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CHEMICAL INVESTIGATIONS OF MEDICINAL PLANTS OF SOUTHERN AFRICA

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Introduction:

Southern Africa is one of the rich centres of plant biodiversity in the world. Not only does it support a large number of species (*ca* 30 000 higher plants in South Africa alone), but also has many species endemic to the area. The Cape Floristic Region with over 6000 endemic species is one of the world's richest floral regions (Cowling and Hilton-Taylor, 1994). The great variation in climatic types from the sub-tropical eastern coast to the semi-desert vegetation of much of the region to the Mediterranean climate of the Western Cape has resulted in a wide variety of types of plants adapted to the different habitats. The indigenous peoples of Southern Africa have a long history of traditional plant usage for medicinal purposes. The trade in medicinal plants in Southern Africa is an important part of the economy. Over 700 plant species are reported as being traded in the region (Mander, 1998). In South Africa there are 27 million indigenous medicine consumers. This is causing demand to exceed supply and several species such as *Walburgia salutaris* (black stinkwood) and *Siphonochilus aethiopicus* (wild ginger) becoming extinct outside protected areas in Kwazulu-Natal (Mander, 1998).

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The value of trade in medicinal plants in KwaZulu-Natal alone was estimated to be worth R60 million ($10 million) in 1998, around one-third the value of the maize crop, which is the largest crop in the province. Most households spend between 4 and 8% of their annual income on indigenous medicine services. In addition, in KwaZulu-Natal between 20 000 and 30 000 people derive an income from trading indigenous plants. Most of these are rural black women, the most marginalized group in South African society (Mander, 1998). It is estimated that in 1998 the trade in medicinal plants was 20 000 tonnes with a value of $110 million (Mander 1998). Apart from traditional plant usage, plants such as *Aspalanthus linearis* (Rooibos), *Harpagophytum procumbens* (Devil's claw) and *Hypoxis hemerocallidea* (African potato) are exported to the East and Europe.

The use of sub-Saharan African medicinal plants has been, until relatively recently, largely undocumented. With the urbanization and westernization of many African people much traditional knowledge is being lost. It is important to preserve the traditional knowledge of indigenous peoples by documenting the types of plants used and their uses. It is also important to investigate the chemistry of these plants with the aim of isolating compounds that can be screened for a variety of activities.

80% of the world's inhabitants rely on traditional medicines for their primary health care.

The importance of plants in Western medicine is illustrated by the fact that 119 chemical substances derived from 90 plant species are considered important. 74% of these were discovered as a result of chemical studies directed at the isolation of plants used in traditional medicine (Farnsworth *et al.*, 1985). The use of compounds from other organisms, such as the penicillins from fungi, and compounds from novel sources such as the spongistatins and bryosytatins from marine organisms, and important highly active compounds from sources such as amphibians and marine molluscs also need to be considered.

The thorough investigation of a medicinal plant requires the collaboration of a number of people with a range of expertise. The traditional healer is an integral part of such a research effort with his knowledge of plant usage. His intellectual property has to be protected and means of benefit sharing should any active compounds that could be commercialized, be found. The ethnobotanist is essential in collecting, correctly identifying the plants, retaining voucher specimens and documenting the plant usage. His input can widen the scope of projects by introducing aspects of chemotaxonomy. The isolation of particular secondary metabolites can assist taxonomists in their work. The natural products chemist's role is to isolate, purify, quantify and identify compounds present in the organisms being investigated. Plant material is usually dried and extracted and the extracts obtained separated into pure compounds using a range of chromatographic techniques. The structures of pure compounds isolated are determined using spectroscopic (infra red, mass spectrometric and nuclear magnetic resonance) and chemical techniques. The most important spectroscopic technique is nuclear magnetic resonance spectroscopy which is an essential tool for the natural products chemist. Chemical techniques usually involve simple derivitisations, such as oxidations, reductions, esterifications to obtain a range of derivatives, analysis of whose NMR spectra will assist in structural determination of the compound. Pure compounds can be screened for a range of activities-e.g. anti-cancer, anti-fungal and anti-malarial. The development of robotic high throughput screening techniques where very small amounts of compounds can be tested in a large number of screens is becoming more important.

One of the major areas of research of the Natural Products Research Group at the University of Natal is the investigation of medicinal plants of southern Africa. Results of our investigations into the chemistry of the Hyacinthaceae family are described in this paper.

The Hyacinthaceae of Southern Africa.

The Hyacinthaceae, formerly part of the monocotolydenous Liliaceae *sensu lato,* is a large, chemically and morphologically diverse group of plants. The ethnobotanical usage of plants from this family has recently been reviewed (Pohl et al., 2000).

Many Hyacinthaceae species are important in the local medicinal plant trade. A recent survey revealed that of the most important species marketed by street traders, seven occurred within the top 70, with three of these (*Scilla natalensis, Eucomis autumnalis* and *Bowiea vo-*

lubilis) ranked in the top 10 (Mander, 1998). Southern African Hyacinthaceae species are well known for their ornamental value, in particular the genera *Eucomis* (pineapple lilies), *Ornithogalum* (chincherinchees), *Lachenalia, Galtonia and Veltheimia.*

Interest in the chemistry of the Hyacinthaceae was initiated over one hundred years ago after stock losses were noted to occur following ingestion of aerial parts of *Ornithogalum thyrsoides* (Hutcheon, 1904). A number of other *Ornithogalum* species have subsequently been implicated in stock poisoning. These observations led to feeding trials being undertaken on almost 40 members of the Hyacinthaceae at the Onderstepoort Veterinary Research Institute which positively linked members of the *Ornithogalum* genus as well as species belonging to *Scilla, Dipcadi* and *Urginea* to poisonings (Bullock, 1952). Although most Hyacinthaceae species are considered poisonous, some taxa are locally considered edible (Anderson and Mc Gregor, 1995; Heinz and Maguire; Obermeyer, 1964; Story, 1964).

Connections between human death resulting from homicide and traditional medicine preparations containing Hyacinthaceae species have been established. *Bowiea volubilis* is notorious in this respect. Extensive work has been done on this species which has been shown to contain bufadienolides (Tschesche and Dolberg, 1958; Gsell and Tamm, 1969). The therapeutic value of some members of the Hyacinthaceae (eg some members of *Ledebouria* and *Drimiopsis*) may be as a result of mucilage produced by the plant. This may account for the laxative effect of *Drimiopsis maculata* preparations in the treatment of infantile stomach disorders (Hutchings and Terblanche, 1989). The pharmacological properties of isolates from this family have been insufficiently studied; however the anti-inflammatory activity of homoisoflavanones (Amschler et al., 1996; Della Logia *et al.*, 1989) would validate the rational ethnomedical use of such species as *Scilla natalensis* and *Scilla nervosa* (Crouch *et al.*, 1999; Bangani *et al.*, 1999).

We have recently investigated species from all three subfamilies of the Hyacinthaceae and have isolated a wide range of compounds: homoisoflavanones, stilbenoids, dibenzo -pyranones, spirocyclic nor-triterpenoids, bufadienolides, nor-lignans, chalcones and steroidal spirocyclic compounds. It was thought that homoisoflavanones were unique to the Hyacinthoideae subfamily, but our work shows that they are also present in the Urginiodeae and Ornithogaloideae. Our work also shows that bufadienolides occur not only in the Urginiodeae, but are more widespread, occurring also in the Ornithogaloideae.

The Chemistry of the Southern African Hyacinthoideae.

This is the subfamily we have investigated most extensively and our investigations include species from *Scilla, Eucomis, Ledebouria* and *Drimiopsis*. The most common secondary metabolites isolated from these genera are the homoisoflavanones. Four types of homoisoflavanones, as illustrated in Figure 1 have been isolated. Homoisoflavanones are formed from cyclisation of 2-methoxychalcones thus it is not surprising that chalcones such as 2'-methoxychalcone, **1,** have been isolated along with the homoisoflavanones *from Ledebouria ovatifolia* (Pohl *et al.*, 2001) and also the chalcone derivative **2.** We have isolated a range of spirocyclic nor-triterpenoids, **3-9,** from *Ledebouria* and *Scilla* species (Pohl *et al.*, 2001; Mulholland *et al.*, unpublished), some of which have been shown to have anti-fungal activity. Stilbenoids are common in *Scilla* species and (*E*)-resveratrol, **10,** and rhapontigenin, **11,** have been isolated from *Scilla nervosa* (Bangani *et al.*, 1999). These compounds have anti-oxidant activity. *Drimiopsis maculata* has been shown to produce scillascillin-type homoisoflavanones (Koorbanally *et al.*, 2001) and a series of dibenzopyranones of the type illustrated in structure **12** were also isolated from this source. *Drimiopsis burkei* and *Ledebouria ovatifolia* have also yielded the norlignans as shown in structure **13.** It is interesting to note that although norlignans have been isolated, no lignans have been isolated from this family.

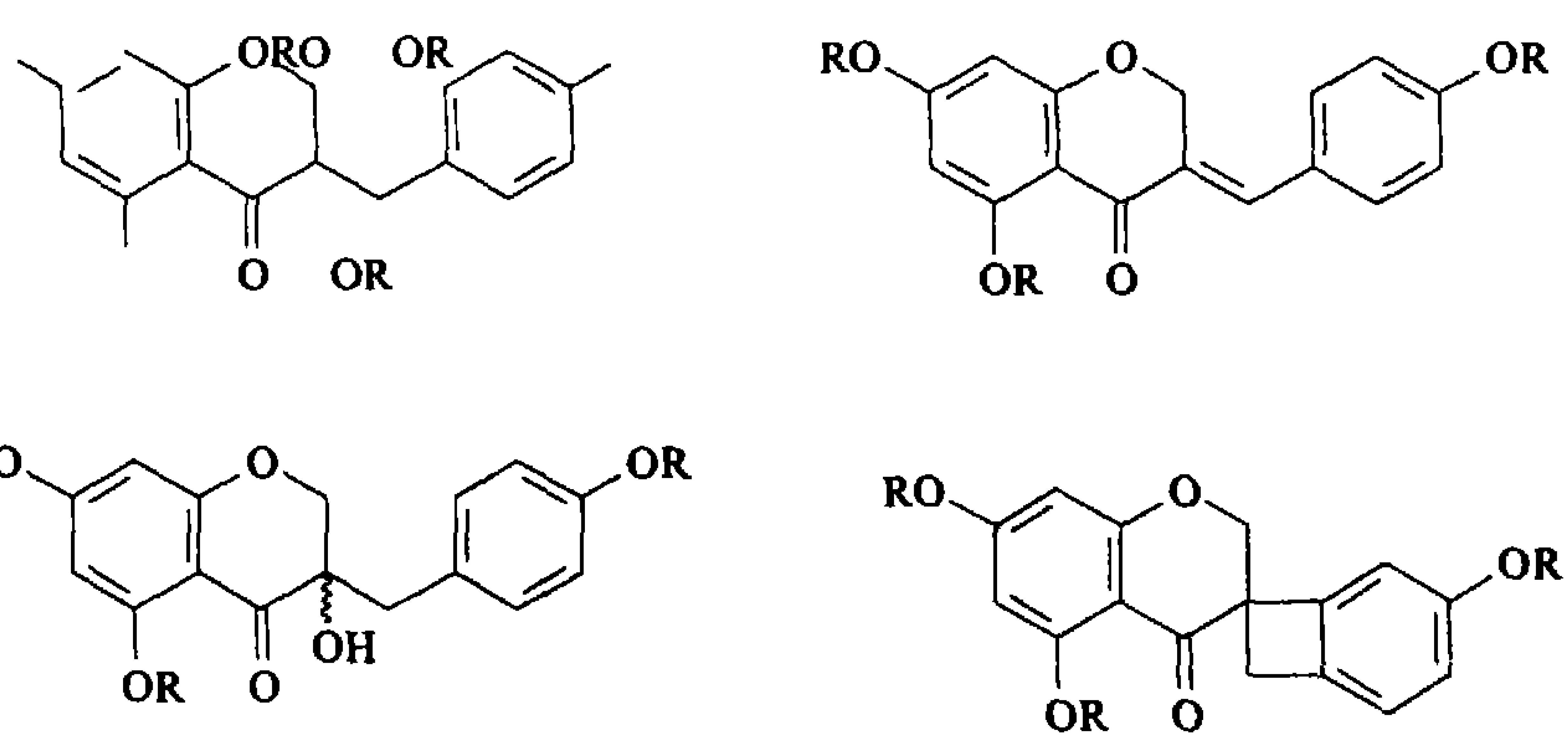
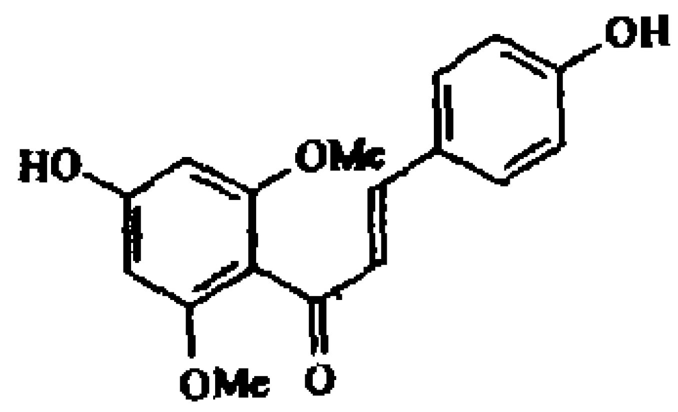


Figure 1. Types of homoisoflavanones isolated from the Hyacinthoideae.

(R=H, CH_3)



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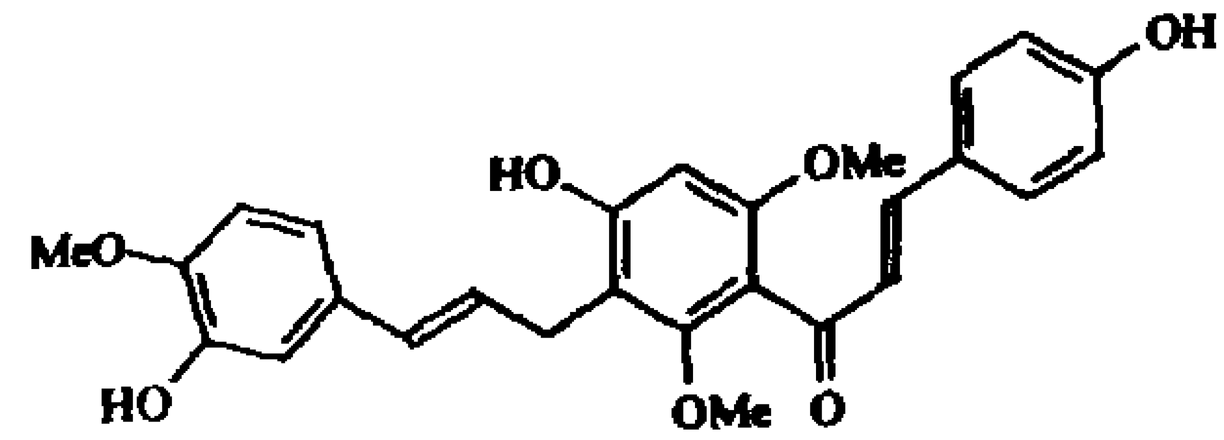

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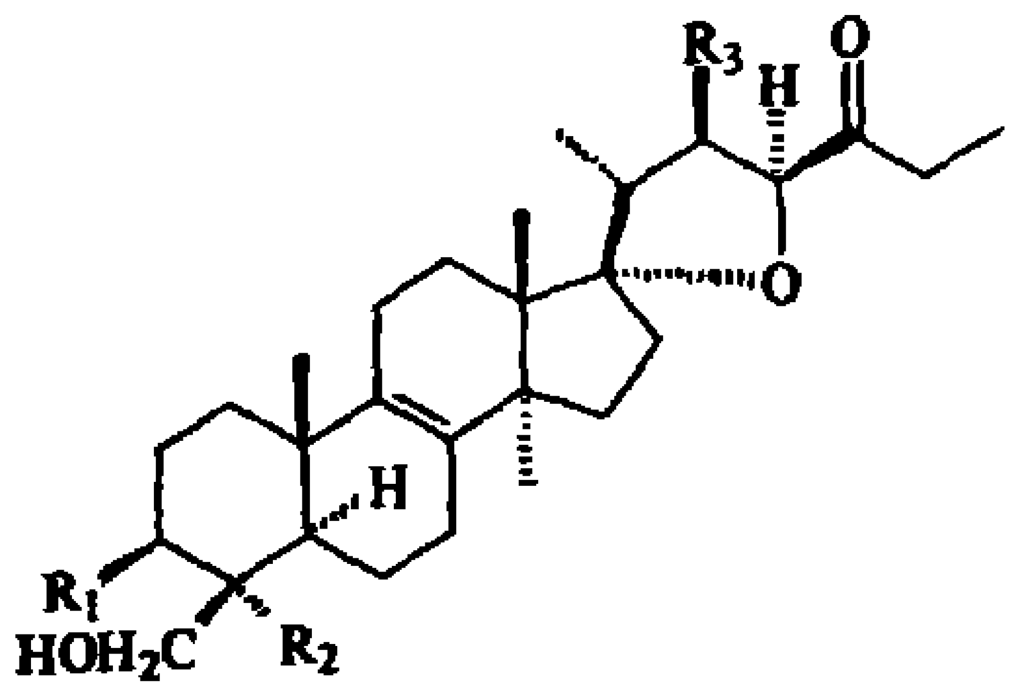
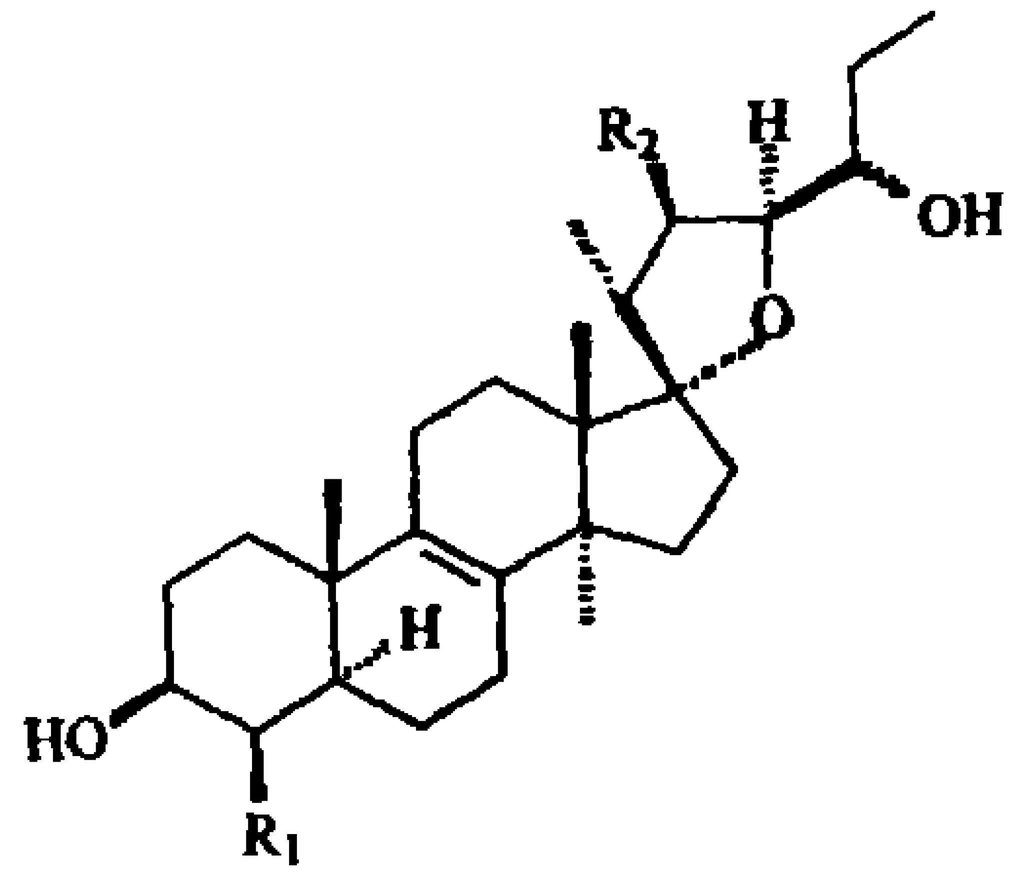
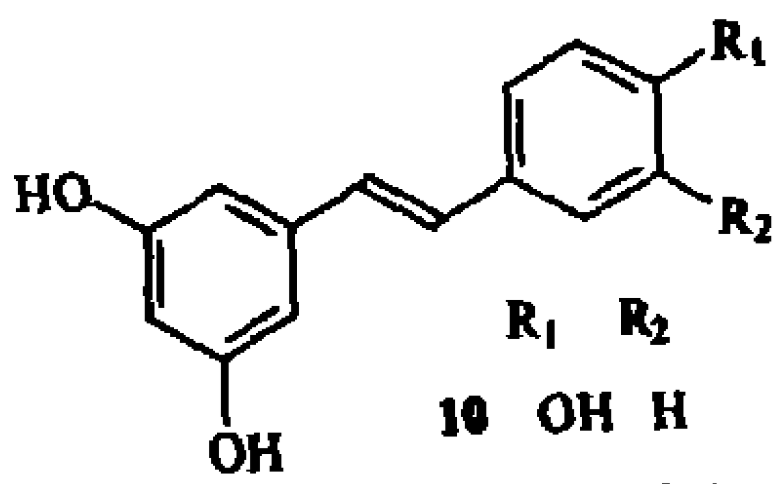


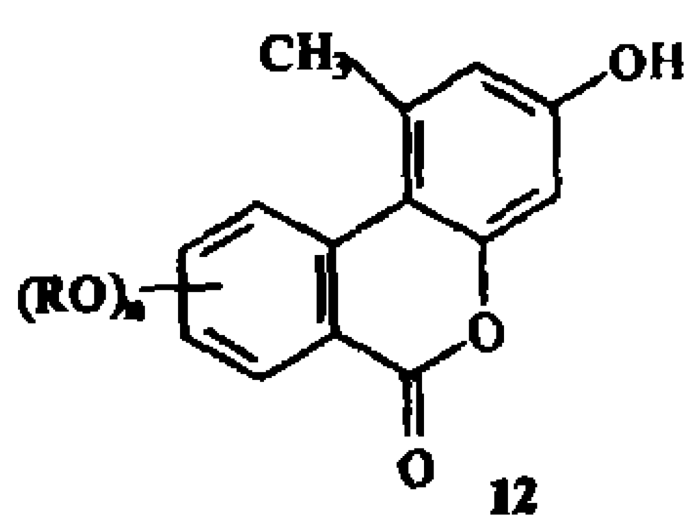
3	R_1-OH	R_2-CH_3	R_3-OH
4	R_1-OH	R_2-CH_2OH	R_3-H
5	R_1-OH	R_2-CH_3	R_3-OAc
6	R_1-OH	R_2-CH_3	R_3-H
7	R_1=O	R_2-CH_3	R_3-OH



8	R_1-H	R_2-H
9	R_1-CH_3	R_2-OH



	R_1	R_2
10	OH	H
11	H	OH



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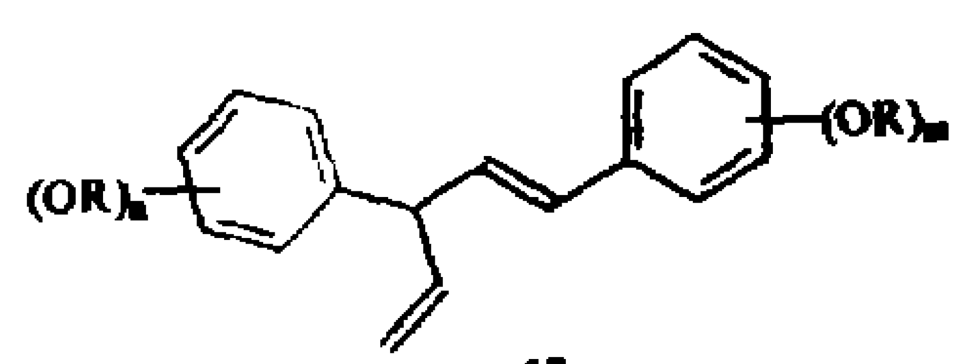

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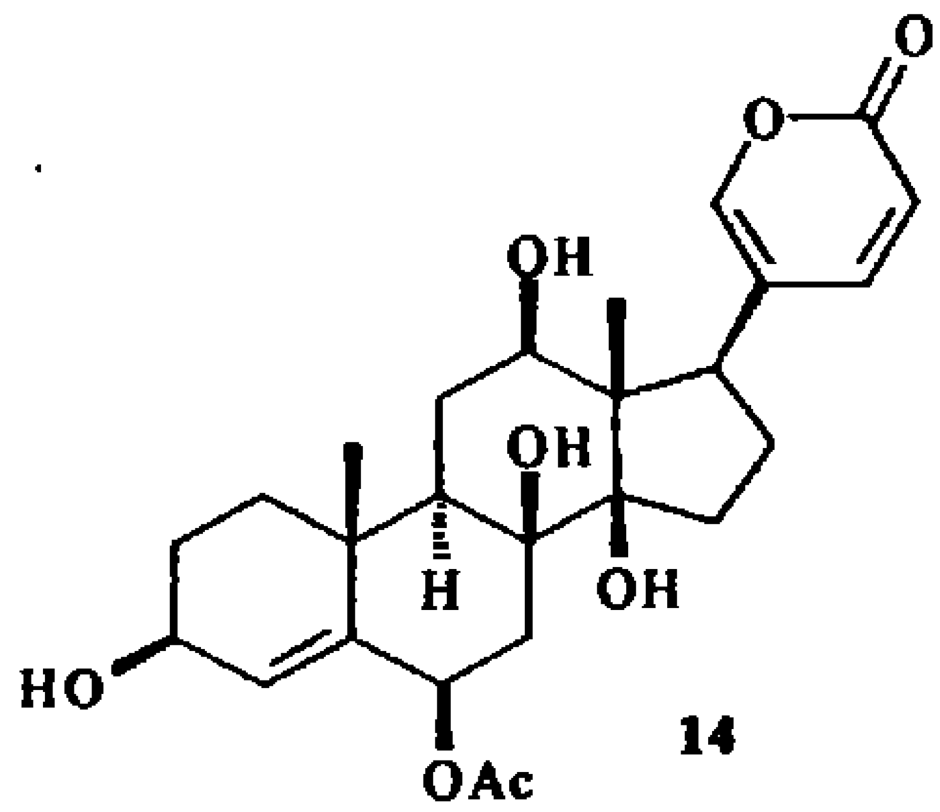
The Chemistry of the Southern African Urginiodeae.

Specimens from two genera, *Urginea* and *Drimia* have been investigated. The bufadienolide **14** (Pohl *et al.*, 2001) was isolated from *Drimia robusta* and a homoisoflavanone from *Urginea delegoensis.*

Our interest in the chemistry of *Urginea altissima* was aroused by the reported isolation of the typically Amaryllidaceae-type isoquinoline alkaloids lycorine and acetylcaranine from its bulbs (Miyakado *et al.*, 1975). This species was re-investigated but no alkaloids were found but rather the novel bufadienolide glycoside, urginin, **15.** Confirmation of the glycosidic linkages was obtained from NMR (NOESY and HMBC) and LC MS studies. Successive MS-MS experiments confirmed the branched structure of the sugar side-chain (Pohl *et al.*, 2001). Verdcourt and Trump (1969) have stated that the cottony appearance of the torn leaf bases of *U. altissima* could lead to its confusion with some Amaryllidaceae bulbs, including *Crinum* and *Boophane*, which seems probable in this case.

The Chemistry of the Southern African Ornithogaloideae.

Representatives from three genera of the Ornithogaloideae have been investigated. A steroidal spirocyclic compound, **16,** has been isolated from *Ornithogalum tenuifolium*, The homoisoflavanone, 7-O-methyleucomin, **17,** has been isolated from two species from this subfamily, *Galtonia princeps* and *Ornithogalum longibracteatum. Albuca nelsonii* has yielded the phenolic acid **18.** Recently, a bufadienolides have been isolated from *Ornithogalum flexuosum,* closely related to the toxic rubellin, **19,** previously isolated from *Urginea rubella* (Steyn *et al.*, 1986) from. This is the first isolation of a bufadienolide from the Ornithogaloideae and would help to account for the toxicity of members of the subfamily.



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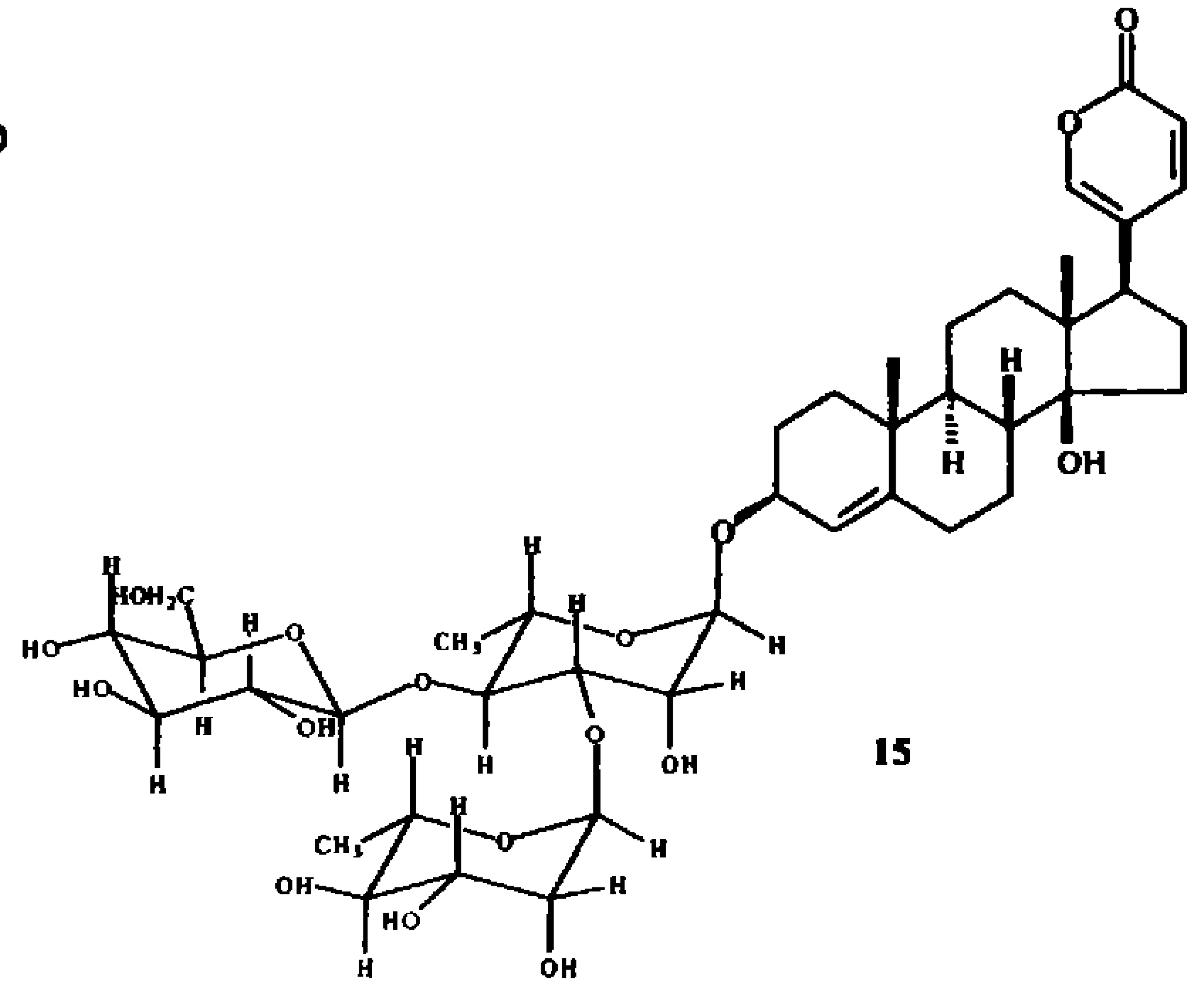

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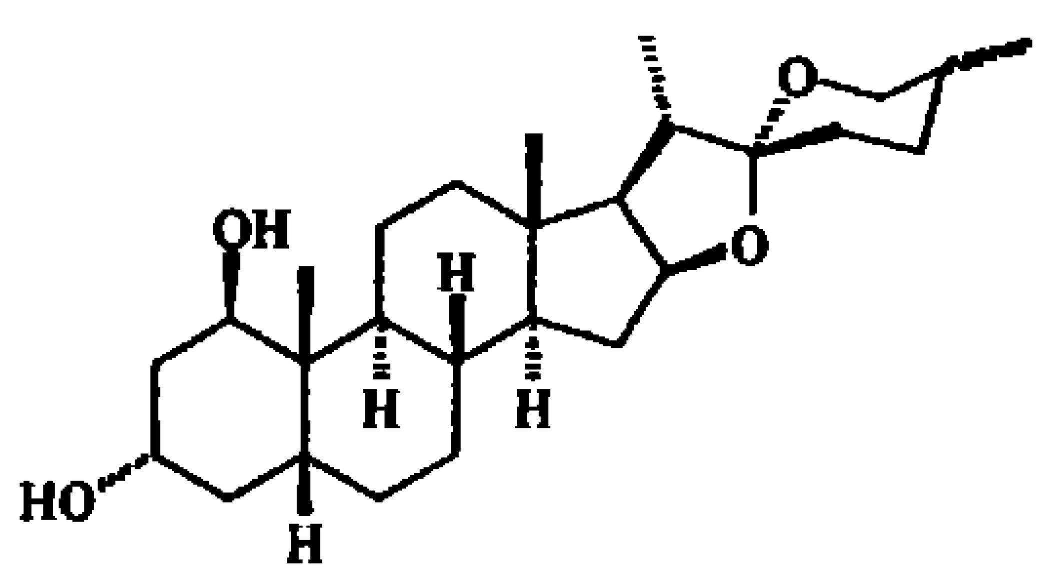

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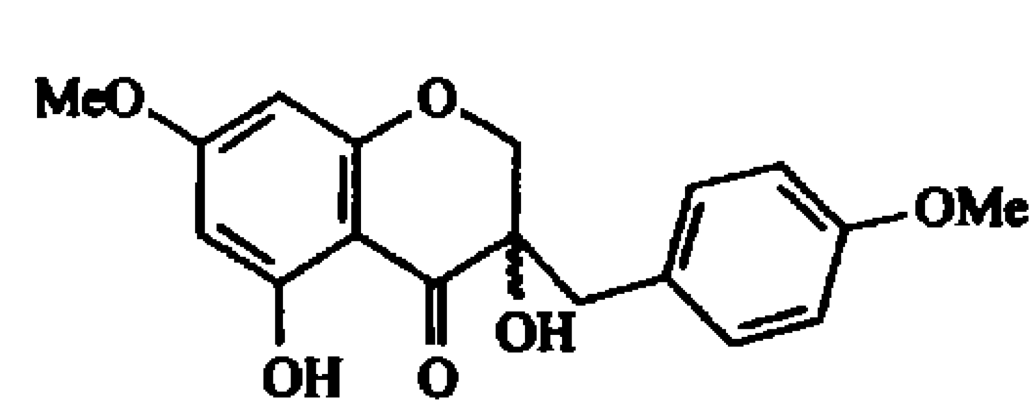

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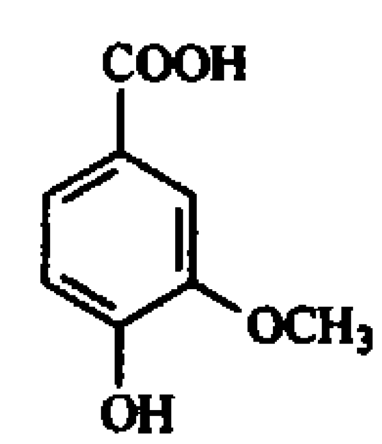

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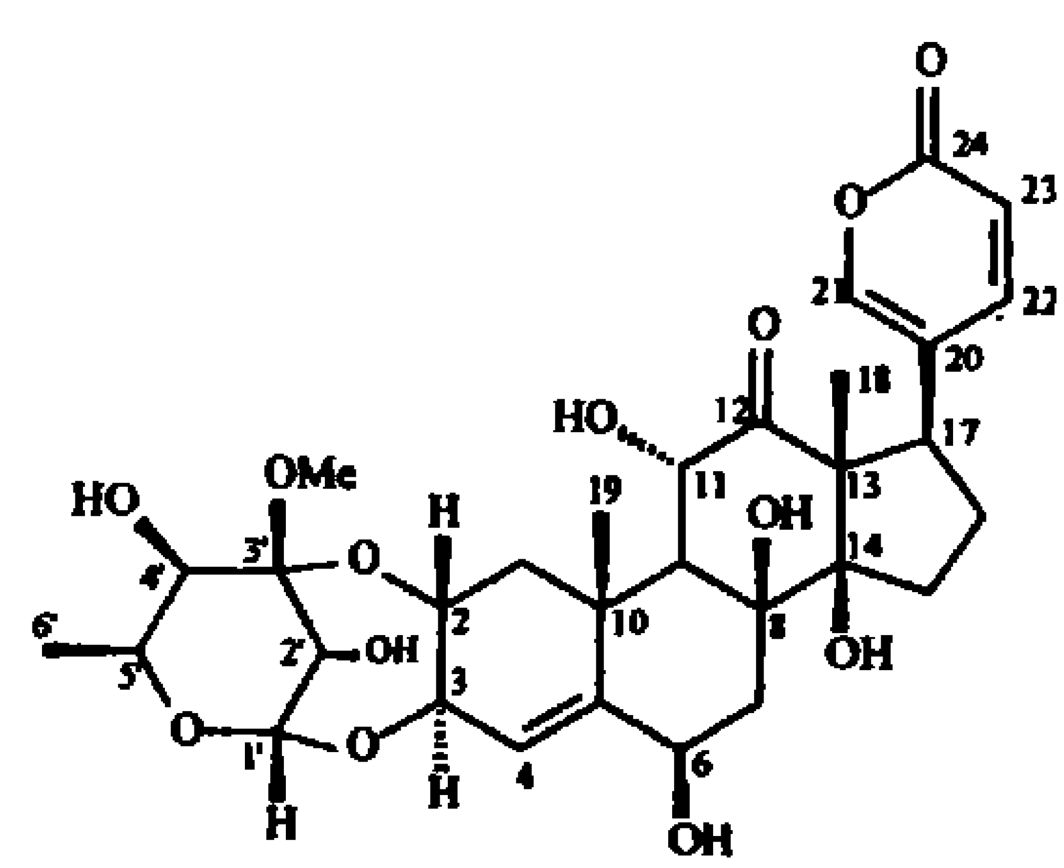

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بحوث التركيب الكيميائي للنباتات الطبية في أفريقيا

للأستاذة الدكتورة دولسي مولهولند

جامعة ناتال - ديربان - جنوب أفريقيا

ملخص

إن أفريقيا الجنوبية من أغني مناطق العالم في التنوع البيولوجي فعدد أنواع النباتات الراقية يبلغ في جنوب أفريقيا ما يزيد عن ٣٠,٠٠٠ نوع وهناك أيضا عدة أنواع متفردة في هذه المنطقة فمنطقة الكاب (رأس الرجاء الصالح) تملك وحدها ما يزيد عن ٦,٠٠٠ نوع نباتي متفرد ويعود هذا الثراء النوعي المتميز إلي تباين المناخات من المناخ شبه المداري علي الساحل الشرقي إلي المناخ شبه الصحراوي ومناخ البحر المتوسط في الكاب الغربي وللسكان الأصليين في أفريقيا الجنوبية خبرة واسعة في الاستخدامات التقليدية للنباتات الطبية ، كما أن تجارتها عنصر هام في الاقتصاد فهناك ما يقرب من ٧٠٠ نوع تدخل السوق ولهذه النباتات حوالي ٢٧ مليون مستهلك مما يجعل الطلب يزيد عن المعروض وهناك عدة أنواع مهددة بالإنقراض لهذا السبب ، خارج مناطق المحميات في ناتال وقد قدرت قيمة ما يباع من النباتات الطبية في منطقة ناتال وحدها بمبلغ ١٠ مليون دولار أمريكي عام ١٩٩٨ ، وهي تقريبا ثلث قيمة محصول الذرة الشامية ، أكبر محاصيل الأقليم ويقال إن الأسر تنفق ما بين ٤,٨٪ من دخلها علي الخدمات الطبية التقليدية وإن هناك ما بين ٢٠ ألف وثلاثين ألف يحصلون علي معاشهم من التجارة في النباتات الطبية ، ومعظمهم من السيدات السود المهمشات وخلاف ذلك هناك تجارة تصديرية لبعض النباتات إلي أوروبا وآسيا.

وتتناول الورقة نتائج الدراسات التي تجريها مجموعة بحوث المنتجات الطبيعية في جامعة ناتال عن التركيب الكيميائي للنباتات التي تدخل في الطلب التقليدي في أفريقيا الجنوبية ، وخاصة نباتات من عائلة الياسنت وعائلة نباتات بصل العنصل وغيرها ، مع بيان ماهية الجوهر الكيميائي والتركيب الجزيئ لهذه المواد الفعالة المستخلصة من تلك النباتات.

محاضرة ألقيت بالمعهد في ربيع ٢٠٠٢ عند استضافة المعهد للمحاضرة كأستاذ زائر.