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Colourful chemistry of South African latrunculid sponges

Marine sponges – in common with many other sessile marine invertebrates seemingly devoid of obvious physical forms of defence against predators, e.g. spines or shells – are the sources of a diverse array of organic chemical compounds known as marine natural products or secondary metabolites. Recent research has indicated that the production of natural products via cellular secondary metabolic pathways in some sponge species may not occur within the sponge cells themselves, but rather in microbial endosymbionts which inhabit the surface and interstitial spaces within the sponge tissue. Regardless of their biosynthetic origin, the bioactivity, e.g. toxicity, of many of these marine natural products may be utilised by sponges as chemical feeding deterrents to discourage predation or to provide a chemical anti-fouling competitive edge in the intense competition for living space amongst filter-feeders on space-limited benthic reefs. Paradoxically, a small number of sponge natural products have serendipitously shown potential as new pharmaceuticals, e.g. novel anti-cancer drugs. Marine biodiscovery (or bioprospecting) is the search for new pharmaceuticals from marine organisms. Exploration of the taxonomy, natural products chemistry and biomedical potential of the rich diversity of South African latrunculid sponges (family Latrunculidae), at Rhodes University, the South African Department of Environmental Affairs and the University of the Western Cape has continued unabated for over a quarter of a century as part of a collaborative marine biodiscovery programme. A short review of this multidisciplinary latrunculid sponge research is presented here.

Significance:

- Research into the taxonomy, chemistry and microbiology of latrunculid sponges is the most comprehensive, multidisciplinary investigation of any group of African marine sponges.
- The potent cytotoxicity of the pyrroloiminoquinone alkaloid pigments isolated from latrunculid sponges may have biomedical applications.
- This review underlines the importance of conserving and protecting South Africa's unique marine invertebrate resources.

Introduction

The first marine biodiscovery programme centred at a South African university was initiated by a SCUBA collection of approximately a dozen marine sponges by a team of Rhodes University ichthyologists, from a sub-tidal reef in the Tsitsikamma National Park, situated on the Southern Cape coast of South Africa during the spring of 1990. This small collection of marine sponges unearthed a single specimen of a dark brown coloured sponge (Figure 1). This sponge was identified by Samaai and Kelly as *Tsitsikamma favus*, the first species from a new genus in the family Latrunculidae Topsent, 1922.¹ Subsequent detailed studies of the taxonomy, marine natural products chemistry and marine microbiology of *T. favus* formed the basis of the first PhD studies at the University of the Western Cape in sponge taxonomy², and in marine sponge natural products chemistry^{3,5} and marine sponge microbiology⁶ at Rhodes University.

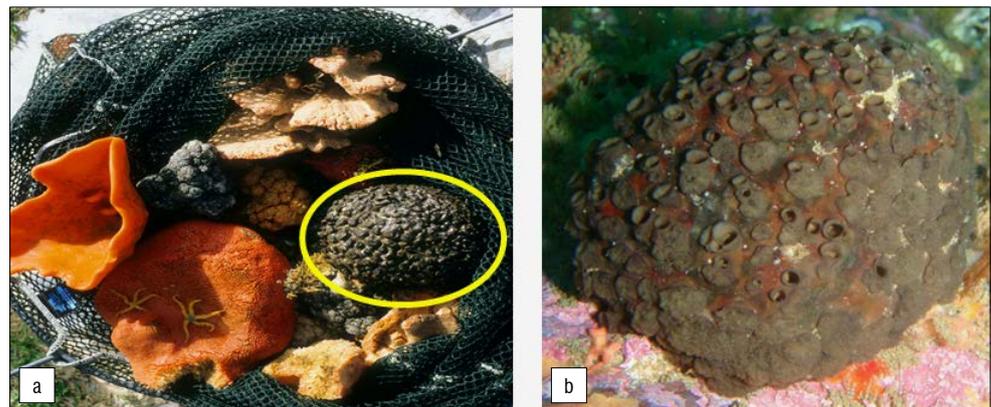


Figure 1: (a) *Tsitsikamma favus* (circled) in a mixed collection of sponges and soft corals from the Tsitsikamma National Park and (b) an underwater photograph of *T. favus* in Algoa Bay, South Africa (photos: M. Davies-Coleman and T. Samaai).

Biodiversity of South African latrunculid sponges

In the southern hemisphere, sponges belonging to the family Latrunculidae (Demospongia, Poecilosclerida; Figure 2) are commonly found on exposed coastal environments attached to hard rocky substrata (<50 m depth) in the cold, inshore, upwelled water environments around South Africa, New Zealand, southwestern Australia and Tasmania.⁷ The

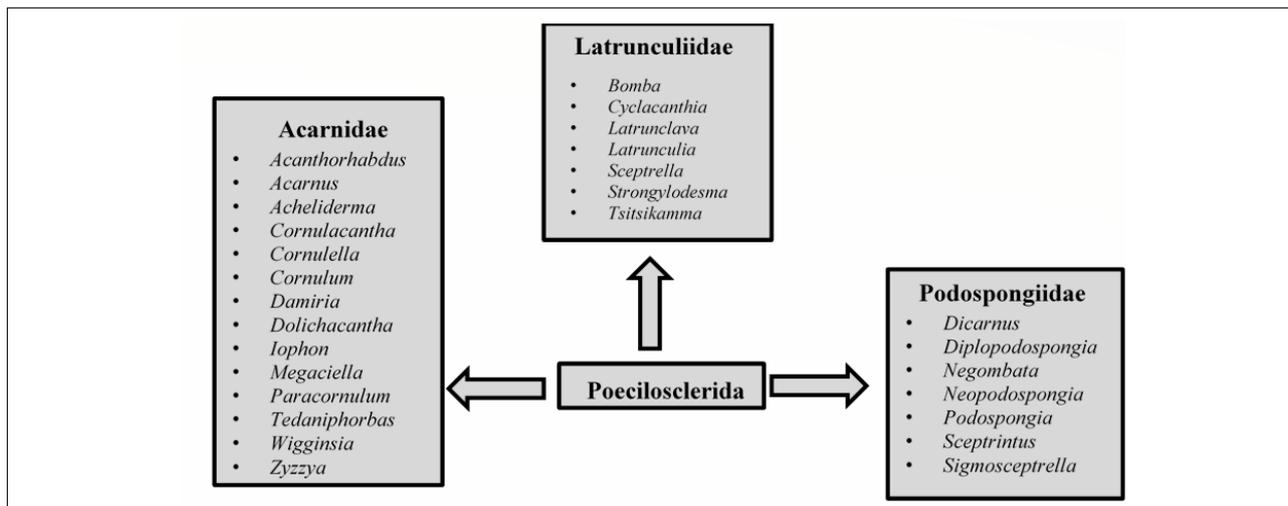


Figure 2: Three taxonomic families ascribed to the sponge order Poecilosclerida.^{7,8}

family Latrunculiidae was retained in the order Poecilosclerida, following a recent revised proposal for the classification of the Demospongiae (Figure 2).⁹ The family comprises seven genera⁷, of which four (*Latrunculia*, *Cyclacanthia*, *Strongyloidesma* and *Tsitsikamma*) include species that are endemic to the Agulhas ecoregion of South Africa.⁹ *Tsitsikamma* and *Cyclacanthia*, known from six species respectively⁷, are genera endemic to South Africa. The coastal regions of South Africa are recognised as a global hotspot of latrunculid sponge biodiversity.^{1,10}

The pioneering, collaborative, marine invertebrate biodiscovery expeditions, coordinated from Rhodes University (1990–2004),¹⁰ revealed for the first time the significant latrunculid sponge diversity off South Africa. The continual discovery of new latrunculid species and genera from these expeditions fuelled increasing interest in these sponges and ultimately led to a taxonomic revision of the family Latrunculiidae in parallel with the natural products chemistry and bioactivity studies of the isolated natural products.^{1,2,11,12} Four genera – *Latrunculia*, *Sceptrella*, *Strongyloidesma* and *Tsitsikamma* – were recognised in this revision (Figure 2). The genus *Tsitsikamma* is endemic to South Africa.¹³ The identification of sponges belonging to this family was predominantly based on a number of key morphological features, including, in most genera, the presence of the characteristic silica-based discorhabd microscleres which differ structurally between the different genera (Figure 3).

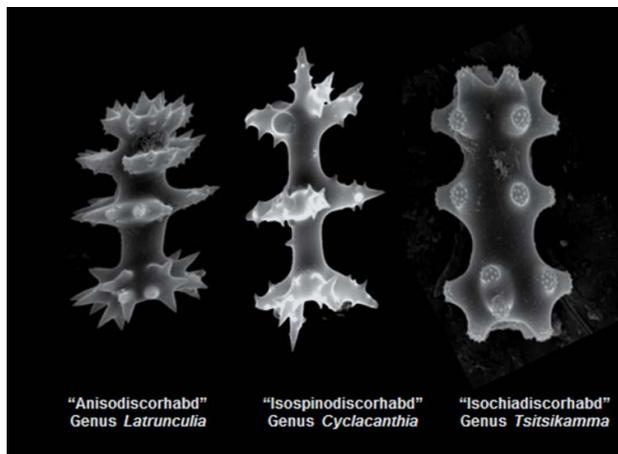


Figure 3: Silicon discorhabd microscleres characteristic of the genus *Latrunculia* and the two endemic South African genera *Cyclacanthia* and *Tsitsikamma*.

However, the genus *Strongyloidesma* is an enigma within the family Latrunculiidae, because species within this genus do not contain these distinctive discorhabd microscleres.¹³ Shortly after this taxonomic revision was published, the family Latrunculiidae was further expanded to include another new endemic South African genus, *Cyclacanthia*, which incorporated three new species collected from the Agulhas ecoregion (*C. bellae*, *C. cloverlyae* and *C. mzimayensis*).¹⁴ The type specimen for this genus, *C. bellae*, described from Algoa Bay, was originally misidentified as *L. bellae* (Samaai and Kelly, 2003) and placed in the genus *Latrunculia*.¹³ Interestingly, *Cyclacanthia* differs from the genus *Latrunculia*, inter alia in ontogeny, morphology and presence of isospinodiscorhabd microscleres, in which there are three major whorls of projections, as opposed to the four characteristic of the anisodiscorhabds of the genus *Latrunculia* (Figure 3).¹⁵

The genus *Latrunculia*, comprising some 30 species of which over a half occur in the southern hemisphere, was further expanded to include another three new South African species: *L. algoensis*, collected from Algoa Bay and *L. gotzi* and *L. kerwathi* collected from deep water reefs situated on the Agulhas continental shelf off South Africa.¹⁶ Latrunculid sponges from the genus *Sceptrella* are also deep water sponges; however, no representatives of this genus have yet been discovered off the South African coast and this genus appears confined to the northern and western Atlantic Ocean.^{1,17,18} The genera *Bomba* and *Latrunclava* have recently been added to the family Latrunculiidae, and representatives of these two genera are similarly not known to occur off southern Africa.^{7,18} A list of the new latrunculid sponges species collected off South Africa, their sites of collection, and references to their published taxonomic data are presented in Table 1.

Pyrrroloiminoquinone alkaloids isolated from South African latrunculid sponges

The general name pyrrroloiminoquinone refers to the central chemical structural motif common to the group of alkaloid secondary metabolites isolated from sponges belonging to the families Latrunculiidae and Acarnidae (Figure 2).²¹ The pyrrroloiminoquinone structure is characterised by a five-membered pyrrole ring (A) fused to a six-membered iminoquinone moiety (B), as typified by the chemical structure of the ubiquitous discorhabdin A (Figure 4).

Biosynthetically, the pyrrroloiminoquinone motif is derived from tryptophan via decarboxylation and oxidative cyclisation. Subsequent addition of tyramine to a putative tricyclic pyrrroloiminoquinone intermediate, affords a group of alkaloids known as the makaluvamines, which may be further elaborated via oxidative, intramolecular cyclisation to yield the discorhabdins and tsitsikammamines (Scheme 1).²²

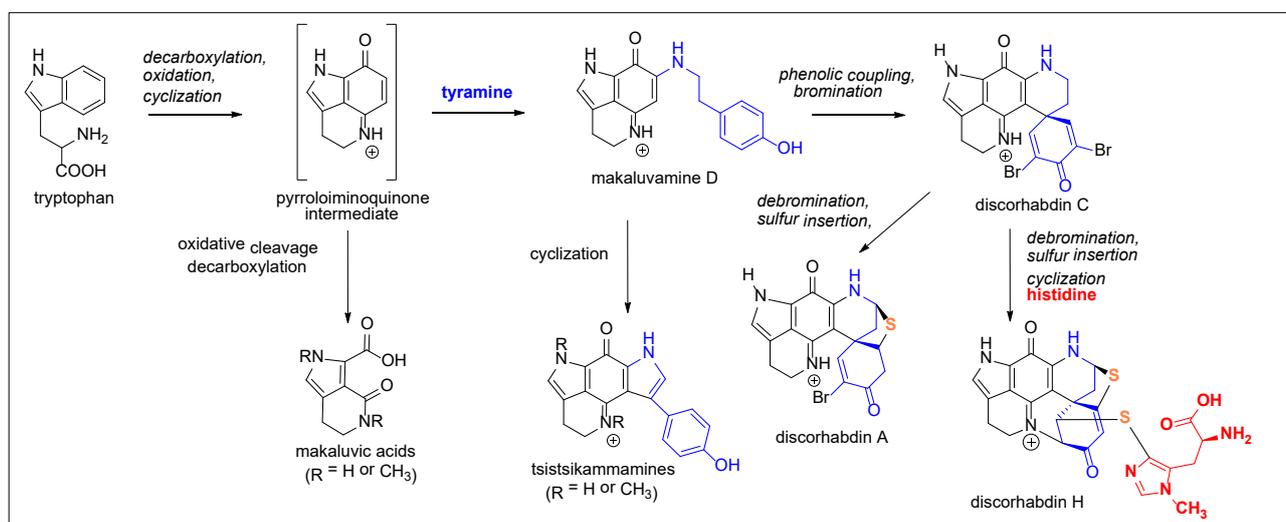
The name 'discorhabdin' originates from the name given to the discorhabd microscleres used by sponge taxonomists to identify latriunculid sponges, and was given to this group of marine natural products by Munro and colleagues, who isolated and identified the first discorhabdin compounds from a New Zealand *Latriunculia* sponge in 1986.²³ Varying in colour from red and orange to dark green, pyrroloiminoquinone metabolites have been shown to be concentrated in the outer 0–2 mm of sponge tissue in the dark green or brown coloured sponges in which they are produced.²⁴ Accordingly, pyrroloiminoquinone metabolites serve a dual purpose in latriunculid sponges, both as pigments and, because of their potent cytotoxicity and general bioactivity *vide infra*, as feeding deterrent compounds to deter predators.²⁴

The isolation of the highly polar pyrroloiminoquinone compounds from methanolic extracts of marine sponges, and the subsequent determination of the chemical structures of these compounds, is not trivial. Nuclear magnetic resonance (NMR) spectroscopy is the pre-eminent spectroscopic technique used to elucidate the chemical structures of natural products.

In the contemporary NMR spectroscopy toolbox, inverse detection, two-dimensional NMR spectroscopy experiments, e.g. heteronuclear single quantum coherence, heteronuclear multiple bond correlation are among the most useful to establish the chemical structure of an unknown organic compound.²⁵ These experiments are designed to define the position in the chemical structure of magnetically insensitive nuclei with a low relative abundance and gyromagnetic ratio, e.g. carbon nuclei (¹³C), via a radio frequency pulse sequence that exploits the highly magnetically sensitive surrounding hydrogen protons (¹H). ¹H has an approximate four-fold greater gyromagnetic ratio compared to ¹³C and is normally more than twice as abundant as carbon atoms in organic compounds. Unfortunately, the relative paucity of hydrogen atoms in pyrroloiminoquinones in comparison with carbon atoms, as reflected, for example, by the molecular formula of discorhabdin A (C₁₈H₁₅BrN₃O₂S), often hampers the structure elucidation of these complex, highly conjugated, polycyclic compounds by NMR spectroscopy and thus provides an intriguing challenge for marine natural product chemists.

Table 1: Latriunculid sponge species collected off South Africa (1990–2016)

Species	Collection site	Ecoregion	Year(s) collected	Depth range
<i>Cyclacanthia bellae</i> ^{13,14}	Algoa Bay, Ryi Banks	Agulhas	1998, 1999	20–22 m
<i>C. cloverlyae</i> ¹⁴	Christmas Reef, Umhlali, Tugela Banks, Durban	Natal	2003	17 m
<i>C. mzimayensis</i> ¹⁴	Mzimayi Reef, Sizela, Umkomaas, Aliwal Shoal, Durban	Natal	2003	18–29 m
<i>Latriunculia algoensis</i> ¹⁶	Algoa Bay, Port Elizabeth	Agulhas	2010	22–30 m
<i>L. gotzi</i> ¹⁶	Alphard Banks	Agulhas	2009	41 m
<i>L. kerwathi</i> ¹⁶	45-Mile Banks	Agulhas	2009	85 m
<i>L. lunaviridis</i> ^{13,19}	Ouderkraal, Cape Town; Hout Bay	Southern Benguela	1996, 2003	17–32 m
<i>L. biformis</i> ^{13,19}	Rheders Bay, Tsitsikamma National Park	Agulhas	1995	28 m
<i>L. microacanthoxea</i> ^{13,19}	Rheders Bay, Tsitsikamma National Park	Agulhas	1995	28 m
<i>Strongyloidesma algoensis</i> ¹³	Algoa Bay, Port Elizabeth	Agulhas	1994	15 m
<i>S. tsitsikammaensis</i> ^{13,20}	Rheders Bay, Tsitsikamma National Park; Algoa Bay, Port Elizabeth	Agulhas	1996	1.5–15 m
<i>S. aliwaliensis</i> ¹⁵	Umkomaas, Aliwal Shoal, Durban	Natal	1994, 2003, 2004	15–18 m
<i>Tsitsikamma favus</i> ^{1,13}	Rheders Bay, Tsitsikamma National Park; Algoa Bay, Port Elizabeth, Jeffreys Bay, St Francis Bay, Plettenberg Bay	Agulhas	1990, 1993, 1994, 1995, 1998, 1999, 2010, 2016,	13–40 m
<i>T. pedunculata</i> ¹³	Thunderbolt Reef, Algoa Bay, Port Elizabeth	Agulhas	1999	40 m
<i>T. scurra</i> ¹³	Hout Bay	Southern Benguela	2000, 2003	28 m



Scheme 1: Proposed biosynthesis of pyrroloiminoquinone alkaloids.

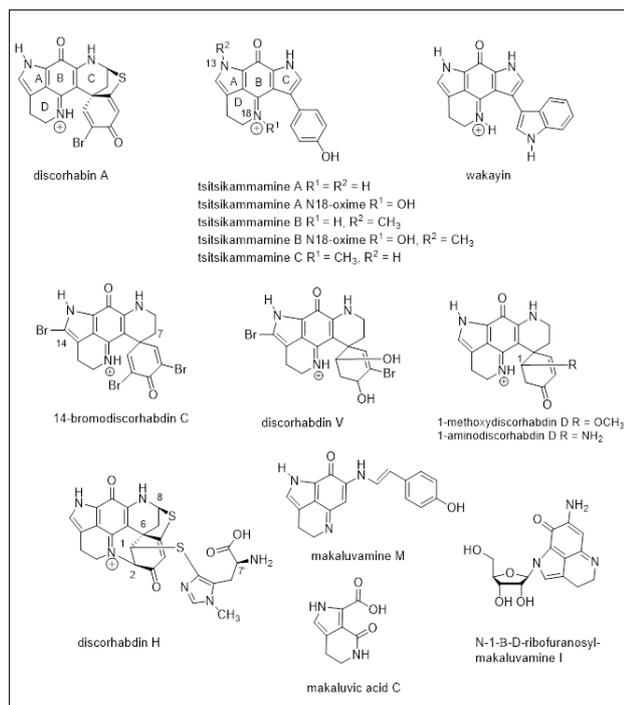


Figure 4: Chemical structures of selected pyrroloiminoquinone pigments isolated from South African latriunculid sponges: tsitsikammamine C from the sponge *Zyzygia fulingosa* and wakayin from a *Clavelina* ascidian.

Over 100 marine pyrroloiminoquinone natural products have been isolated from marine organisms collected from across the globe and the chemistry and bioactivities of this group of compounds have been regularly reviewed in the chemistry literature.^{21,26-28} Of the pyrroloiminoquinones isolated thus far from marine sponges, 30 (of which 16 were new compounds) have been isolated from five South African latriunculid sponge species: *T. favus*^{12,29}, *T. pedunculata*¹², *C. bellae* (formerly *L. bellae*)¹², *S. algoensis*¹² and *S. aliwaliensis*^{30,31} (Figures 1 and 5), and the names of these compounds are presented in Tables 2 and 3. Selected compounds from Tables 2 and 3, with novel chemical structural features observed for the first time in this group of compounds, are presented in Figure 4 and the significance of their discovery will be briefly discussed here.

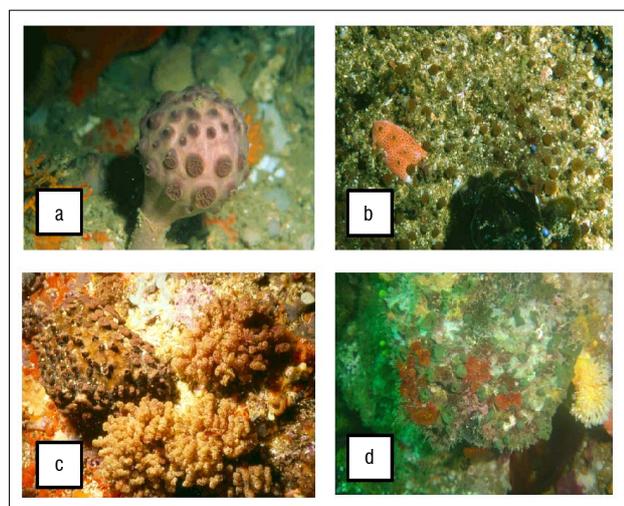


Figure 5: Underwater photographs of (a) *Tsitsikamma pedunculata*, (b) *Cyclacanthia bellae*, (c) *Strongylodesma algoensis* and (d) *S. aliwaliensis* (photos: P. Colin and T. Samaai).

Table 2: Pyrroloiminoquinone alkaloids isolated from *Tsitsikamma favus* and *T. pedunculata*. IC₅₀ (μM) cytotoxicity against human colon tumour cell line (HCT 116)¹² presented in parentheses.

South African latriunculid sponge species	Pyrroloiminoquinone alkaloids
<i>Cyclacanthia bellae</i>	damirone B (3.10 μM)
	makaluvamine C (1.09 μM)
	makaluvic acid A (28.40 μM)
	discorhabdin G* (0.33 μM)
	discorhabdin M (2.25 μM)
	1-amino-discorhabdin D (0.12 μM)
<i>Strongylodesma algoensis</i>	1-methoxy-discorhabdin D (0.23 μM)
	1-alanyl-discorhabdin D (0.36 μM)
	1-amino-discorhabdin D (0.12 μM)
	3-dihydro-discorhabdin C (0.32 μM)
	discorhabdin A (0.007 μM)
<i>S. aliwaliensis</i>	discorhabdin D (0.60 μM)
	discorhabdin H
	damirone C [55.7; 78.3; 77.8]
	makaluvamine I
	makaluvamine M [0.7; 6.8; 3.2]
	makaluvic acid C [>150; >150; >150]
	<i>N</i> -1-β- <i>D</i> -ribofuranosyl-damirone C [37.9; 85.5; 66]
<i>N</i> -1-β- <i>D</i> -ribofuranosyl-makaluvic acid C [60.6; >200; >200]	
<i>N</i> -1-β- <i>D</i> -ribofuranosyl-makaluvamine I [1.6; 5.7; 3.2]	

Tsitsikammamine A and B were isolated from a 1:1 methanol:chloroform extract of *T. favus* (Figure 1) specimens collected from the Tsitsikamma National Park, along with the first discorhabdin analogues substituted at C-14 e.g. 14-bromodisorhabdin C (Figure 4).²⁹ The tsitsikammamines were the first bis-pyrroloiminoquinone (with two pyrrole rings A and C fused to either side of the central iminoquinone ring B) to be isolated from a sponge²⁹, but were not the first compounds from this structural class to be isolated from a marine organism. Wakayin, which also possesses a bis-pyrroloiminoquinone structural scaffold (Figure 4), had previously been isolated from an ascidian, *Clavelina* sp.³² The biosynthesis of marine natural products, in common with the biosynthesis of terrestrial plant natural products, is not random and the chemical structures of the major natural products usually reflect family and genus structural generalities and species specificity. Therefore, the occurrence of natural products with almost identical chemical structures in two different marine phyla is unexpected and may be a possible indicator of a shared microbial endosymbiont primary producer of the natural product(s), as opposed to serendipitous convergent evolution of secondary metabolic pathways in phyletic disparate marine organisms. In an effort to unequivocally establish the biosynthetic origin of the tsitsikammamines, a detailed community structure analysis of the symbiotic bacteria found in *T. favus* sponges collected from Algoa Bay is currently underway at Rhodes University.^{9,33} The microbial community analyses are coupled to a metagenomic search for microbial biosynthetic gene clusters that might ultimately be responsible for the biosynthesis of the tsitsikammamines.

The structural novelty and bioactivity of the tsitsikammamines has attracted interest from synthetic chemists and tsitsikammamine A was first synthesised by Delfourne and co-workers.³⁴ A follow-up natural products study of Tsitsikamma National Park specimens of *T. favus* afforded two further minor metabolite analogues of the tsitsikammamines, both of which contain an N18-oxime moiety (Figure 4).¹² Marine natural products possessing either N-oxides or N-oximes moieties are rare and these two are the only examples of N-oximes amongst the known pyrroloiminoquinone metabolites. The closely related sponge, *T. pedunculata* (Figure 5a), collected from Algoa Bay yielded the same suite of discorhabdin compounds as that found in *T. favus*, in addition to four new minor discorhabdin metabolites also with C-14 substituents, e.g. discorhabdin V (Figure 4).¹² Interestingly, the tsitsikammamines were not present in extracts of *T. pedunculata*, and are therefore not genus-specific chemotaxonomic markers as tentatively initially proposed.²⁹

Table 3: Pyrroloiminoquinone alkaloids isolated from *Cyclacanthia bellae*, *Strongyloidesma algoensis* and *S. aliwaliensis*. IC₅₀ (μM) cytotoxicity towards either human colon tumour cell line (HCT 116)¹² or oesophageal cancer cell lines (WHCO1; WHCO6; KYE30)⁴⁰ presented in parentheses. The paucity of discorhabdin H and makaluvamine I isolated from *S. algoensis* and *S. aliwaliensis* respectively, prevented an investigation of their cytotoxicity towards either human colon tumour or oesophageal cancer cell lines.

South African latrunculid sponge species	Pyrroloiminoquinone alkaloids
<i>C. bellae</i>	damirone B (3.10 μM)
	makaluvamine C (1.09 μM)
	makaluvic acid A (28.40 μM)
	discorhabdin G* (0.33 μM)
	discorhabdin M (2.25 μM)
	1-amino-discorhabdin D (0.12 μM)
	1-methoxy-discorhabdin D (0.23 μM)
<i>S. algoensis</i>	1-alanyl-discorhabdin D (0.36 μM)
	1-amino-discorhabdin D (0.12 μM)
	3-dihydro-discorhabdin C (0.32 μM)
	discorhabdin A (0.007 μM)
	discorhabdin D (0.60 μM)
<i>S. aliwaliensis</i>	discorhabdin H
	damirone C [55.7; 78.3; 77.8]
	makaluvamine I
	makaluvamine M [0.7; 6.8; 3.2]
	makaluvic acid C [>150; >150; >150]
	<i>N</i> -1-β- <i>D</i> -ribofuranosyl damirone C [37.9; 85.5; 66]
<i>N</i> -1-β- <i>D</i> -ribofuranosyl makaluvic acid C [60.6; >200; >200]	
<i>N</i> -1-β- <i>D</i> -ribofuranosyl makaluvamine I [1.6; 5.7; 3.2]	

Natural product investigations of two other Algoa Bay latrunculid sponges, *C. bellae* (Figure 5b) and *S. algoensis* (Figure 5c), yielded a further 11 pyrroloiminoquinone pigments, including the known compound discorhabdin A and makaluvamine C and two new compounds,

namely 1-methoxydiscorhabdin D and 1-aminodiscorhabdin D from the specimens of the former species (Figure 4).¹² Interestingly, discorhabdin H (Figure 4) isolated from *S. algoensis* had also been previously identified from *L. lunaviridis* and *L. microcanthoxea*.⁴ The isolation of discorhabdin H provided an opportunity to unequivocally establish the absolute configuration of this compound. Degradative hydrolysis of the (-)-discorhabdin H, followed by comparative chiral gas chromatographic analysis of derivatised hydrolysis products with the equivalent derivative of *L*-histidine, confirmed the 7'S configuration of the C-1 thiomethylhistidine residue.¹² The configuration of the remaining four chiral centres in discorhabdin were established, in collaboration with Copp in New Zealand, as 1*R*, 2*R*, 6*R*, 8*S* (Figure 4) by comparison of the electronic circular dichroism spectrum of (-)-discorhabdin H with that of a closely related model compound, discorhabdin L, to which the application of time-dependent density functional theory calculations had been used to unequivocally establish the absolute configuration of this latter compound.³⁵

A second *Strongyloidesma* species, *S. aliwaliensis* (Figure 5d), collected from Aliwal Shoal, a sub-tropical reef system off Umkomaas in southern KwaZulu-Natal, South Africa, afforded three known pyrroloiminoquinone compounds: e.g. makaluvamine M, a new pyrroloquinoline, makaluvic acid C, and three novel *N*-β-*D*-ribofuranosyl substituted pyrroloiminoquinone and pyrroloquinoline metabolites e.g. *N*-β-*D*-ribofuranosyl makaluvamine I (Figure 4).^{30,31} The sugar moiety in the latter three compounds was identified by chiral gas chromatography comparison of the peracetylated aldononitrile derivative of the acid hydrosylate derived from each compound with a similarly peracetylated aldononitrile derivative of *D*-ribose. The three ribofuranosyl-containing metabolites from *S. aliwaliensis* remain the only known pyrroloiminoquinone glycosides isolated thus far from marine organisms.

Biomedical potential of pyrroloiminoquinone alkaloids

The impressive bioactivity of pyrroloiminoquinone metabolites, consistent with their ecological role as feeding deterrents in sponges *vide supra*, is continuously reported in the chemistry literature. Pyrroloiminoquinones have been shown to exhibit cytotoxicity in a variety of whole-cell biomedical screening programmes, including screens designed to discover new chemical entities with anti-cancer, anti-malaria and anti-microbial activity.^{28,36,37} In addition to whole cell screens, the bioactivity of marine pyrroloiminoquinones against medicinally relevant enzyme targets is also of interest.^{28,38,39} The isolation of a large cohort of pyrroloiminoquinone metabolites from four species of South African latrunculid sponges provided a unique opportunity to explore the cytotoxicity (Tables 2 and 3) and structure activity relationship of 20 of these compounds against a human colon tumour cell line (HCT-116).¹² Discorhabdin A, with an IC₅₀ of 7 nM, was the most active compound against this cancer cell line.¹² The tetracyclic pyrroloiminoquinone core structure was found to be essential for activity, while a Δ⁷ olefin and substitution at C-1 in discorhabdins were found to enhance cytotoxicity.¹² A subsequent screening of the *S. aliwaliensis* metabolites against oesophageal cancer cell lines (WHCO1, WHCO6 and KYE30; Table 3) revealed that makaluvamine M (Figure 4) was the most cytotoxic compound amongst those isolated from *S. aliwaliensis*.⁴⁰

Research into the biomedical potential and the possible mechanisms of cancer cell cytotoxicity of the tsitsikammamines has not abated. We initially established that tsitsikammamine A's inhibition of the topoisomerase I enzyme, responsible for catalysing the relaxation of super-coiled DNA, and this compound's DNA binding affinity were both comparable with that observed for the structurally homologous wakayin.¹² In a subsequent comprehensive medicinal chemistry study, based around the chemical structure of tsitsikammamine A,³⁴ and a series of 43 analogues of this South African latrunculid sponge natural product^{41,42}. Two of these analogues, in which pyrrole ring C was exchanged for a pyrazole ring, exhibited improved topoisomerase I inhibitory activity of tsitsikammamine A⁴¹, while a ring D-opened, bis-pyrroloquinone analogue of tsitsikammamine A exhibited low μM in vitro



growth inhibitory (IC₅₀) cytotoxicity against three different cancer cell lines⁴². The ensuing isolation of tsitsikammamine C⁴³ (Figure 4) from an Australian sponge *Zyzya* sp. (family Acarnidae; Figure 2) with potent low nanomolar IC₅₀ in vitro anti-malarial activity against chloroquine-sensitive and chloroquine-resistant *Plasmodium falciparum* malaria parasites, has opened the door to a new era of tsitsikammamine anti-malarial drug research.⁴⁴

Conclusion

The taxonomy, chemistry, symbiotic microbial community structure and biomedical potential of South African latrunculid sponges continues to attract interest a quarter of a century after the first investigations of the natural products chemistry and cytotoxicity of extracts of *T. favus*, a widely distributed, endemic subtidal sponge within the Agulhas ecoregion. South Africa's position as a global hotspot of latrunculid sponge biodiversity is well established and the search for new latrunculid sponge species continues. The generally non-specific, potent cytotoxicity of pyrroloiminoquinone metabolites continues to hamper their development as new pharmaceuticals. However, research into new targeted drug delivery systems, incorporating pyrroloiminoquinone compounds and currently underway at the University of the Western Cape, may open new opportunities for marine pyrroloiminoquinone metabolites as possible anti-cancer or anti-malarial drugs.

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Authors' contributions

M.T.D.-C. is the leader of the original research group working on South African latrunculid sponges and conceptualised the review and prepared the initial draft. E.M.A. and D.R.B. are key members of the original research group working on latrunculid sponge chemistry and bioactivity and provided critical review and commentary and assisted with the correction and editing of the original draft. T.S. is a key member of the original research group working on latrunculid sponge taxonomy and provided critical review and commentary and assisted with the correction and editing of the original draft.

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