidence for two genera in the subfamily Urgineoideae in the Mediterranean region, *Urginea* Steinh. and *Charydbis* Speta. Phytochemical investigations to date support this generic distinction.

With much of the early research on *Charydbis maritima* focused on the plant then known as *Scilla maritima*, the trivial names of isolates of this urgineoid accordingly reflect this nomenclatural association. Notably, *Scilla* is a distinct genus currently assigned to the subfamily Hyacinthoideae, and has a very different chemical profile. Kopaczewski isolated a toxic component from the bulbs of *C. maritima* (as *Scilla maritima*) which he termed scillitin.183 It was found to be a diuretic but the whole extract from the bulbs was found to be more poisonous to guinea pigs and rabbits than scillitin itself.181 In contrast, Smith found scillitin to be more toxic to rats than the crude extract.184 The bufadienolides scillaren A224, scilliroside 430, prosclolaridin A223 and scillaren F431 have also been isolated from *C. maritima* (reported as *Scilla maritima* and/or *Urginia maritima*).185–189 Using HPLC, with prosclolaridin A223 as a reference, Tittel and Wagner showed the possible presence of bufadienolides in a plant identified as *Scilla rubra* L. (here considered synonymous with *C. maritima*).190 Petrol extracts of bulbs of this species (as *Scilla maritima* and *Urginia maritima*) were found to contain fatty acids (lauric acid, myristic acid,

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Image 123: This journal is © The Royal Society of Chemistry 2013

![Image 124](https://example.com/image.png)
palmitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid and linolenic acid) and sterols (sitosterol, stigmasterol, campesterol and cholesterol).

Investigations carried out in the early 1920s focused primarily on Charybdis maritima (squill). Both the extracts of fresh bulbs and dried powdered bulbs showed digitalis-like activity on the heart when tested on frogs and cats. Markwalder found no difference in activity between the fresh and dried bulbs and noted that neither the dried outer leaves nor the heart of the bulb exhibited much activity, while the mature middle layers of the bulb were rich in active components. The structure of scillaren A, the principle active component of C. maritima (reported as Urginia maritima) was elucidated by Stoll et al. in 1933. The interesting activity shown by the squill bufadienolides resulted in some comparative studies with digitoxigenin and strophanthidin as well as the effects of combination therapy. Ever since, work on the bulbs of C. maritima (as Urginia maritima) over the following years resulted in the isolation and identification of a large number and variety of bufadienolides. They can be divided into those having a double bond at C-4 (e.g., 224), those having a double bond at C-3 (e.g., 431) and those without either (dihydro C-4) (e.g., 432). Without exception, within C. maritima they contain a β-hydroxy group at C-14, a trans junction of rings B and C and a cis junction of rings C and D. They have been isolated as the aglycones as well as a variety of glycosides, with scillaren A 224 and proscillaridin A 223 being present in all specimens of C. maritima investigated. Samples of the plant from across its Mediterranean, European and Middle Eastern range have been investigated and this would account for the great diversity of bufadienolides isolated.

Von Wartburg and Renz isolated five bufadienolides from C. maritima (as Urginia maritima), scilliroside 430, scillaren A 224, scillaren F 431, proscillaridin A 223 and scillarenin-β-D-glucopyranoside 433. The structures reported at that time were subsequently revised and the structures shown here reflect that revision. Gorlich found proscillaridin A 223, scillaren A 224, scilliglucoseide (scillaren F) 431 and scillicyanoside 434 in crystalline form as well as minor amounts of scillicoeloside (no structure given) and glucoscillaren 435. Later work on this plant resulted in the isolation of further minor components, scilliphoside 436 and glucoscilliphoside 437. A reinvestigation of the bulbs of C. maritima (as Urginia maritima) in 1991 by Krenn et al. resulted in an additional four new bufadienolides, identified as 5α-4,5-dihydroproscillaridin A 432, 5α-4,5-dihydroglucoscillaren A 438,
gamabufotalin-3-O-α-L-rhamnopyranosyl-β-D-glucopyranoside 439 and 19-oxo-5α,4,5-dihydroprosclarin A 440. Forty-one bufadienolides were isolated from an Egyptian sample of C. maritima (as Urginia maritima). Proscillarin A 223, scillaren A 224 and scilliroside 430 were found as expected. In addition to 15 known bufadienolides found (223, 224, 430, 433, 435, 436, 441–449), 10 new glucosides of known aglycones (450–459) and sixteen new compounds were isolated (460–475). An unusual 9-hydroxy bufadienolide 476 was later isolated, also from Egyptian material.

Forty-one bufadienolides were isolated from an Egyptian sample of C. maritima (as Urginia maritima). Two of the compounds 477 and 478 were isolated from Spanish material and nine (479–487) from a plant cultivated in Japan (provenance undisclosed). A comparative study of the bulbs of C. maritima collected in the northern and southern regions of the Mediterranean area showed some differences in both the quantity and type of bufadienolides isolated. Both samples contained scilliroside 430, scillarenin.

From 2000 until 2012 a total of eleven additional new bufadienolides (477–487) have been isolated from C. maritima (as Urginia maritima). Two of the compounds 477 and 478 were isolated from Spanish material and nine (479–487) from a plant cultivated in Japan (provenance undisclosed). A comparative study of the bulbs of C. maritima collected in the northern and southern regions of the Mediterranean area showed some differences in both the quantity and type of bufadienolides isolated. Both samples contained scilliroside 430, scillarenin.
3-O-β-D-glucopyranoside 433, proscillaren A 223, scilliphaesidin 3-β-D-glucopyranoside 441, proscillaren A 223, scilliphaesidin 3-β-D-glucopyranoside 441, scilliglaucoside 431, scilliphaoside 436 and 12-epi-scilliphaeoside. In addition, the bulbs from Tunisia contained glucoscilliphaeoside 437, 12-epi-glucoscilliphaeoside, 12β-hydroxyscilliglaucosidin 3-O-β-D-glucopyranoside 488, 12-epi-scilliphaeosidin 3-O-β-D-glucopyranoside 443 and 12-epi-scilliphaeosidin 3-O-α-L-rhamnopyranosyl-β-D-glucopyranoside 489. Bulbs sourced from Sardegna also contained gamabufotalin 3-O-α-L-rhamnopyranoside 490, scillirubrosidin 3-O-α-L-rhamnopyranoside 491, scillirubroside 492, 12β-hydroxyscillirosidin 446, 5α-4,5-dihydroscillirosidin 3-O-α-L-thevetopyranosyl-β-D-glucopyranoside 475, deacetylsclirrosid 443, 10-carboxy-5β,14β-hydroxybufa-3,20,22-trienolide 5-O-β-D-glucopyranoside 493 and scilliglaucogenin 494.

The flavonoid, anthocyanin and sterol content of the bulbs of C. maritima (as Urginia maritima) have been investigated. The ethanol extract of the bulbs was studied by gas-liquid chromatography and the sterols identified by comparison to known reference compounds. Sitosterol, stigmasterol, campesterol, cholesterol, Δ7-avenasterol and Δ5-avenasterol were found to be present.213,214 Red bulbs of C. maritima (as Urginia maritima), collected in the Balearic Islands contained cyanidin 495, cyanidin-3-monoglucoside 496 and pelargonidin-3-monoglucoside 497, both in the free form and acylated with p-coumaric acid.212–216 The proportion of anthocyanin was found to be higher in tetraploids than in triploids or hexaploids.217 The flavonoids isolated included kaempferol-7-O-β-D-glucopyranoside-3-O-β-D-triglucopyranoside 498, kaempferol-7-O-β-D-glucopyranoside-3-O-α-L-rhamnopyranosyl-β-D-glucopyranoside 499, kaempferol-7-O-β-D-glucopyranoside-3-O-β-D-diglucopyranoside 500 and kaempferol-7-O-α-L-rhamnopyranosyl-β-D-glucopyranoside 501.218 In addition the
flavonoid O-glycosides 502–505, have been isolated.219 Five C-glycosylflavones have been isolated from the ethyl acetate extract of the bulbs. They have been identified as vitexin 506, isovitexin 507, orientin 508, isoorientin 509, and isoscoparin 511.220–223 Fernandez et al. identified twenty-five flavonoids in a Spanish sample of C. maritima bulbs (as Urginia maritima). They followed a parallel series: pelargonidin, kaempferol, cyaniding, quercetin and taxifolin. A complex mixture of both C- and O-glycosides was obtained.224 A fructan, sinistrin, has been isolated from C. maritima (as Urginia maritima) and found to be a mixed type β-D-fructan, with (2→1) linked and (2→6) linked unbranched β-D-fructofuranosyl and α-D-glucopyranoside residues.225,226

C. maritima (reported as Urginia maritima) has been used as a form of rodenticide since the 13th century.202 The toxic component has been found to be scilliroside 430, which affects the cardiovascular and central nervous systems, resulting in death.202 Scilliroside has an emetic effect on humans, cats, dogs and pigeons, but rats and mice are unable to vomit and as such they die within a few hours of ingesting the bulbs. The flavonoid fraction has been found to have a diuretic effect227 and the ethanolic extract of Spanish squill has shown good insecticidal activity against the stored grain pest Tribolium castaneum (red flour beetle).228 Twelve wild populations of the bulbs were studied with the red bulbs giving 60–90% mortality if applied at 20–30 μg insect−1.228 An extract of the bulbs of C. maritima (as Urginia maritima) growing in Turkey has been found to exhibit greater toxicity than cisplatin against the A549 non-small cell lung cancer (NSCLC) cell line.229 Tissue cultures of C. maritima (as Urginia maritima) grown both in the dark and under light showed no sign of the bufadienolides commonly associated with this species. The cultures grown in the light did though produce anthocyanins.220

The range of bufadienolides found in the bulbs of Charybdis hesperia (Webb & Berthel.) Speta (as Urginea hesperia Webb & Berthel.) indicates a close relationship to C. maritima. Thirteen bufadienolides have been isolated including scillarenin (512) and a variety of associated glycosides.231 Urginea fugax (Moris) Steinh. is a species which is widespread in the Mediterranean area. In contrast to C. maritima and C. hesperia, cardenolides

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and Charybdis lends chemotaxonomic support to recognition of both glucopyranosyl-glucopyranoside and rhamnosyl-3 and C-2, unlike any seen in fugaxin.

by the Zulu as a vermifuge (as plant has also been implicated in stock mortality and it is used as a substitute for squill. (as Urginea macrocentra (Baker) Speta (as Urginea maritima (C. maritima) and C. hesperia, which lends chemotaxonomic support to recognition of both Urginea and Charybdis in the Mediterranean region. Six bufadienolides have been isolated from the bulbs of Charybdis pancriation (Steinh.) Speta (as Urginea pancriation), scilliglucoside, scilliroside, transvaalin and rubellin were isolated previously from other members of the Urgineoideae. Two bufadienolides, scillaren A and scillabiose (disaccharide). Zoller and Tamm (1969) found to be toxic to animals and having a digitalis-like effect on the heart as well as a diuretic effect, and a white compound which resulted in paralysis of the central nervous system and respiration. Additional work on S. burkei (as Urginea burkei) and Urgineopsis modesta (Baker) Speta (as Urginea rubella) in the 1940s and 1950s resulted in the isolation and identification of two cardiac glycosides, transvaalin and rubellin 516 respectively. Rubellin was found to behave as a cardiac poison towards rats while transvaalin was found to kill rats primarily by its effect on the central nervous system. Further work by Louw et al. (1970) transvaalin led to the conclusion that it was either isomeric with scillaren A 224 or a stable complex of scillaren A and scilliroside. This was based on melting point analysis, toxicity tests and the fact that hydrolysis of transvaalin led to the same products as the hydrolysis of scillaren A, namely scillaridin A 517 and scillabiose (disaccharide). Zoller and Tamm (1969) and Tschesehe and Hottemann (1969) all concluded that transvaalin and scillaren A were identical compounds. The structure of rubellin 516 was fully elucidated by Steyn et al. in 1986 using high-field NMR spectroscopy. In 1927, work by Watt on South African Sekanama burkei (Baker) Speta (as Urginea burkei), yielded two glucosides, a red compound found to be toxic to animals and having a digitalis-like effect on the heart as well as a diuretic effect, and a white compound which resulted in paralysis of the central nervous system and respiration. Additional work on S. burkei (as Urginea burkei) and Urgineopsis modesta (Baker) Speta (as Urginea rubella) in the 1940s and 1950s resulted in the isolation and identification of two cardiac glycosides, transvaalin and rubellin 516 respectively. Rubellin was found to behave as a cardiac poison towards rats while transvaalin was found to kill rats primarily by its effect on the central nervous system. Further work by Louw et al. (1970) transvaalin led to the conclusion that it was either isomeric with scillaren A 224 or a stable complex of scillaren A and scilliroside. This was based on melting point analysis, toxicity tests and the fact that hydrolysis of transvaalin led to the same products as the hydrolysis of scillaren A, namely scillaridin A 517 and scillabiose (disaccharide). Zoller and Tamm (1969) and Tschesehe and Hottemann (1969) all concluded that transvaalin and scillaren A were identical compounds. The structure of rubellin 516 was fully elucidated by Steyn et al. in 1986 using high-field NMR spectroscopy. Later work by Krenn et al. on Sekanama sanguinea (Schinz) Speta (as Urginea sanguinea) yielded eight bufadienolides as well as a steroidal sapogenin and stigmasterol. The first six bufadienolides, namely scillaridin A 518, scillaridin B 519, scillaridin C 520, scillaridin D 521, scillaridin E 522, scillaridin F 523 and scillaridin G 524 were isolated from other members of the Urgineoideae. Two

As early as 1923, Juritz reported the presence of a glucoside in the toxic South Africa plant Boosia macrocentra (Baker) Speta (as Urginea macrocentra Baker) with digitalis-like activity and he noted that it could be used as a substitute for squill. This plant has also been implicated in stock mortality and it is used by the Zulu as a vermifuge (as Drimia macrocentra). The major component was identified as rubellin 516 by NMR spectroscopy. In 1927, work by Watt on South African Sekanama burkei (Baker) Speta (as Urginea burkei), yielded two glucosides, a red compound found to be toxic to animals and having a digitalis-like effect on the heart as well as a diuretic effect, and a white compound which resulted in paralysis of the central nervous system and respiration. Additional work on S. burkei (as Urginea burkei) and Urgineopsis modesta (Baker) Speta (as Urginea rubella) in the 1940s and 1950s resulted in the isolation and identification of two cardiac glycosides, transvaalin and rubellin 516 respectively. Rubellin was found to behave as a cardiac poison towards rats while transvaalin was found to kill rats primarily by its effect on the central nervous system. Further work by Louw et al. (1970) transvaalin led to the conclusion that it was either isomeric with scillaren A 224 or a stable complex of scillaren A and scilliroside. This was based on melting point analysis, toxicity tests and the fact that hydrolysis of transvaalin led to the same products as the hydrolysis of scillaren A, namely scillaridin A 517 and scillabiose (disaccharide). Zoller and Tamm (1969) and Tschesehe and Hottemann (1969) all concluded that transvaalin and scillaren A were identical compounds. The structure of rubellin 516 was fully elucidated by Steyn et al. in 1986 using high-field NMR spectroscopy. Later work by Krenn et al. on Sekanama sanguinea (Schinz) Speta (as Urginea sanguinea) yielded eight bufadienolides as well as a steroidal sapogenin and stigmasterol. The first six bufadienolides, namely scillaridin A 518, scillaridin B 519, scillaridin C 520, scillaridin D 521, scillaridin E 522, scillaridin F 523 and scillaridin G 524 were isolated from other members of the Urgineoideae. Two

| 514 | R₁ = α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside, R₂ = CH₃, R₃ = H, R₄ = O, R₅ = H, R₆ = H, R₇ = H, R₈ = H, R₉ = H, R₁₀ = H |
| 515 | R₁ = α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside, R₂ = CH₃, R₃ = OAc, R₄ = β-OH, R₅ = OH, R₆ = H, R₇ = H, R₈ = H, R₉ = H, R₁₀ = H, R₁₁ = H |
| 521 | R₁ = H, R₂ = CH₃, R₃ = OAc, R₄ = β-OH, R₅ = OH, R₆ = H, R₇ = H, R₈ = H, R₉ = H, R₁₀ = H, R₁₁ = H |
| 531 | R₁ = β-D-glucopyranoside, R₂ = CHO, R₃ = H, R₄ = β-OH, R₅ = H, R₆ = H, R₇ = H, R₈ = H, R₉ = H |
| 537 | R₁ = α-L-rhamnopyranoside, R₂ = CH₃, R₃ = H, R₄ = O, R₅ = H, R₆ = H, R₇ = H, R₈ = β-OH, R₉ = H, R₁₀ = H |
| 542 | R₁ = H, R₂ = CH₃, R₃ = H, R₄ = H, R₅ = β-OH, R₆ = H, R₇ = H, R₈ = H |
| 543 | R₁ = β-D-galactopyranoside, R₂ = CH₃, R₃ = H, R₄ = β-OH, R₅ = H, R₆ = H, R₇ = H, R₈ = H, R₉ = H |
| 557 | R₁ = H, R₂ = CHO, R₃ = H, R₄ = H, R₅ = H, R₆ = H, R₇ = β-OH, R₈ = H, R₉ = H |
| 558 | R₁ = β-D-glucopyranoside, R₂ = CHO, R₃ = H, R₄ = H, R₅ = H, R₆ = H, R₇ = β-OH, R₈ = H, R₉ = H |
| 559 | R₁ = β-D-glucopyranoside, R₂ = CHO, R₃ = H, R₄ = H, R₅ = H, R₆ = H, R₇ = β-OH, R₈ = H, R₉ = H |
| 560 | R₁ = β-deoxy-3-O-methyl-β-L-glucopyranoside, R₂ = CHO, R₃ = H, R₄ = H, R₅ = H, R₆ = H, R₇ = H, R₈ = H, R₉ = H |
| 561 | R₁ = β-D-glucopyranoside-(1→2)-β-deoxy-3-O-methyl-β-L-glucopyranoside, R₂ = CHO, R₃ = H, R₄ = β-OH, R₅ = H, R₆ = H |
| 562 | R₁ = β-deoxy-3-O-methyl-β-L-glucopyranoside, R₂ = CHO, R₃ = H, R₄ = β-OH, R₅ = H, R₆ = H, R₇ = H, R₈ = H |
| 563 | R₁ = H, R₂ = CH₃, R₃ = H, R₄ = H, R₅ = H, R₆ = H, R₇ = H, R₈ = H, R₉ = H |
new compounds, 12β-hydroxyscillirubrosidin-3-one 522 and 12β-
hydroxyscillirubrosidin-3-one 523 were identified using NMR
spectroscopy. The steroidal saponin, 7β,15α-dihydrox-
xyramogenin 524 was the first such compound to be isolated
from a member of the Urgineoideae. Majinda et al. investigated
another stem member of the same plant, and found stig-
masterol, phloroglucinol 525, phloroglucinol 1-β-glucopyranoside, scillaren A 224 and the novel 5α,4,5-dihy-
droscillaren A. In addition, salicylic acid and 3-hydroxy-4-
methylenzoic acid were isolated. An ethnopharmacological
study of S. sanguinea, using patient records from Ga-Rankuwa
Hospital in South Africa revealed a number of cases of
poisoning as a result of ingestion. The amount usually
prescribed by traditional healers does not result in adverse side
effects, but the patients admitted to the hospital had taken
more than the prescribed dose. A brine shrimp assay showed a
seasonal variation in toxicity, with the plant being more toxic in
February (late Summer) than in September (Spring). Seka-
nama sanguinea has traditionally been used for many different
conditions, including asthma and it is often taken by pregnant
women. A study by Marx et al. showed significant damage to chick embryos after exposure to this
plant. They concluded that it should be used with extreme care
by traditional healers. Undoubtedly the bufadienolides dominate the chemistry of the Urgineoideae, including the
Sekanama species. However, the isolation of a novel homoiso-
flavonoid from the bulbs of Sekanama delagoensis (Baker) Speta (as Crinum delagoensis (Baker) Jessop) indicates that a broader
range of secondary metabolites can be expected, if not
commonly found. The homoisoflavonoid 526 and 3-methoxy-
4-hydroxybenzoic acid 527, were isolated from the dichloro-
methane and methanol extracts of the bulbs respectively.

Other sub-Saharan members of the Urgineoideae to receive
attention include Urginavia altissima (L.f.) Baker (as Urginea altissima (L.f.) Baker and Drimia altissima (L.f.) Baker), Fusitum
physodes (Jacq.) Raf. ex Speta (as Urginea physodes (Jacq.) Baker),
Urginavia epigea (R.A.Dyer) Speta (as Urginea epigea R.A.Dyer),
Urginea lydenburgensis R.A.Dyer and Urginea riparia Baker. Characteristic bufadienolides have been isolated and identified,
many of which include either an aldehyde group at C-10 or a
rubellin type carbohydrate group doubly linked to the aglycone at
positions 2α and 3β. The best known of this group is the wide-
spread Urginavia altissima (often referred to as Drimia altissima or Urginea altissima). Rat populations need to be controlled to limit
threats to public health and minimise crop damage. The toxicity
of U. altissima has been investigated with respect to the field rat,
Arvicanthis abyssinicus. Synthetic rodenticides affect non-target
species and can be expensive. The powdered bulb was tested and
found to be toxic at levels of 5% of the daily food intake. If the
percentage was lower, no mortality was noted. Urginavia bra-
chystachys (Baker) Speta has (as Drimia branrystachys (Baker)
Stedje) reportedly been used as an arrow poison.

Both bufadienolides and alkaloids have been isolated from U. altissima. The alkaloids, lycorine 528 and acetylcaranine 529 have not been found by any subsequent investigators and the identity
of the plant investigated by Miyakado and coworkers has been
called into question as bulbs of U. altissima may be easily
confused with those of some Amaryllidaceae, especially the genus
Crinum L. Six bufadienolides have been isolated from U. altissima collected in Kenya, all of which have an aldehyde at C-10 (530–533). A South African sample of this plant was found to
contain 12β-hydroxyscillirubrosidin 445 (which has been isolated
from S. sanguinea previously and urginin 536 with an interesting
trisaccharide substituent at C-3). A specimen from Ethiopia yielded different bufadienolides again, gambufotalin-3-O-α-L-
hannopyranoside 490 and arenobufagin-3-O-α-L-hannopyrano-
side 537. It would appear that significant regional differences exist in the type of bufadienolide found in U. altissima. U. altissima is widely used for the treatment of gout, rheumatism
and a number of respiratory conditions, including asthma. This plant is also used by Zimbabwean traditional healers to treat
skin conditions. It has been found to produce a mild
inflammation and itching if rubbed on the skin. This effect has been found to be due to the presence of calcium oxalate raphides in the bulbs and as such the appropriateness of its use as a skin treatment has been questioned.262

*Fusilium physodes* (as *Urginea physodes* (Jacq.) Baker) was found to contain four bufadienolides, physodines A 538, B 539, C 540 and D 541. Two of which, physodines A and B, both having a C-10 aldehyde group, were found to be toxic to weaned guinea pigs (fractions not causing death in 48 h at 200 mg kg⁻¹ were considered non toxic). Physodines C and D were of interest in that they were the first naturally occurring 14-deoxybufadienolides to be isolated.263 An ethanolic extract of the bulbs has been shown to have antifungal activity.264 The methanol extract of the bulbs of *Fusilium depressum* (Baker) U.Müll.-Doblies J.S.Tang & D.Müll.-Doblies (as *Drimia depressa* (Baker) Jessop) was found to contain two bufadienolides, 542 and 543.265 The leaves of this plant are toxic to cattle, sheep and rabbits and the plants are used by the Sotho as a good luck charm or to cause harm to one’s enemy.266 Novel rubellin type bufadienolides, riparianin 544 and lydenburgigenin 545, have been isolated from *Urginea riparia* and *Urginea lydenburgensis* R.A.Dyer respectively.237,268 In addition, *Urginea lydenburgensis* was found to contain the novel bufadienolide, scillicyanosidin 546, with an aldehyde group at C-10. Riparianin 544 showed moderate activity against MCF7 (breast), TK10 (renal) and UACC62 (melanoma) cell lines (total growth inhibition of <3.5, 544 and 545 show moderate activity against MCF7 (breast), TK10 (renal) and UACC62 (melanoma) cell lines (total growth inhibition of <3.5, <7 and <10.5 ppm respectively). *Urginavia epigea* is used locally to treat backaches or as a soap. The smoke from smouldering bulbs is also used as a treatment for headaches and colds.269 In addition to the bufadienolide 517,270 six deoxypseudo sesquiterpenoids were isolated, 547 and 548. These were the first to be reported from the Hyacinthaceae and due to their occurrence in *U. epigea* but not the oft-confused *U. altissima*, provide species level taxonomic markers.267 The bufadienolide 517, has an unusual 3,5-diene system, readily obtained synthetically, but not commonly isolated directly from plant sources.268 The butanol extract of the bulbs of *U. epigea* was found to have significant molluscicidal activity against the bilharzia-carrying snail, *Bulinus africanus*. This result has raised some concern with regards its use as soap and the potential toxic affect it may have on other aquatic biota.269

An Indian member of the Urgineoideae, known locally as ‘jungli-piyaz’ or ‘bhukanka’ and Indian squill has been used traditionally for stomach complaints, as a cardiac stimulant, a diuretic, as well as to treat asthma, cough or bronchitis and various infections.270 Commercially available samples vary with some plants having a truncated bulb and others a scaly bulb.271 For much of the work reported, the plant has been identified as *Urginea indica* (Roxb.) Kunth or *Scilla indica* Baker. The name *Indurga indica* (Roxb.) Speta is currently accepted. Extracts of the bulbs have shown some activity against *Neisseria gonorrhoeae* infections272 and have had outstanding antimicrobial activity attributed to them in a survey of medicinally used plants in India.273 The ethanolic extract of the bulbs of *I. indica* (as *Scilla indica* Baker) has been found to have good antioxidant activity (protection against lipid peroxidation induced by ferrous sulphate in a dose-dependant manner, with 49% protection for hydroxyl radical-mediated hydroxylation at a concentration of 250 μg ml⁻¹) as well as to possess cardiac activity on a par with ouabain.274 Rao and Rangashwami have detected bufadienolides in extracts of the bulbs of *I. indica* (as *Scilla indica* Roxb.) and have isolated scillaren A 224 as the principle active component.275,276 Jha and Sen, however, found no trace of scillaren A 224 in a plant identified as *Scilla indica* at the time.277 The principle bufadienolides isolated from this plant (as *Urginia indica* Kunth) by various investigators are scillaren A 224 and prosccillaridin A 223,278,279 with scillaren A being reported as early as 1956. These are also the principle bufadienolides of the European squill *C. maritima*. In small doses, the action of *I. indica* is the same as *C. maritima*, in that it slows the heart beat and increases urine flow and it can successfully be used as a substitute for *C. maritima*.282 Jha and Sen277,280 have studied the twelve different cytotypes of *I. indica* (as *Urginea indica*), belonging to four ploidy levels. Scillaren A 224 and prosccillaridin A 223 were present in all twelve. Bulbs were investigated through three successive years. The tetraploids showed the highest concentration of these bufadienolides, followed by diploids and then triploids. Significant variation in the bufadienolide concentration was also noted between samples collected in northern and southern India, with the northern samples showing much lower levels of prosccillaridin A 223 and scillaren A 224.281 In addition, two minor components, scilliphaeoside 436 and anhydroscilliphaeosidin, were found to be present in the tetraploid cytotypes and...
scilliphaseoside 436 in the triploids. Likewise the sterol content was investigated with only minor differences noted between the ploidy levels. Stigmasteryl predominated, with sitosterol and campesterol being found in the tetraploid cytotypes and some of the triploids respectively. 284,285 Kopp and Danner284 found the bulbs of I. indica (as Urginia indica) to contain six bufadienolides, scillaren A 512, proscillaren A 223, scillaren A 224, scilliphaseosidin 3-0-α-L-rhamnopyranoside 549, scilliglauco- sidin 3-0-α-L-rhamnopyranoside 534 and scilliglaucesidin 3-0-β-D-glucopyranoside 535, while Saxena and Chaturvedi isolated 6-desacetoxy scillirosidin 550. 286 In addition to the bufadienolides and sterols, Sultana et al. have isolated three novel flavonoid glycosides (551–553) from bulbs collected in Bangladesh. 287 Seasonal variation in the glycosidal content of the bulbs has been observed with the highest such levels found during October at the onset of dormancy. The levels steadily decrease to a minimum in June. 288 Sterol content has been found to peak during the pre-flowering and pre-vegetative growth stages and it has been suggested that the sterols could be a trigger for the onset of reproductive and vegetative growth in the species. 289 Significant antifungal activity has been noted and attributed to the presence of a 29-kDa glycoprotein which inhibited growth of Fusarium oxysporum at a concentration of 10 µg protein well−1. 290,291 This protein has in addition shown good antitumour activity against the growth of an ascites tumour and mouse mammary carcinoma (tested in vivo using 6–8 week old female mice). 292 The bulbs of I. indica (as Urginia indica L.) collected in Nigeria were found to contain six alkylresorcinols of the structure types shown in 554 and 555. 293 An ethanolic extract of I. indica (as Scilla indica), has reportedly shown good inhibition of the Semliki Forest Virus and the active principal found to be a diosgenin saponin. 294 The genus Drimia Jacq. is closely related to Urginea. Drimia robusta Baker is widely used in southern Africa by traditional healers. It has been used as a diuretic, as a treatment for feverish colds, to promote the healing of broken bones, to treat diseases of the uterus and to relieve stabbing pains in the chest. 258,295 Luyt et al.295 investigated the biological activity of this plant in order to substantiate its use in traditional medicine. Anti-bacterial activity was found to be present in the ethyl acetate extract of the bulbs. An ethanolic extract of the bulbs showed higher inhibitory activity than indomethacin in the screening for inhibition of cyclooxygenase. This inhibition of prostaglandin synthesis (tested for with the cyclooxygenase assay) could explain the plant’s use as a treatment for feverish colds. Further work on the COX-1 inhibition of a water extract of the bulbs showed activity above 70%. 296 Evidence for the presence of proscillaridin A 223 was presented: TLC and NMR data were compared with a standard sample. Luyt et al.297 then compared bulbs derived from tissue culture with those grown naturally. A standard proscillaridin A 223 was used for comparison and the UV spectra and qualitative TLC results were compared. The results indicated that the bufadienolide content was the same in the in vitro-derived plants as in those grown naturally. This is in contrast to the work done on C. maritima, where no bufadienolides were found in the tissue cultured bulbs. 298 Phytochemical studies of the bulbs of D. robusta yielded eight bufadienolides, 12β-hydroxyciscilli- soroside 445, 6β-acetoxy-3β,8β,14β-trihydroxy-12-oxobuta-4,20,22- trienolide 556, scillirosidin 430, 12β-hydroxyciscilliroside 446, hellebrigenin-3-O-β-glucopyranoside 531, 16β-hydroxyhelle- brigenin 557, 16β-hydroxylellebrigenin-3-O-β-glucopyranoside 558 and 5β,16β-dihydroxybufalin-3-O-β-glucopyranoside 559 as well as three common aromatic acids, 4-hydroxy-3-methoxybenzoic acid, 3,4-dihydroxybenzoic acid and trans-3-{4′-hydroxyphenyl}-2-propenoic acid.258,259,297 The toxicity of Rhodoceon madagascariensis Baker, a plant endemic to Madagascar, has been tested against the embryo-larvae of medaka fish (Oryzias latipes) and an LD50 of 1 mg ml−1 was established. 298 Work on the genus Boweia Harv. ex Hook.f. has centred on Boweia volubilis Harv. ex Hook.f. Most of the investigations were carried out in the 1950s and early 1960s. This African species is
The Ornithogaloideae are widespread throughout Africa, Europe and southwest Asia. This group consists of approximately 280 species, with a recent phylogenetic analysis by Martinez-Azorin et al. recognizing nineteen monophyletic genera. Phytochemical studies on the Ornithogaloideae have centred on Ornithogalum L. and Galtonia Decne., primarily driven by the significant biological activity attributed to the compounds isolated. In addition, a small amount of work has been done on Albuca L., Eliokarmos Raf., Stellarioide Medik., Loncomelos Raf. and Honorius Gray. The types of compounds isolated are strongly linked to the geographic region the plant species derive from, with the African taxa containing primarily cholestane glycosides and spirosterols, and the European taxa cardenolides. Some flavonoids and sterols have been isolated from plants sourced from all regions studied. Additionally, a limited number of homoisoflavonanes have been identified from the bulbs.

The genus Albuca L. is widespread in southern Africa, with some species occurring in the Arabian Peninsula. The bulbs of Albuca fastigiata Dryand. have been investigated and only one compound was isolated, a homoisoflavonoid, 564. Albuca fastigiata is found on the East coast of South Africa and is used by the Zulu as a protective charm and to treat malicious food poisoning. Another southern African species, Albuca setosa Jacq., has been tested for anti-inflammatory activity in a carrageenan-induced rat paw edema assay. This plant is used by traditional healers to treat wounds, among other conditions, and was found to significantly inhibit carrageenan-induced paw edema for a 3-hour challenge (43–55% over 3 h at 150 mg kg⁻¹ and 68–85% for 300 mg kg⁻¹). Albuca setosa has also been used by traditional healers in the Nkonkobe municipality in South Africa for the treatment of diabetes. As part of a study on the steroidal sapogenins of various monocot families, Okanishi et al. found Albuca nelsonii N.E.Br. to contain ruscogenin. This was identified by comparison of melting points, mixed melting points, optical rotations, infrared and mass spectra with an authentic sample.

Galtonia candicans (Baker) Decne. is native to South Africa, and was investigated by the laboratories of Kuroda and Mimaki who used bioassay-directed fractionation to isolate the active components of the bulbs. The methanol extract was found to be active against leukemia HL-60 cells (IC₅₀ = 0.017 μM). This was further partitioned between n-butanol and water, with the activity being retained in the n-butanol fraction (IC₅₀ = 0.0056 μM). This was found to contain the hexacyclic rearranged cholestane diglycoside, candicanoside A 566, the polyoxygenated 5β-cholestane diglycoside galtonioside A 567, six cholestan
bisdessomides 568–573 and six cholestane glycosides 574–579. Candicansoside A 566 and galtonioside A 567 were found to have potent activity against leukemia HL-60 cells (IC50 = 0.032 μM and 0.057 μM respectively) and further testing on a 38 cell line assay showed differential cytotoxicities against breast cancer, CNS cancer and lung cancer lines, while colon cancer, ovarian cancer and stomach cancer cell lines were resistant to them. 568,570 Compound 569 showed moderate activity against leukemia HL-60 cell lines ([IC50 = 6.8 μM]) and compounds 575–578 showed good activity using the same assay (IC50 = 0.00012 μM, 0.00048 μM, 0.0024 μM and 0.053 μM respectively). 571 Tang and Yu have achieved the total synthesis of can- dicansoside A 566, using a 27-step synthesis. 572,573 Another southern African species of Galtonia that has received some attention is Galtonia princeps (Baker) Deacre. 574 A methanol extract of the bulbs yielded the cholestanol derivative 580. Both the bulbs and aerial leaves of Galtonia viridiflora I. Verd. were found to contain monoglycosides of caffeic acid, principally rhamnose and glucose. 575,576

Work on the bulbs of Galtonia saundersiae (Baker) Mart.-Azorin, M.B.Crespo & Juan (as Ornithogalum saundersiae), a native of the East coast of South Africa, began in the early 1990s with the isolation of three acylated cholestanol glycosides 581–583. All three were examined for their inhibitory effect on cyclic AMP phosphodiesterase. Compounds 582 and 583 showed good activity ([IC50 = 0.00025 μM and 0.00020 μM respectively], suggesting that the presence of a benzoyl group attached to the sugar moiety is essential for activity. 577 Six additional cholestane glycosides 584–589 were isolated and tested for their inhibitory activity on cyclic AMP phosphodiesterase. Compounds 585 and 588, with the acyl group at the C-3 hydroxy position of the rhamnose group, showed good activity (IC50 = 9.9 × 10−5 μM and 10.9 × 10−5 μM respectively), as did compound 589 (40% inhibition at 0.08 mg ml−1), while the other compounds were inactive. 579,580 Compound 590, isolated from the bulbs of G. saundersiae (as Ornithogalum saundersiae), showed significant inhibition (IC50 = 3.1 μM) of the proliferation of peripheral blood lymphocytes produced by a patient with chronic renal failure, suggesting potential as an immunosuppressive agent. 581 Rearranged cholestanol glycosides (591–599) with a six-membered hemiacetal ring E, between C-16 and C-23, have been isolated. The conformation of ring E was determined through molecular mechanics and molecular dynamics calculations. 582 These compounds were tested for anti-tumour activity, primarily against leukaemia HL-60 cells and MOLT-4 cells. Compounds 591 (IC50 = 21.0 nM and 18.0 nM), 592 (IC50 = 9.2 nM and 3.2 nM) and 597–599 (IC50 = 0.019, 0.063 and 0.052 μM for HL-60 cells) showed significant cytotoxic activity, primarily through the induction of apoptosis. These results would indicate that the presence of an aromatic ester group at the glyco-

side moiety is essential for good activity. 583 Further investigation of the methanol extract of the bulbs resulted in the isolated of the related cholestanol glycoside 600. 584 In addition to the rearranged cholestanol glycosides mentioned above, ten new (575, 601–609) and three previously isolated (567–569) cholestanol glycosides, with a glycosidic moiety at C-16 have been
tested for their inhibitory activity against leukemia HL-60 cells and MOLT-4 cells. All these compounds showed significant activity, with a loss of activity noted each time the ester group on the sugar moiety was removed.\textsuperscript{150-153} Due to the significant anti-
tumour activity shown by these plant extracts, a number of patents have been filed in Japan and China covering the extract methods used, the use of the saponins and, in some cases, the synthesis of the active components.\textsuperscript{354-358} In particular, 567
(called OSW1) has been the subject of much synthetic work. The full synthesis of the compound itself has been accomplished, and a large number of analogues have been produced for structure–activity relationship studies. Studies indicate that OSW1 acts by damaging the mitochondria and inducing apoptosis through an increase of cytosolic calcium and thus the activation of calcium dependent apoptosis. It has been demonstrated that OSW1 is active against some cells that are resistant to conventional anti-cancer agents, in particular fludarabine-resistant chronic lymphocytic leukemia cells.\(^{299}\) In addition to the work on the anti-tumour activity of \textit{G. saundersii}, the ethanol extract of the whole dried plant has been tested for its protective effects against acute hepatic failure. The authors concluded that it did provide some benefit, primarily through suppressing oxidative stress, lipid peroxidation and apoptosis of hepatocytes, as well as reducing inflammation.\(^{280,281}\)

Species from the genus \textit{Ornithogalum} have received substantial attention. While early work on the genus began in the 1950s on the European members of the genus, later work has included species from Turkey and Iran.

Work on the European species of \textit{Ornithogalum} was initially centred on \textit{Ornithogalum umbellatum} L. (common Star of Bethlehem). European species of \textit{Ornithogalum} are characterised by the presence of cardenolides, with some flavonoids also identified. Extracts of the bulbs of \textit{O. umbellatum} were found to have a digitalis-like effect on frog, rabbit and cat hearts. In all cases, a positive inotropic action was noted, decreased conduction and finally systolic standstill.\(^{262-264}\) A clinical trial found that when tablets of \textit{O. umbellatum} were substituted for digitoxin there was a loss of activity and fluid retention increased. When the tablets were coated to protect them from stomach acid, the digitalis-like effect and less gastrointestinal nausea.\(^{265}\) The principal active component of \textit{O. umbellatum} was found to be the cardenolide convallatoxin.\(^{610}\) The cytotoxicity of convallatoxin \textit{610} was studied. It was found to have an IC\(_{50}\) of 0.02 \(\mu\)g ml\(^{-1}\) when assayed against Eagle’s KB strain of human carcinoma and structure–activity studies showed that the glycosidic portion was essential for activity and that the \(\beta\)-hydroxy groups at C-5 and C-14 and the aldehyde at C-10 significantly enhanced the activity.\(^{267}\) The convallatoxin \textit{610} content in the bulbs can be increased by defoliation of the plant.\(^{268}\) In total, sixteen cardenolides (\textit{610}–\textit{626}) have been isolated from the bulbs of \textit{O. umbellatum} L.\(^{268,271}\) Later phytochemical investigations of the bulbs resulted in the isolation and identification of two flavonoids (\textit{627} and \textit{628})\(^{272}\) while the four flavonoids (\textit{627}–\textit{630}) were isolated from the leaves.\(^{272-273}\) Compounds \textit{629} and \textit{630} were also isolated from the leaves of \textit{Ornithogalum algeriense} Boiss. and \textit{Ornithogalum kochii} Parl.\(^{274}\) Sabudak and Oyman reported the presence of 3-O-(2′-methoxy-4′-(2-pentenal))-phenylsiosteryl in the bulbs of \textit{O. umbellatum}\(^{275}\) and a study of the roots colonized by the fungus \textit{Glomus intraradices} found a complex range of apocarotenoids.\(^{275}\) A range of cardenolides have been isolated from the species \textit{Loncomelos magnus} (Krasch. & Schischk.) Speta (as \textit{Ornithogalum magnus}) \textit{610, 614, 631–635,}\(^{276-282}\) \textit{Honorius nutans} (L.) Gray (as \textit{Ornithogalum nutans}) \textit{610, 631, 632, 636–664,}\(^{283,284}\) \textit{Ornithogalum gussonei} Ten. \textit{631, 635, 665}\(^{285}\) and \textit{Honorius boucheanum} (Kunth) Holub (as \textit{Ornithogalum boucheanum}) \textit{666–673}.\(^{286}\) The aerial parts of \textit{O. gussonei} yielded two flavonoids saponaretin \textit{674} and saponarin \textit{675}.\(^{287}\) A terpene glucoside \textit{676} has been isolated from \textit{Ornithogalum montanum} Cyt.\(^{288}\) and the main water soluble polysaccharide of the bulbs of \textit{Ornithogalum ponticum} (Zahar.) Speta was found to be a neutral glucofructan with a glucose : fructose ratio of \(30:1\).\(^{289}\)

A comparative study on the Bulgarian species \textit{Ornithogalum nanum} Silbth. & Sm., \textit{O. gussonei}, \textit{Loncomelos nanobosphate} (L.) Raf. (as \textit{O. nanobosphate}), and \textit{O. montanum} Cyt. resulted in cardenolides (\textit{677–681}) being found in the bulbs of \textit{O. nanum} and \textit{O. gussonei} but not in the bulbs of the other two species.\(^{290}\)

The leaves and bulbs of the Turkish species \textit{Ornithogalum alpigenum} Stapf. have been tested for antioxidant activity, antimicrobial activity and as free radical scavengers. The leaf extracts were found to be good free radical scavengers (90.9%) and the bulb extracts (methanol, ethanol, acetone and benzene) showed variable activity against \textit{Candida albicans}, \textit{Bacillus subtilis} and \textit{Bacillus cereus}. The highest antioxidant activity was found in the methanol extract of the bulbs (88.1% on a \(\beta\)-carotene-linoleic acid system) and the lowest in the benzene extract of the bulbs.\(^{291}\) The Iranian species \textit{Ornithogalum procerum} Stapf. and \textit{Ornithogalum cuspidatum} Bertol. have received some attention. The aerial parts of \textit{O. cuspidatum} are used in Iran as food additives as well as an anti-irritant and relaxant to soothe the throat when suffering from a dry cough. The essential oils in the leaves, flowers and bulbs have been determined by GC-MS. The flowers and bulbs contained primarily saturated hydrocarbons, while the leaves contained oxygenated hydrocarbons and terpenoid compounds.\(^{292}\) In addition, a GS-MS analysis of the methanol extract of the bulbs has allowed for the identification of thirteen phytosterols (cholesterol, 3,5-didehydrostigman-6,22-diene, 4,4-dimethyl-5x-cholest-7-en-3-one, 4β-methylcholesterol, 5-cholestone-3β,7β-diol, campesterol, cholest-4-ene-3,6-dione, stigmaster-4-en-3-one, stigmasta-3,5-dien-7-one, stigmasterol, \(\Delta^5\)-ergostenol, \(\beta\)-sitosterol and \(\gamma\)-sitosterol).\(^{293}\) A GC-MS analysis of the aerial parts and bulbs of \textit{O. procerum} resulted in the identification of twenty-three essential oils in the aerial parts and four polyester-type compounds in the bulbs.\(^{294}\) \textit{Ornithogalum sintensii} Freyn, another Iranian species, has been tested for antioxidant activity. A higher phenolic and flavonoid content in the aerial parts of the plant relative to the bulbs, accounted for the greater antioxidant activity in those extracts (IC\(_{50}\) for DPPH radical scavenging activity of 368 and 669 \(\mu\)g ml\(^{-1}\) for leaves and bulbs respectively).\(^{295}\)

\textit{Eliokarmon thysoides} (Jacq.) Raf. is found in southwestern South Africa. Although not reportedly used by traditional healers it has been strongly linked to stock poisoning.\(^{296}\) Accordingly, the bulbs have been the subject of many phytochemical investigations. An initial investigation of the methanol extract of the bulbs in 1992 (as \textit{Ornithogalum thysoides}) resulted in the isolation of four cholestane bisdesmosides (\textit{682–685}), with \textit{685} showing some inhibitory activity on cyclic AMP phosphodiesterase (IC\(_{50}\) = 15.3 \times 10^{-5} M).\(^{297}\) Following the discovery that the methanol extract of the bulbs showed potent
cytotoxicity against leukemia HL-60 cells (IC_{50} = 0.79 \mu g ml^{-1}),
fractionation of this extract resulted in the isolation of twelve
desmosidic cholestane glycosides (577–578, 686–694),
seven cholestane glycosides (695–701) and nine spirocyclic
glycosides (702–710). The desmosidic cholestane
glycosides with an aromatic acyl group at the C-16 diglycoside
were found to be the most cytotoxic (686 and 576) with IC_{50}
values of 0.00016 and 0.00013 \mu g ml^{-1} respectively. Compounds
687 and 696, the deacyl derivatives of compounds 688 and 689
and compounds 691 and 692 respectively did not show any
activity at all. Only moderate activity against leukemia HL-60
cells was found for the spirocyclic glycosides (IC_{50} of 1.6–5.3 \mu g
ml^{-1}). An arabinogalacturonan oligosaccharide has been isolated
from the leaves of *E. thyrsoides* (as *O. thyrsoides*). South
African bulbs of *Stellarioides longibracteata* (Jacq.) Speta are
used extensively by the Zulu as an anti-inflammatory, and
regionally to treat diabetes. A phytochemical investigation of
the bulbs (as *Ornithogalum longibracteatum* Jacq.) revealed one
compounds, the homoisoavanone 711. The water extract of the bulbs produced a significant increase in glucose
utilisation in Chang liver cells. *Stellarioides longibracteata*
was introduced to China many years ago and it is used in Chinese
folk medicine to treat cancer, as an antimicrobial, anti-inflammatory and to treat hepatitis and parotitis. This species
was known earlier as *Ornithogalum caudatum* Ait. and as such many
papers and in particular patents, have been filed under that
name. Spirosteroles, caudaside A 712 and hecogenin 713 have
been isolated as well as \( \alpha \)-sitosterol and three homoiso-
flavonones (714–716). Compounds 714–716 were tested for
anti-tumour activity against P388 (mouse leukemia) and A-549
(human pulmonary adenocarcinoma) but no activities were noted. Later investigations of the bulbs of *S. longibracteata* (as *O. caudatum*) resulted in the isolation of n-butyl pyroglumate 717, 26 additional known flavonoids, sterols and acids\(^a\)\(^b\)\(^c\)\(^d\)\(^e\) and a monoterpene lactone (6-hydroxy-4,4,7α-trimethyl-5,6,7,7α-tetrahydro-4H-benzofuran-2-one).\(^f\)\(^g\) A number of patents have been filed in China and Russia outlining methods for the extraction of *S. longibracteata* (as *O. caudatum*) and use as a treatment for cancer,\(^a\)\(^b\)\(^c\)\(^d\)\(^e\) cholecystitis and cholecystitis-related diseases\(^a\)\(^e\)\(^f\)\(^g\) and for the isolation of the flavonoid components for use as an anti-inflammatory and analgesic.\(^a\)\(^e\)\(^f\)\(^g\) Extracts from *S. longibracteata* (as *O. caudatum*) have shown some benefit in the treatment of liver conditions.\(^a\)\(^e\)\(^f\)\(^g\) Four water soluble polysaccharide fractions have been extracted from *S. longibracteata* (as *O. caudatum*) and have been found to have potential as antitumour agents.\(^a\)\(^e\)\(^f\)\(^g\) Further work on the anti-cancer effects of this species has shown inhibition of MDA-MB-231 breast cancer cells in a dose and time dependant manner.\(^a\)\(^e\)\(^f\)\(^g\) The bulbs of *Stellarioideae tenuifolia* (Redoute) Speta (as *Ornithogalum tenuifolium* Delaroche) yielded a crystalline steroidal saponin, 718, with an unusual 5β configuration.\(^a\)\(^b\)\(^c\)\(^d\)\(^e\)\(^f\)\(^g\) This unusual configuration at C-5, together with the 1β,3α hydroxy group configuration, results in a molecule with a shape that is able to undergo self-recognition, similar to single-strand DNA, and thus form a supramolecular zipper. A review of steroidal glycosides isolated from various monocot families (including *Galtonia saundersiae*, as *Ornithogalum saundersiae*) and their biological activities has been published as well as a review of cholestan glycosides from *G. saundersiae*, *G. candidans* and *Eliokarpos thysoides* (as *Ornithogalum thysoides*).\(^a\)\(^b\)\(^c\)\(^d\)\(^e\)\(^f\)\(^g\)

4 The Oziroëeideae

The genus *Oziroë* Raf. (syn. *Fortunatia* Macbr.), is widespread in South America and can be found in Peru, Chile, Bolivia, Paraguay and north to central Argentina.\(^a\)\(^b\)\(^c\)\(^d\) No phytochemical investigations have been recorded on these plant species.

5 Conclusions

Research into the chemistry of the Hyacinthaceae has spanned over 90 years and resulted in the isolation of over 700 compounds. The need to understand the chemistry was largely fuelled by both the toxicity of the plants to stock and the significant ethnomedicinal applications associated with representative species. In addition to the isolation of many compounds of medicinal significance, the phytochemical studies have shed light on the classification of many of the species. A thorough understanding of the chemistry and pharmacology of these important plant species allows for the potential discovery of new medical applications and further aids the conservation of those taxa threatened with unsustainable utilisation by indicating alternatives with similarly active constituents.

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7 References


