Namibian marine algae as a potential source of novel bioactive natural products

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Abstract

A literature review shows that the medicinal chemistry and bioactivity of very few Namibian species has ever been investigated. In southern Africa, marine red algae such as species of *Plocamium*, *Laurencia* and *Portieria* are known to contain bioactive natural products. Of these three species, only *Plocamium* species are currently found in Namibia. *In vitro* testing of secondary metabolites from South African *Plocamium* species have demonstrated antibacterial, cytotoxic, antiplasmodial, and anti-fouling properties. Whilst the commercial benefits of some Namibian marine algae are well established, this review highlights the shortage of knowledge and research related to the pharmaceutical potential of Namibian marine algae, and how marine algae could possibly benefit the health and wellbeing of Namibians in the future.

Keywords: Namibian marine algae, bioactivity, cytotoxic, antiplasmodial, antimicrobial, halogenated monoterpenes, drug discovery, *Plocamium*

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1 Introduction

1.1 Commercial importance of marine algae

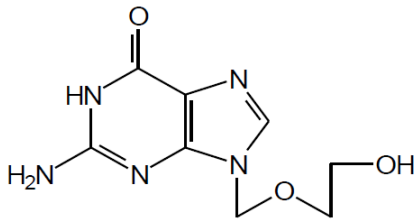
Mankind uses seaweed for a number of different functions, but most often seaweed is used as a rich source of food and nutrition, as well as being an abundant source of agar. For example, in South Africa, Western Cape kelps such as *Ecklonia maxima* and *Laminaria pallida* are collected for alginates (Hay *et al.*, 1983). Both of the above mentioned kelps are also found in Namibia. *Ecklonia* and *Laminaria* are also harvested as feed for commercially farmed abalone (Shuuluka, 2011). Worldwide, *Gracilaria* and *Gelidium* species are commonly used in the production of agar (Baghel *et al.*, 2014). *Gracilaria* species are farmed and harvested in Lüderitz, Namibia (Molley *et al.*, 1995).

In China and Japan, diseases due to iodine deficiency are often treated by consuming iodine containing marine algae. In addition to this seaweeds have also been used as wound dressings and in many beauty preparations. Seaweeds have also been used to treat various intestinal disorders, vitamin shortages and have even been used as hypoglycaemic agents (Lamela *et al.*, 1989). Macroalgae have been used as an important source of food in Japan and China for a long time. Several red algae are eaten, the most popular are known as dulse or *Palmaria palmata*, which is a good source of fibre, and carrageen moss (*Chondrus crispus* and *Mastocarpus stellatus*) from which carrageenan is isolated. Carrageenan is a thickener and stabiliser which is commonly used in various milk products such as ice-cream. Globally, the red algae *Kappaphycus* and *Betaphycus* are also important sources of carrageenan (El Gamal, 2010). Nori is the Japanese name for various edible seaweed species which come from the red alga *Porphyra*, including most notably, *P. yezoensis* and *P. tenera*. Namibia also has *Porphyra* species. Of all the red algae, nori is utilised the most. Amongst other things, nori is an indispensable ingredient in the making of sushi. This valuable marine crop is mainly grown by means of aquaculture in China, Japan and South Korea. Total nori production is estimated to be worth over two billion US$ per year (El Gamal, 2010). Various brown algae are also eaten and are known to be rich in carbohydrates such as laminarin (Deville *et al.*, 2004).

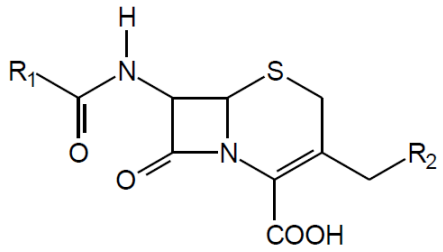
1.2 Biological importance of marine natural products

The biodiversity of earth is heavily in favour of the oceans. With the barely explored biodiversity that is offered by the oceans, the potential for discovering new pharmaceutical compounds from the ocean is enormous. Over the past 30 years, a number of natural products (or secondary metabolites) with potent pharmacological activities have been isolated

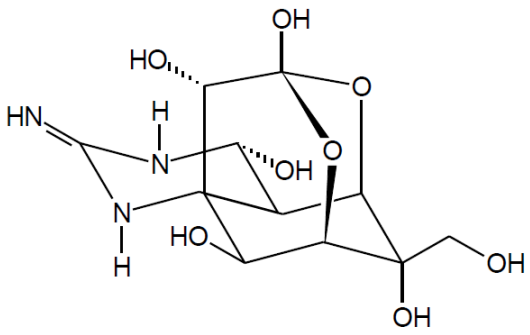
or derived from lead compounds originating in the ocean (Munro *et al.*, 1994). For example; antiviral compounds such as Ara-A, which was the lead compound used for the synthesis of acyclovir (**1.1**) (Munro *et al.*, 1994), antibiotics such as cephalosporin (**1.2**), toxins such as tetrodotoxin (**1.3**) (Delgado and Remers, 1998) and anti-tumour compounds such as halomon (**1.4**) (Fuller *et al.*, 1992) all come from marine sources such as marine algae, marine fungi or marine organisms. See Table 1 for further examples of experimental anti-cancer agents obtained from the ocean.



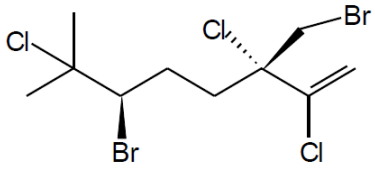
Acyclovir (**1.1**)



Cephalosporin (**1.2**)



Tetrodotoxin (**1.3**)



Halomon (**1.4**)

1.3 Drug discovery and natural product chemistry of Southern African marine algae

The coastline of Southern Africa (from northern Namibia to southern Mozambique) has over 10 000 species of marine fauna and flora which amounts to approximately 15% of all the coastal marine species known worldwide. Of this amazing assemblage, approximately 12% of these species are endemic (Branch *et al.*, 1994). According to the present data, the

Table 1: Marine derived experimental anti-cancer agents (Schwartsmann *et al.*, 2001)

Organism	Group	Metabolite	Location
Tridemnum soldium	Tunicate	Didemnin B	Caribbean
Bugula neritina	Bryozoan	Bryostatin 1	Gulf of California
Ecteinascidia turbinate	Tunicate	Ecteinascidin-743	Caribbean
Halichondria okadai	Sponge	Halichondrin B	Okinawa
Dolabella auricularia	Sea hare	Dolastatin 10	Indian Ocean
Portieria hornemannii	Red alga	Halomon	Philippines
Apidium albicans	Tunicate	Aplidine	Mediterranean
Aplysia kurodai	Sea hare	Aplyronine A	Japan
Elysia rubefescens	Mollusc	Kahalalide F	Hawaii
Mycale ap.	Sponge	Mycaperoxide B	Thailand
Micromonospora marina	Actinomycete	Thiocoraline	Mozambique Strait
Ascidian didemnum granulatum	Tunicate	Granulatimide	Brazil

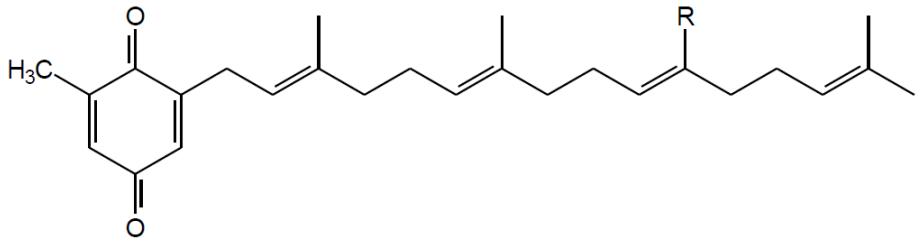
marine benthic flora of Namibia comprises 196 taxa (147 Rhodophyceae, 20 Phaeophyceae, 15 Ulvophyceae, 6 Cladophorophyceae and 8 Bryopsidophyceae) (Lluch, 2002).

Literature reports on the natural product chemistry of Southern African marine algae are limited. One study screened 56 South African crude extracts of marine algae for antimicrobial activity; however, this was a pharmacological study in which characterisation of the compounds responsible for activity were not investigated (Vlachos *et al.*, 1997). In another study, the antiplasmodial and antimicrobial activities of 78 crude South African marine algal extracts also provided valuable insight into the interesting pharmacological potential of marine *flora* (Lategan *et al.*, 2009).

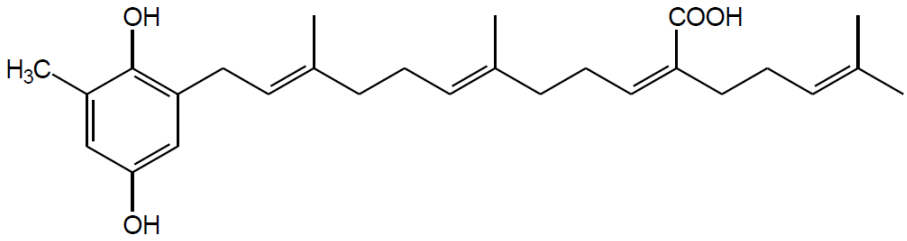
Metabolites were isolated from *Sargassum heterophyllum*, namely; sargaquinoic acid (**1.5**), sargaquinal (**1.6**) sargahydroquinoic acid (**1.7**) and fucoxanthin (**1.8**) (Afolayan *et al.*, 2008). Fucoxanthin and sargaquinal showed good antiplasmodial activity toward a chloroquine-sensitive strain of *Plasmodium falciparum*, while sargaquinoic acid and sargahydroquinoic acid were only moderately active. *Sargassum heterophyllum* has not been reported off the Namibian coast.

Other South African marine algae such as *Laurencia* and *Portieria* species have also demonstrated good *in vitro* bioactivity on a number of different cell lines; however these species have also not been reported off the Namibian coast.

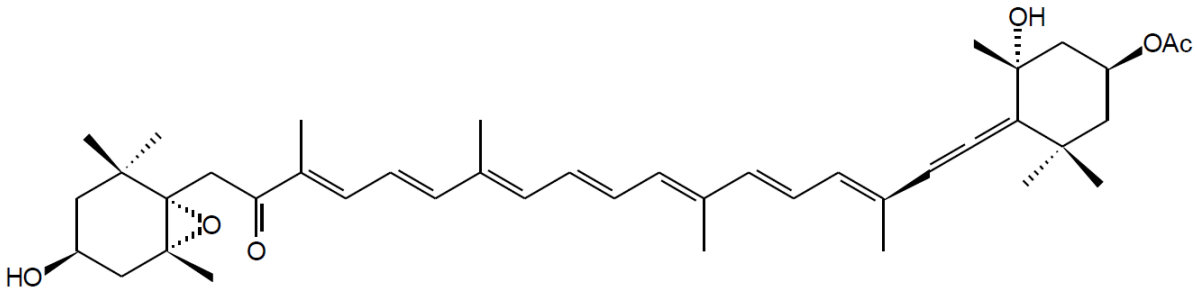
A number of new cytotoxic halogenated monoterpenes were also isolated from *Plocamium corallorhiza* (Knott *et al.*, 2005; Mann *et al.*, 2007) (See Table 2). Further halogenated monoterpenes (**1.9-1.10**) were also later isolated from *Plocamium cornutum*, and these compounds showed *in vitro* antiplasmodial activity (Afolayan *et al.*, 2009).



Sargaquinoic acid, R = COOH (**1.5**) Sargaquinal, R = CHO (**1.6**)

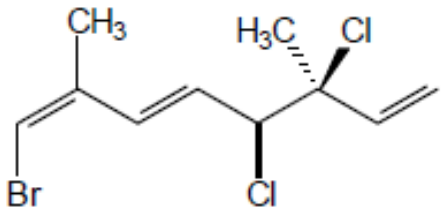


Sargahydroquinoic acid (**1.7**)



Fucoxanthin (**1.8**)

The identification and *in vitro* anti-oesophageal cancer activity of a series of halogenated monoterpenes isolated from *Plocamium suhrii* and *P. cornutum* was also reported (Antunes *et al.*, 2011) (See Table 2).



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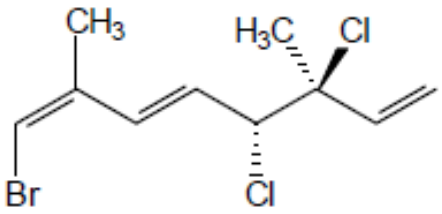

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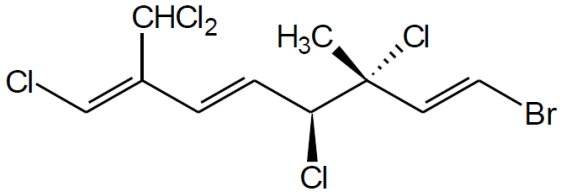
Table 2: IC_{50} (μM) data for cytotoxic compounds isolated from *Plocamium* species using oesophageal cancer (WHCO1) cell lines. For this test, the known anticancer drug cisplatin has an IC_{50} value of 13μM (Knott, 2012).

Plocamium Species	Compound Number	$IC_{50} - \mu$M Values	Reference
Plocamium suhrii	**1.11**	6.6	(Antunes *et al.*, 2011)
Plocamium corallorhiza	**1.12**	7.5	(Mann *et al.*, 2007)
Plocamium suhrii	**1.13**	7.9	(Antunes *et al.*, 2011)
Plocamium suhrii	**1.14**	8.4	(Antunes *et al.*, 2011)
Plocamium suhrii	**1.15**	8.5	(Antunes *et al.*, 2011)
Plocamium corallorhiza	**1.16**	9.3	(Knott *et al.*, 2005)
Plocamium suhrii	**1.17**	9.3	(Antunes *et al.*, 2011)
Plocamium suhrii	**1.18**	9.9	(Antunes *et al.*, 2011)
Plocamium suhrii	**1.19**	15.1	(Antunes *et al.*, 2011)
Plocamium corallorhiza	**1.20**	17.2	(Knott *et al.*, 2005)
Plocamium cornutum	**1.21**	17.8	(Antunes *et al.*, 2011)
Plocamium corallorhiza	**1.22**	18.1	(Knott *et al.*, 2005)
Plocamium corallorhiza	**1.23**	33.8	(Knott *et al.*, 2005)
Plocamium corallorhiza	**1.24**	34.8	(Knott *et al.*, 2005)
Plocamium cornutum	**1.25**	40.2	(Antunes *et al.*, 2011)
Plocamium cornutum	**1.26**	47.3	(Antunes *et al.*, 2011)
Plocamium corallorhiza	**1.27**	64.8	(Antunes *et al.*, 2011)
Plocamium cornutum	**1.28**	87.6	(Antunes *et al.*, 2011)
Plocamium cornutum	**1.29**	87.6	(Antunes *et al.*, 2011)



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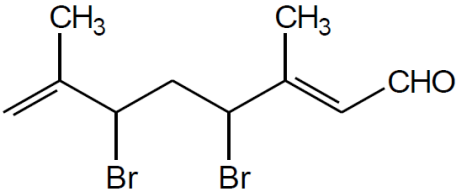

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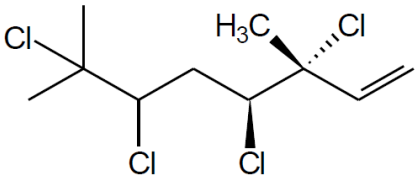

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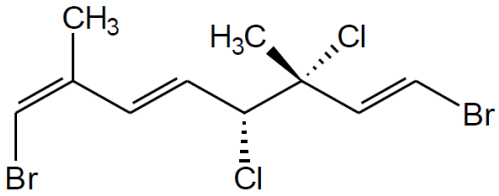

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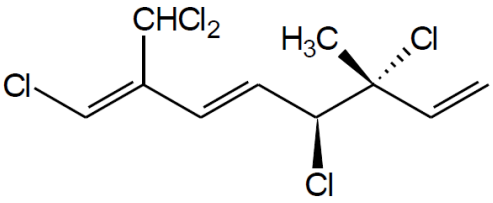

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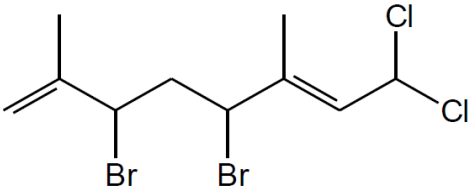

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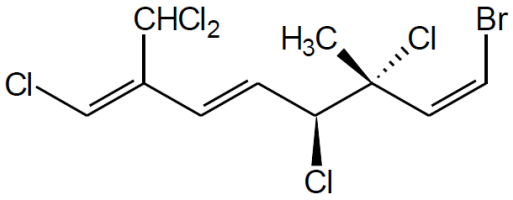

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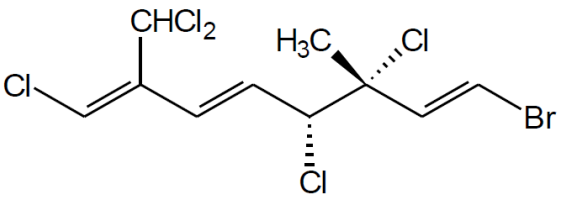

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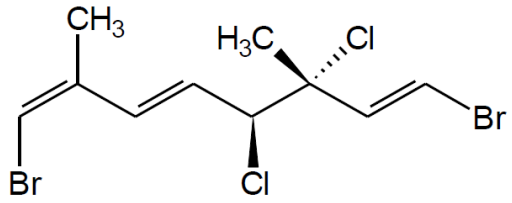

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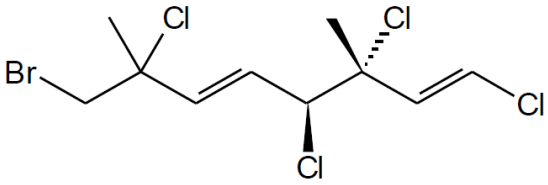

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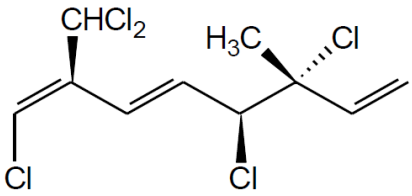

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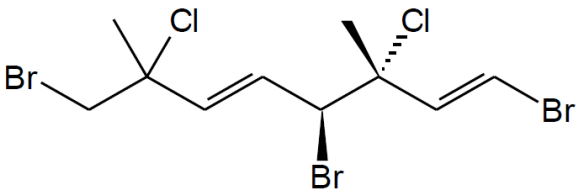

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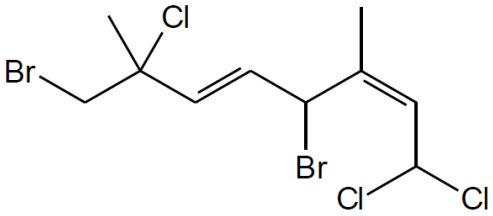

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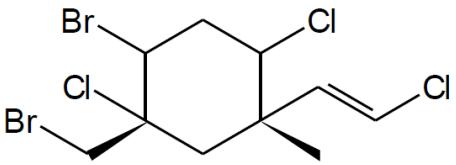

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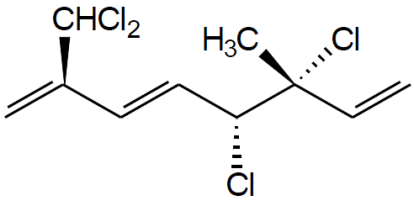

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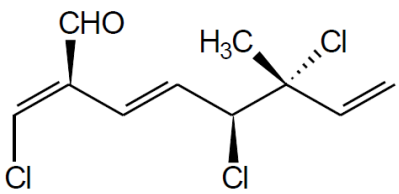

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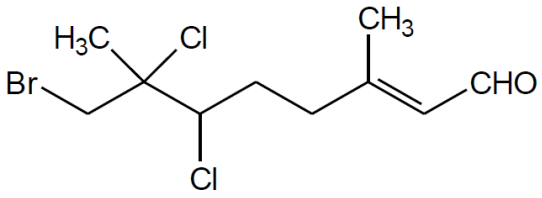

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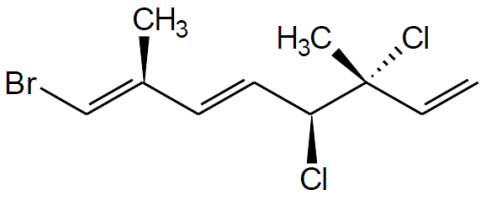

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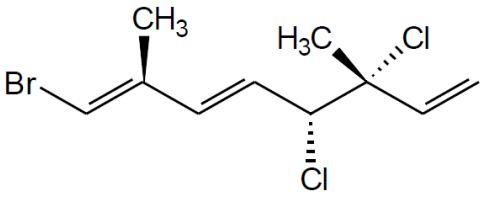

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2 Findings

A literature review could not find publications when it comes to looking at the medicinal chemistry and biological screening of Namibian marine algae for the purposes of novel drug discovery. This raises the question, what is Namibia currently doing with its abundant marine algal reserves to enhance pharmaceutical research and novel drug discovery?

With regards to Namibian *Plocamium* species, there are at least six well known different kinds of *Plocamium* species found off the Namibian coast, namely *P. cartilagineum, P. corallorhiza, P. cornutum, P. glomeratum, P. rigidum* and *P. suhrii.*

To date, the chemistry of *P. cartilagineum*, and *P. glomeratum,* from Southern Africa has not yet been published or identified. The chemistry of South African samples of *P. corallorhiza, P. cornutum, P. maxillosum, P. rigidum* and *P. suhrii* is published. Different compounds isolated from *Plocamium* species have demonstrated antiplasmodial, antimicrobial, cytotoxic and antifouling activity (Afolayan *et al.*, 2009; Antunes *et al.*, 2011). Several compounds isolated from South African *Plocamium* species are indicated in Table 2 in decreasing order of IC_{50} values. These compounds are most likely also present in Namibian *Plocamium* species. Although this still needs to be confirmed by means of Nuclear Magnetic Resonance (NMR).

3 Conclusion

The authors of this paper believe that further research needs to be conducted into Namibian *Plocamium* species as a source of novel bioactive compounds with possible pharmaceutical applications.

In a paper written by Davies-Coleman (2010) entitled, '*Natural products research in South Africa: End of an era on land or the beginning of an endless opportunity in the sea*?' it was concluded that marine natural products cannot be ignored as a source of new drugs. The reason for this is that natural products are often required to bind to other proteins to execute the bioactivities for which they were produced by a living organism (Davies-Coleman, 2010). Natural products have privileged structures over random synthetic products as they are designed to be able to bind to specific protein receptors. Davies-Coleman (2010) further suggests that South Africa's marine *fauna* and *flora* remain a relatively untapped source of novel bio-molecules with unfulfilled pharmaceutical and agrochemical potential, and that endemic South African marine *fauna* and *flora* offer rich rewards for marine natural product chemists in search of novel bioactive secondary metabolites with possible medicinal properties.

The authors believe that the suggestions made by Davies-Coleman can also be extended to the Namibian context. Based on the above-mentioned findings, the authors also suggest that Namibian marine algae should to be thoroughly investigated for possible pharmaceutical applications and novel drug discovery.

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