

# Antimicrobial properties and metabolite profiling of the ethyl acetate fractions of *Sinularia polydactyla* and *Cespitularia simplex* surrounding Mauritius Island

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**Abstract.** Jahajeeah D, BhoYROO V, Ranghoo-Sanmukhiya M. 2023. Antimicrobial properties and metabolite profiling of the ethyl acetate fractions of *Sinularia polydactyla* and *Cespitularia simplex* surrounding Mauritius Island. *Indo Pac J Ocean Life* 7: 133-142. Soft corals form an integral part of the reef ecosystem. This study assessed the antibacterial activities of Mauritius Island's soft corals and their different natural compounds having important biological properties. Antimicrobial assays and GCMS-MS analysis were performed using ethyl acetate extracts of *Sinularia polydactyla* and *Cespitularia simplex*. The results for both species indicated significant activity against most clinically pathogenic bacterial strains tested. In addition, *S. polydactyla* and *C. simplex* extracts gave the most potent action spectra yielding the largest inhibition zone diameter, especially against the Gram-positive *Staphylococcus aureus* ( $8.73 \pm 2.87$  and  $6.00 \pm 1.20$  mm), respectively. The MIC also confirmed that the Gram-positive *Bacillus subtilis* and *S. aureus* strains were the most susceptible bacteria when exposed to the soft coral extracts, while *Pseudomonas aeruginosa* and *Escherichia coli* were the most resistant Gram-negative strains. The biochemical profile of the extracts showed the presence of terpenoids, steroids, flavonoids, coumarins, and quinones. GCMS-MS analysis also identified 151 compounds in *S. polydactyla* and 91 compounds in *C. simplex*. Several previously published studies have shown the biological activities of different species of *Cespitularia*; however, this is the first study to demonstrate the antibacterial activity and compound profiling of *C. simplex*. Although studies have been carried out on *S. polydactyla* extracts, compounds such as 25-Hydroxycholesterol and spathulenol have not yet been reported. The results from the study suggest that both *S. polydactyla* and *C. simplex* are potential sources of novel antibiotics and possess a myriad of chemical compounds which may lend themselves to bioprospecting.

**Keywords:** Antibacterial activity, biochemical compounds, GCMS-MS, Mauritius, soft corals

## INTRODUCTION

Soft corals have been studied since the nineteenth century as a natural product source (Aratake et al. 2012). Extreme ocean conditions change can lead marine organisms such as soft corals to synthesize various natural biological and chemical products. Soft corals, sessile organisms, have strong chemical defense systems, which produce diverse and complex secondary metabolites (Choudhary et al. 2017; Kusmita et al. 2021; Nurrachma et al. 2021). Over the past 50 years, more than 20,000 natural products have been reported in the marine environment (Blunt et al. 2017). The soft corals' bioactive secondary metabolites, such as terpenoids, cembranoids, and steroids, have exhibited interesting biological properties, including cytotoxic, antifungal, antibacterial, anti-inflammatory, and antifouling activity (Carroll et al. 2020; Tammam et al. 2020). The bioactive compounds found in soft corals have antibacterial properties against a wide range of Gram-positive and Gram-negative bacteria. More than 5,800 secondary metabolites are produced by soft corals (Li et al. 2019), including unique fatty acids, terpenoids, quinones, alkaloids, glycosides, and steroids (Ermolenko et al. 2020). The most studied soft coral species for its bioactive

compounds is *Sinularia* sp. This soft coral contains toxins such as diterpenes, sesquiterpenes, norditerpenes, polyhydroxylated steroids, and polyamine compounds, which have been used for drug development (Chen et al. 2012).

The inhibitory activity of these bioactive compounds varies across different bacterial species (Tanod et al. 2018). In addition, the polarity of compounds plays a role in the sensitivity of bacteria. Gram-negative bacteria are generally sensitive to polar antimicrobial compounds, whereas Gram-positive are more sensitive to non-polar antibacterial compounds. The variation in sensitivity of different bacteria is mainly due to the cell wall structure. The outer membrane observed in Gram-negative bacteria is the main reason for the resistance to a wide range of antibiotics (Breijyeh et al. 2020). Moreover, differences in antibacterial activity can be observed within the same soft coral species. A plausible explanation could be the environmental factors that might affect the bioactive compounds present in the organism (Tanod et al. 2018).

Antimicrobial resistance is a worldwide phenomenon, which includes Mauritius Island. Although non-communicable diseases remain the leading cause of death in Mauritius, an increase in deaths due to infectious

diseases has also been recorded in recent years (MNAP 2017). The AMR global surveillance report revealed 43.5% and 57.6 % resistance of *Escherichia coli* to 3<sup>rd</sup> generation cephalosporins and fluoroquinolones, respectively. Those reports also stated 55.8% and 1.9% resistance of *Klebsiella pneumoniae* to 3<sup>rd</sup> generation cephalosporins and carbapenems, and lastly, 51.5% resistance of *Staphylococcus aureus* to methicillin in Mauritius during one month in 2012 (MNAP 2017). Thus, searching for novel antimicrobial compounds is very important for the well-being of humanity. Furthermore, Mauritius is known to have one of the world's largest Exclusive Economic Zones (EEZ), extending over a surface area of 1.9 million km<sup>2</sup>. However, it has not yet been fully exploited. Undoubtedly, the soft marine corals in this area hold potential pharmaceutical drugs and must be inventoried for their antimicrobial and other biological properties.

Previous research showed that *Sinularia* sp. has antibacterial potential (Afifi et al. 2016; Tanod et al. 2018). However, until now, no work has been carried out on the antimicrobial properties and the chemical profiling of *Sinularia polydactyla* and *Cespitularia simplex* around Mauritius Island. *S. polydactyla* and *C. simplex* are the most abundantly present soft corals around Mauritius (Jahajeeah et al. 2021). Compounds, such as spathulenol, 25-hydroxycholesterol, batilol, and others, were identified on GCMS analysis and have been reported from *S. polydactyla* and *C. simplex* for the first time. This study demonstrated the antimicrobial properties of soft corals from Mauritian waters and identified the compounds with myriad biological importance.

## MATERIALS AND METHODS

### Study area

Samples of the two soft corals, *S. polydactyla* and *C. simplex*, were collected from Albion (57°24'2.99"E: 20°12'42.01"S) and Pereybere (57°35'19.21"E: 19°59'56.67"S) (Figure 1). Both samples were collected at less than 2 m depth during low tides. They were transferred to the lab in zip-lock bags containing seawater, where they were cleaned and frozen at -80°C before a freeze-drying step. The soft corals were previously identified at the molecular level using the COI-COII intergenic spacer marker (Jahajeeah et al. 2021).

### Extract preparation

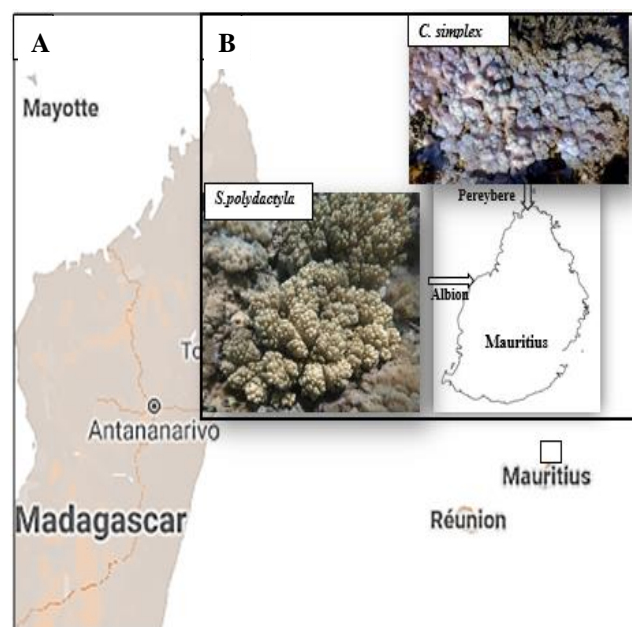
The soft corals were cut into small pieces, weighed, and freeze-dried. The freeze-dried soft corals (70-200g) were exhaustively macerated with ethyl acetate for 48 h. Next, the solution was filtered and evaporated using a rotatory vacuum evaporator set at a temperature of 55°C. The obtained extracts were weighed and stored in sterile corning tubes at 4°C. Finally, the crude extracts were stored for phytochemical and antimicrobial analyses against selected bacteria and GCMS-MS analysis.

### Microorganisms and Inoculum preparation

The following microbial strains were obtained from the American Type Culture Collection (ATCC): *Bacillus subtilis* (ATCC 6633), *S. aureus* (ATCC 51153), *E. coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 27853). All isolates were maintained in nutrient broth at 4°C. The strains were activated by subculture at 37°C for 24 h with fresh Muller Hinton agar (MHA) prior to any antimicrobial tests.

### Antibacterial activity

The in vitro antibacterial activity of the soft coral extracts total crude extracts was evaluated using the disc diffusion method using Müller–Hinton agar with the determination of inhibition zone diameters measured in millimeters (mm) (CLSI 2008). Bacterial cultures were adjusted to a turbidity of 0.5 McFarland (absorbance 0.08–0.1 at 600 nm), and 100 µL of the standardized test strain cultures were plated onto Muller–Hinton agar using an inoculating loop. The plates were dried for approximately 15 min and then used for the sensitivity test. Sterile filter paper discs were saturated with 10 µL of the soft coral extracts and then placed on inoculated Petri dishes. A negative control (ethyl acetate) and a positive control (chloramphenicol) were used for each bacterial strain. All the tests were carried out in triplicate to ensure reliable and accurate results. The plates were inverted and incubated at 37°C for 18 to 24 h. The inhibition zone diameter defines active or inactive soft coral extracts.



**Figure 1.** A. Location of Mauritius in the Western Indian Ocean; B. Location of the sample collection sites, Albion and Pereybere around Mauritius Island, with representative images of the soft coral colonies *S. polydactyla* and *C. simplex* present at each sample site

### Determination of minimal inhibitory concentration

The soft coral extracts which showed the ability to inhibit the growth of microorganisms were tested for their Minimum Inhibitory Concentration (MIC) using the microdilution technique (Eloff 1998). Test strains were cultured as before and were diluted to a concentration of  $1 \times 10^6$  CFU/mL and plated on sterile 96 well microplates. All the wells used were filled with 100  $\mu$ L of Muller-Hinton broth (MHB) except the negative control, which contained only 100  $\mu$ L of solvent and 100  $\mu$ L of bacteria. Each sample consisted of 4-5 replicates, with the 5<sup>th</sup> row containing 10 mg/mL chloramphenicol as the positive control. Apart from the negative control, all the wells were two-fold serially diluted. In addition, 100  $\mu$ L of inoculum was added to each well, making a total volume of 200  $\mu$ L. The last column contained only MHB and the inoculum as the control. The microplate was incubated at 37°C for 24 h. P-iodonitrotetrazolium chloride (0.2 mg/mL) was used to indicate microbial growth. Viable bacteria reduced the yellow dye to pink color.

### Biochemical analysis

The ethyl acetate aqueous extracts were subjected to several chemical tests to evaluate the presence of secondary metabolites such as alkaloids, flavonoids, saponins, tannins, phenols, anthraquinones, steroids, coumarins, and terpenoids using standard procedures described by Deyab et al. (2016).

### GCMS-MS analysis and Compound identification

GCMS carried out the identification and analysis of chemical compounds in the crude extracts. The GC-MS Shimadzu model GC 2010 was used. Exactly 1  $\mu$ L of the sample was injected in the GC column (SP®-2560; fused silica, 100m $\times$ 0.25mm $\times$ 0.2 $\mu$ m, Sigma-Aldrich). Helium was used as the carrier gas at a working constant flow rate of 1 mL/min. The injection volume was 1.0  $\mu$ L, the injection temperature was 250°C, and the interface temperature was 250°C. The injection took place at an initial oven temperature of 60°C maintained for 5 min, and raised at a rate of 15°C/min till 165°C. That was maintained for 1 min and then raised to 225°C for 20 min at a rate of 2°C/min. Identification of components was achieved based on their retention indices, and the mass spectra were interpreted using the National Institute of Standards and Technology (NIST) database, Wiley library, and GC/MS Forensic Toxicological Database. Each of the compounds identified was verified for their biological importance through published data, and the structure of the biologically important compounds was obtained from NIST.

## RESULTS AND DISCUSSION

### Antibacterial activity

Both *S. polydactyla* and *C. simplex* ethyl acetate extracts showed significant activity against the bacterial strains. The *S. polydactyla* extract had greater antibacterial activity than the *C. simplex* extract against the pathogenic

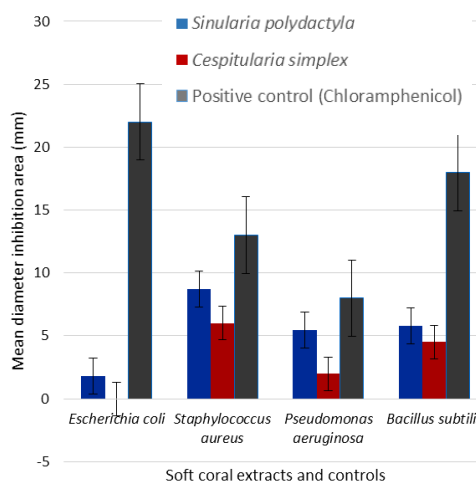
strains *B. subtilis*, *S. aureus*, *E. coli*, and *P. aeruginosa*. The *S. polydactyla* extract had the most potent action spectra, yielding the largest inhibition zone diameter, especially against the Gram-positive strain *S. aureus* ( $8.73 \pm 2.87$  mm). *C. simplex* showed high inhibition against *S. aureus* ( $6.00 \pm 1.20$  mm) compared to the other bacterial strains. The positive control chloramphenicol showed an inhibition zone diameter of  $13.0 \pm 1.41$  against *S. aureus*, similar to the inhibitory effect of the *S. polydactyla* extract. Low antibacterial activity ( $1.80 \pm 1.93$  mm) and no inhibition were observed for Gram-positive *E. coli* by *S. polydactyla* and *C. simplex*, respectively, when compared to the positive control, which showed the highest inhibition zone diameter of  $22.0 \pm 2.82$  mm (Figure 2).

### Minimum Inhibitory Concentration (MIC)

The antibacterial activity of each soft coral extract was further probed to determine its MIC using the microdilution assay. The MIC of *C. simplex* for *E. coli* was not performed due to the absence of an inhibition zone using the agar disc diffusion method. The *S. polydactyla* extract had the highest inhibitory effect on the Gram-positive strains *S. aureus* and *B. subtilis*, with a MIC value of 3.26 mg mL<sup>-1</sup>. *E. coli* and *P. aeruginosa* seemed less sensitive, with a MIC value of 6.51 mg mL<sup>-1</sup>. Similarly, the ethyl acetate extract of *C. simplex* showed a higher inhibitory effect on *S. aureus* and *B. subtilis*, reporting a MIC value of 1.59 mg mL<sup>-1</sup>, while *P. aeruginosa* seemed less sensitive, with a MIC value of 6.35 mg mL<sup>-1</sup> (Table 1). The MIC data confirmed that Gram-positive bacteria were more susceptible than Gram-negative bacteria.

### Biochemical analysis

The soft coral extracts were screened for their biochemical components using standard protocols. Both *S. polydactyla* and *C. simplex* showed similar results (Table 2). The presence of terpenoids, steroids, flavonoids, coumarins, and quinones was recorded for both soft corals. However, Alkaloid was only recorded in the *S. polydactyla* extract.



**Figure 2.** Antimicrobial activity of the two soft coral extracts on different bacteria

### GCMS-MS result of soft corals

The current study determined the GCMS-MS spectra of the ethyl acetate extracts of the two soft corals. The compounds identified through the GCMS-MS system were classified into different classes based on their biosynthetic origins: terpenoids, sesquiterpenoids, fatty acid derivatives, sterols, pyrans, alkaloids, ketones, aldehydes, and naphthalene derivatives, with each having a specific retention time. GCMS-MS analysis identified 151 compounds in the *S. polydactyla* ethyl acetate extract and 91 compounds in the *C. simplex* ethyl acetate extract. Sesquiterpenoids (23.84% and 28.60%, respectively) were the class of the most dominant compound found in *S. polydactyla* and *C. simplex*. The compounds produced by the studied soft corals also possess biological activities (Tables 3 and 4).

One hundred and fifty-one compounds were identified in the *S. polydactyla* ethyl acetate extract, and 50 compounds were found to have biological properties based on previous literature. Of the 50 compounds, 21% had antimicrobial properties (antibacterial, antiviral, and antifungal), 18% and 16% had anti-inflammatory and anticancer properties, respectively, and 45% had other biological properties such as antiarthritic, anti-hypercholesterolemic, and anti-oxidative. For the soft coral *C. simplex*, out of the 91 compounds, 17 were found to have biological properties. Of the 17 biologically important compounds, 24% were found to have anti-inflammatory activities, while 17% and 10% had antimicrobial and anticancer properties, respectively. In addition, 49% had other important biological activities such as application in neurodegenerative diseases, treatment of hepatitis, and many more (Figure 3).

### Discussion

The current study was conducted to screen the ethyl acetate extracts of Mauritius's most abundant soft corals and test their inhibitory potential on the growth of pathogenic bacterial strains. The soft corals *S. polydactyla* and *C. simplex* were selected as they have 100% coverage at the selected sites. *S. polydactyla* formed large colonies of about 2.5 m at Albion, and *C. simplex* grows extensively on

the rocks at Pereybere. The results indicated that the ethyl acetate extracts of *S. polydactyla* and *C. simplex* possess antibacterial activity against most of the tested bacterial strains. Moreover, the data obtained from the Disc diffusion and MIC showed that the Gram-positive strains *B. subtilis* and *S. aureus* were the most susceptible to the soft coral extracts, while *P. aeruginosa* and *E. coli* were the most resistant Gram-negative strains. Soares et al. (2012) reported that Gram-negative bacteria have a unique outer membrane that prevents certain drugs and antibiotics from entering the cell, making them less susceptible. However, the bacteria are not completely protected even with a double membrane. Gram-negative bacteria have hydrophilic ends such as carboxyl, amino acids, and hydroxyl, thus making them more sensitive to polar compounds (Madigan et al. 2000).

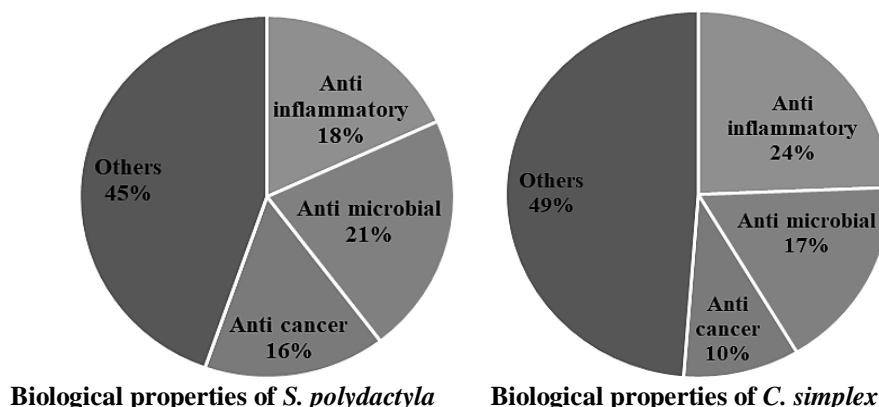
**Table 1.** MIC values of both *S. polydactyla* and *C. simplex* extracts against pathogenic bacteria.

Bacteria	Samples	
	<i>Sinularia polydactyla</i> (mg mL <sup>-1</sup> )	<i>Cespitularia simplex</i> (mg mL <sup>-1</sup> )
<i>Escherichia coli</i>	6.51	-
<i>Staphylococcus aureus</i>	3.26	1.59
<i>Pseudomonas aeruginosa</i>	6.51	6.35
<i>Bacillus subtilis</i>	3.26	1.59

**Table 2.** Biochemical components in the soft coral extracts.

Biochemical tests	<i>Sinularia polydactyla</i>	<i>Cespitularia simplex</i>
Alkaloids	+	-
Terpenoids	+	+
Steroids	+	+
Tannins	-	-
Saponins	-	-
Flavonoids	+	+
Phenols	-	-
Coumarins	+	+
Quinones	+	+
Glycosides	-	-

Note: +: Present/detected, -: Absent/Not detected



**Figure 3.** Biological properties of the ethyl acetate extracts of *Sinularia polydactyla* and *Cespitularia simplex*

**Table 3.** Biological properties of the compounds found in the *Sinularia polydactyla* extract

Biochemical compound	Biological properties	References
Caryophyllene	Anti-inflammatory, antimicrobial, anticancer	Dahham et al. (2015), Hameed et al. (2016)
1H-Cycloprop[e]azulen-7-ol, decahydro-1,1,7-trimethyl-4-methylene-/ Spathulenol	Antimicrobial, anti-proliferative, anti-inflammatory, immunomodulatory activities	Goud et al. (2002), Ziaei et al. (2011), Tan et al. (2016)
(E)- $\beta$ -Farnesene	Application in neurodegenerative diseases as an alarm pheromone	Russo and Marcu (2017)
1,4,7-Cycloundecatriene, 1,5,9,9-tetramethyl-, Z,Z,Z-7-epi-cis-Sesquisabinene hydrate	Anti-aging, anti-hyperlipidemia, antimicrobial activities	Mohammad et al. (2016)
Cyclohexene, 3-(1,5-dimethyl-4-hexenyl)-6-methylene-, [S-(R*,S*)]-	Anticancer	Shareef et al. (2016)
$\beta$ -Bisabolene	Anti-viral	Joshi et al. (2020)
Caryophyllene oxide	Anti-cancer	Yeo et al. (2016)
1,6,10-Dodecatrien-3-ol, 3,7,11-trimethyl-, (E)-	Anticancer, antifungal, anti-coagulant, anti-inflammatory	Sain et al. (2014), Fidyt et al. (2016)
12-oxabicyclo[9.1.0]dodeca-3,7-diene, 1,5,5,8-tetramethyl-, [1R-(1R*, 3E, 7E, 11R*)]	Anti-trypanosomal activity, antimicrobial, anti-biofilm, anti-oxidative, anti-parasitic, skin-penetration enhancer, skin-repellent, anti-nociceptive, anti-inflammatory, anticancer	Chan et al. (2016)
Tetracyclo[6.3.2.0(2,5).0(1,8)]tridecan-9-ol, 4,4-dimethyl-	Antimalarial activities	Da Silva et al. (2004)
1,2-15,16-Diepoxyhexadecane	Antifungal	Narayanasamy et al. (2011)
1-Naphthalenol, 1,2,3,4,4a,7,8,8a-octahydro-1,6-dimethyl-4-(1-methylethyl)-, [1R-(1 $\alpha$ ,4 $\beta$ ,4a $\beta$ ,8a $\beta$ )]-	Anti-tumorigenic, anti-inflammatory	Shareef et al. (2016)
Ar-Turmerone	Anti-fungal	Chang et al. (2008)
alpha-Bisabolol	Antitumor, neuroprotective effect, anti-dermatophytic activity	Mukda et al. (2013), Saga et al. (2020)
Curlone	Anti-inflammatory, anti-tumorigenic, anti-spasmodic, relaxant	Kamatou and Viljoen (2009)
2-Methyltetracosane	Anticancer, anti-inflammatory	Aggarwal et al. (2013)
7-Isopropenyl-1,4a-dimethyl-4,4a,5,6,7,8-hexahydro-3H-naphthalen-2-one / $\alpha$ -cyperone	Free radical scavenging activity	Malarvili et al. (2015)
Jasmolin II	Anti-virulence, anti-genotoxic, antibacterial, anti-depressant, anticancer	Xia et al. (2020)
n-Butyl laurate	Insecticidal activity	Godin et al. (1965)
Heptadecane	Antimicrobial activity	Kavčić et al. (2013)
3,7,11,15-Tetramethyl-2-hexadecen-1-ol /	Anti-inflammatory, sex pheromone	Kim et al. (2013)
Phytol	Anti-hyperalgesic, anti-inflammatory, antiarthritic, antimicrobial, anticancer	Carvalho et al. (2020), Willie et al. (2021)
2-Pentadecanone, 6,10,14-trimethyl-	Antimicrobial	Olaoye et al. (2017)
Bicyclo[7.2.0]undec-4-ene, 4,11,11-trimethyl-8-methylene-, [1R-(1R*,4Z,9S*)]-	Anti-inflammatory, anti-carcinogenic, antibiotic, antioxidant, and local anesthetic properties	Legault et al. (2013)
n-Hexadecanoic acid	Anti-inflammatory, antioxidant, hypocholesterolemic nematocide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor, potent mosquito larvicide	Aparna et al. (2012), Abubakar et al. (2016)
2-Nonadecanone	Anti-inflammatory, anti-depressant, anti-dementia	Lee and Hyun (2018)
Andrographolide	Antidiabetic potential, treatment of hepatitis, anti-inflammatory, antioxidant, antineoplastic properties, antibacterial	Brahmachari (2017); Girish and Pradhan, (2017); Burgos et al. (2020)
Thunbergol	Antibacterial activity	Salem et al. (2014), Mitić et al. (2019)
(-)-Neoclovene-(II), dihydro-	Antimicrobial	Venkata Raman et al. (2012)
n-Nonadecanol-1	Cytotoxic activity	Bernardini et al. (2018)
Cyclohexane, 1-ethenyl-1-methyl-2,4-bis(1-methylethenyl)-	Anticancer,	Jiang et al. (2017), Xie et al. (2020)
cis-(Z)-alpha-Bisabolene epoxide	Anti-inflammatory	Rodríguez-Chaves et al. (2018)
2-Methyltetracosane	Anti-leishmania activity	Malarvili et al. (2015)
Aromadendrene oxide 2	Free radical scavenging activity	Pavithra et al. (2018)
Retinal	Anti-cancer	Pechère et al. (1999)
Ergost-25-ene-3,6-dione,5,12-dihydroxy(5alpha,12beta)-	Anti-bacterial	Saravanan et al. (2021)
1-Heptatriacotanol	Anticancer	Mohammad et al. (2016); Junwei et al. (2018)
Tetratetracontane	Anti-hypercholesterolemic, antioxidant, anticancer, anti-inflammatory, sex hormone activity	Gumgumjee and Hajar (2015)
trans-Z- $\alpha$ -Bisabolene epoxide	Antibacterial	Altameme et al. (2016)
25-Hydroxycholesterol	Anti-inflammatory	Zu et al. (2020)
17-Pentatriacontene	Antiviral effect (on SARS-CoV-2 infection as well)	Dineshkumar et al. (2018)
Batilol	Anti-inflammatory, anticancer, antibacterial, antiarthritic	Hassan et al. (2016)
6beta-Hydroxymethandienone	Anti-bacterial	Hooijerink et al. (1999)
1,6,10,14,18,22-Tetracosahexaen-3-ol,	Growth hormone	Jenecius et al. (2012)
2,6,10,15,19,23-hexamethyl-, (all-E)-	Anti-inflammatory, antiarthritic, antimicrobial, anti-tumorigenic, anti-protozoal, chemopreventive	
Cholesterol	Membrane fluidity	Kohlmeier, (2013)
9,12-Octadecadienoic acid (Z,Z)-	Antibacterial, anti-inflammatory	Rosselli et al. (2007)
Isoaromadendrene epoxide	Antimicrobial, antioxidant, anti-inflammatory	Hameed et al. (2016)
4-Isopropenyl-4,7-dimethyl-1-oxaspiro[2.5]octane	Antimicrobial	Rahman et al. (2014)
Campesterol	Anti-inflammatory, decrease LDL cholesterol	Yuan et al. (2019)
Lupeol	Anticancer, anti-inflammatory, cardioprotective agent	Saleem (2009)

**Table 4.** Biological properties of the compounds from *C. simplex* extract

Biochemical compound	Biological properties	References
(E)- $\beta$ -Farnesene	Application in neurodegenerative diseases As an alarm pheromone	Russo and Marcu (2017)
$\beta$ -Elemene	Anticancer, anti-inflammatory	Jiang et al. (2017), Xie et al. (2020)
Andrographolide	Antidiabetic potential, treatment of hepatitis, anti-inflammatory, antioxidant, antineoplastic properties, antibacterial	Brahmachari (2017), Girish and Pradhan (2017); Burgos et al. (2020)
1H-Cycloprop[e]azulen-7-ol, decahydro-1,1,7-trimethyl-4-methylene-, [1ar-(1a.alpha.,4a.alpha.,7b.beta.,7a.beta.,7b.alpha.)]- / (-)-Spathulenol	Antimicrobial, anti-proliferative, anti-inflammatory, immunomodulatory activities	Goud et al. (2002), Ziaei et al. (2011), Tan et al. (2016)
Viridiflorol	Antimycobacterial, anti-inflammatory, Antioxidant activity	Trevizan et al. (2016)
trans-Z- $\alpha$ -Bisabolene epoxide	Anti-inflammatory effects	Altameme et al. (2016)
Thunbergol	Antibacterial activity	Salem et al. (2014); Mitić et al. (2019)
1-Heptatriacotanol	Anti-hypercholesterolemic effects, antioxidant, anticancer, anti-inflammatory, sex hormone activity	Mohammad et al. (2016) Junwei et al. (2018)
Limonen-6-ol, pivalate	Antioxidant, anti-inflammatory, insect repellent activity	Mohammad et al. (2016)
$\alpha$ -Bulnesene	Paf inhibitor	Tsai et al. (2007)
1-Heneicosanol	Antibacterial activity	Arancibia et al. (2016)
Isoaromadendrene epoxide	Antimicrobial, antioxidant, anti-inflammatory	Hameed et al. (2016)
6-epi-Shyobunol	Anti-inflammatory, antimicrobial, antioxidant	Shareef et al. (2016)
2-Dodecen-1-yl(-)succinic anhydride	Antineoplastic agents, antioxidants, antimicrobial activity	Tanod et al. (2019)
2(3H)-Benzofuranone, 6-ethenylhexahydro-6-methyl-3-methylene-7-(1-methylethenyl)-, [3aS-(3a $\alpha$ ,6 $\alpha$ ,7 $\beta$ ,7a $\beta$ )]-	Anticancer activity	Alotaibi et al. (2021)
Aromadendrene oxide 2	Anti-cancer	Pavithra et al. (2018)
Bicyclo[4.4.0]dec-2-ene-4-ol, 2-methyl-9-(prop-1-en-3-ol-2-yl)-	Local anesthetic, anti-inflammatory	Shareef et al. (2016)

The ethyl acetate extract from *S. polydactyla*, a polar compound, showed a noticeable inhibition zone against *E. coli* and *P. aeruginosa*. The work by Afifi et al. (2016) on the antimicrobial properties of *S. polydactyla* reported effective inhibitory activity in Gram-positive bacterial isolates (*Bacillus* sp. and *S. aureus*). Rozirwan et al. (2014) also reported antibacterial activity against *E. coli* and *S. aureus* from the semi-polar (EtOAc) and polar (MeOH) fractions of *S. polydactyla*. However, Shaaban et al. (2013) showed that the crude extracts and isolate compounds from *S. polydactyla* showed no antibacterial activities against a wide range of bacterial strains, some of which included *B. subtilis*, *S. aureus*, and *E. coli*.

Extracts of *C. simplex* showed antibacterial activities against *S. aureus*, *B. subtilis*, and *P. aeruginosa* but no antimicrobial activity against *E. coli* in this study. The ethyl acetate extract of *C. simplex* showed the highest inhibition zone to *S. aureus*. As an antibacterial control, the chloramphenicol inhibition zone diameters for the test bacteria were greater than those of both soft coral extracts. The ethyl acetate extract of *S. polydactyla* confirmed the presence of multiple compounds responsible for various biological activities, with the most prominent ones being the sesquiterpenoids. Khesli et al. (2008) also reported

that more than 60% of the studied soft coral species of *Sinularia* contained terpenoid compounds. Additionally, Yan et al. (2021) showed that the genus *Sinularia* is well-known for producing different complex secondary metabolites, such as sesquiterpenes (10%), diterpenes (46%), norsesquiterpenes (2%), norditerpenes (9%), steroids/steroidal glycosides (22%), and other types (11%) which exhibit a wide range of biological activities including antimicrobial. Caryophyllene, spathulenol, 1,4,7-Cycloundecatriene, 1,5,9,9-tetramethyl-, Z,Z,Z-, 1,6,10-Dodecatrien-3-ol, 3,7,11-trimethyl-, (E)-,  $\alpha$ -Cyperone, n-Butyl laurate, Phytol, 2-Pentadecanone, 6,10,14-trimethyl-, Andrographolide, Thunbergol, (-)-Neoclovene-(II), dihydro-, Retinal, Tetratetracontane, 17-Pentatriacontene, Batilol, 9,12-Octadecadienoic acid (Z,Z)-, Isoaromadendrene epoxide, 4-Isopropenyl-4,7-dimethyl-1-oxaspiro[2.5]octane identified from the GCMS profile of *S. polydactyla* are known for their antimicrobial properties. The presence of these compounds is accountable for the antimicrobial activities of *S. polydactyla* extract against *B. subtilis*, *S. aureus*, *E. coli*, and *P. aeruginosa*.

Interestingly,  $\beta$ -caryophyllene was previously isolated from soft coral *S. gibberosa*, and *S. nanolobata* were found to possess anticancer properties (Ahmed et al. 2004; Chen



et al. 2006). Spathulenol is a rare sesquiterpenoid compound with multiple biological properties found in *Eucalyptus spathulata* and isolated from *S. kavarattiensis* (Goud et al. 2002). Spathulenol has been recorded previously in *S. mayi* (Beechan et al. 1978). However, until now, no reports have been available on the presence of spathulenol in *S. polydactyla*. Finally, Andrographolide, labeled as a prospective pharmaceutical entity, principally isolates from the medicinal plant *Andrographis paniculata*, has been detected in the ethyl acetate extract of *S. polydactyla* from Mauritius. Andrographolide possesses anti-inflammatory, anticancer, antibacterial, and antiviral properties (Brahmachari 2017). Mitić et al. (2019) reported that diterpene alcohol thunbergol might have important antimicrobial properties, and this compound might have contributed to the antimicrobial effect against the tested bacterial isolates.

Thunbergol has been detected in the soft coral eggs of *Lobophytum compactum* and *L. crissum* and is reported to have Antioxidant potential (Sammarco and Coll 1992; Coll et al. 1985). The compound Batilol was previously identified in the soft coral *L. pauciflorum* and has been shown to have antibacterial activity against *B. subtilis*, *Sarcina lutea*, and *Candida albicans* (Hassan et al. 2016). It was also isolate from the Egyptian soft coral *Heteroxenia fuscescens* (Abdelkarem et al. 2021). However, these compounds have never been reported previously in *S. polydactyla*. Isoaromadendrene epoxide has been reported from the extract of *C. stolonifera* but not in any *Sinularia* sp. and *C. simplex*. The compounds 1,4,7,-Cycloundecatriene, 1,5,9,9-tetramethyl-, Z,Z,Z-, 1,6,10-Dodecatrien-3-ol, 3,7,11-trimethyl-, (E)-,  $\alpha$ -Cyperone, n-Butyl laurate, Phytol, 2-Pentadecanone, 6,10,14-trimethyl-, (-)-Neoclovene-(II), dihydro-, Retinal, Tetratetracontane, 17-Pentatriacontene, 9,12-Octadecadienoic acid (Z,Z)-, 4-Isopropenyl-4,7-dimethyl-1-oxaspiro[2.5]octane, all possess antimicrobial activity. However, they have not yet been reported in soft corals for their antimicrobial properties.

The *S. polydactyla* ethyl acetate extract possesses other metabolic compounds which are well known for their biological activities. 25-Hydroxycholesterol was detected in the extract, and this molecule has been found to have an antiviral effect on SARS-CoV-2 infection in vitro (Zu et al. 2020). Cyclohexene, 3-(1,5-dimethyl-4-hexenyl)-6-methylene-, [S-(R\*,S\*)]- has also been reported to have antiviral properties (Joshi et al. 2020). Some of the compounds have been reported to have various properties. For example, 1,6,10-Dodecatrien-3-ol, 3,7,11-trimethyl-, (E)- has properties ranging from anti-trypanosomal, antimicrobial, anti-biofilm, Antioxidant, anti-parasitic, skin-penetration enhancer, anti-nociceptive, anti-inflammatory to anticancer (Chan et al. 2016). Besides having anti-inflammatory, Antioxidant, anti-androgenic properties, N-Hexadecanoic acid has been shown to be a potent pesticide and larvicide (Aparna et al. 2012; Abubakar et al. 2016). Moreover, Bicyclo[7.2.0]undec-4-ene, 4,11,11-trimethyl-8-methylene-, [1R-(1R\*,4Z,9S\*)]- has local anesthetic properties as well as anti-inflammatory, anti-carcinogenic and Antioxidant properties. Huong et al. (2019) isolated six known compounds, namely

(1R\*,2E,4R\*,7E,10S\*,11S\*,12R\*)- 10,18-diacetoxy-dolabella-2,7-dien-6-one, emblide, sarcophine, (3R)-4-[(2R,4S)-4-acetoxy-2-hydroxy-2,6,6-trimethylcyclohexylidene-3-en-2-one, 3 $\beta$ -hydroxypregna-5,16-dien-20-one, and 3  $\beta$ -hydroxyandrost-5-en-17-one from the methanol extract of *S. digitata*. The steroid constituent, (22R, 23R, 24R)-5 $\alpha$ , 8 $\alpha$ -epidioxy-22, 23-methylene-24-methylcholest-6-ene-3 $\beta$ -ol, ergosterol peroxide, and 3 $\beta$ -hydroxyandrost-5-ene-17-one, were isolate from the methanol extract of the soft coral *Lobophytum crissum* from Vietnam (Thao et al. 2015). However, none of these compounds were identified in this study. The extraction and isolation of compounds using different polar and non-polar solvents will extract a wider range of compounds in the soft corals.

The GCMS analysis from the extracts of *C. simplex* identified several compounds which have vital biological activities. The ethyl acetate extract of the latter showed an antimicrobial effect against the test isolates, *B. subtilis*, *S. aureus*, and *P. aeruginosa*. Compounds include Andrographolide, Viridiflorol, (-)-Spathulenol, Thunbergol, 1-Heneicosanol, Isoaromadendrene epoxide, 6-epi-Shyobunol, 2-Dodecen-1-yl(-)succinic anhydride identified from the GCMS analysis might be responsible for the antimicrobial activity in *C. simplex*. 2-Dodecen-1-yl(-)succinic anhydride has been reported in *Sinularia* sp. and *Sarcophyton* sp. showing antineoplastic agents, antioxidants, and antimicrobial activity (Tanod et al. 2019). However, none of these compounds were previously reported in *C. simplex* before.  $\beta$ -Elemene, 2(3H)-Benzofuranone, 6-ethenylhexahydro-6-methyl-3-methylene-7-(1-methylethenyl)-, [3aS-(3a $\alpha$ ,6 $\alpha$ ,7 $\beta$ ,7a $\beta$ )]-, Aromadendrene oxide 2 identified by GCMS analysis possess anticancer properties.  $\beta$ -Elemene induces antitumor effects against various cell lines such as melanoma cells (Chen et al. 2012), glioblastoma cell lines (Zhu et al. 2014), leukemia cell lines (Yu et al. 2011), breast cancer cell line (Cai et al. 2013) and many more cell lines. 2(3H)-Benzofuranone, 6-ethenylhexahydro-6-methyl-3-methylene-7-(1-methylethenyl)-, [3aS-(3a $\alpha$ ,6 $\alpha$ , 7 $\beta$ , 7a $\beta$ )]- also known as dehydrosaurea lactone has an inhibitory effect against breast cancer cell growth (Peng et al. 2017). Aromadendrene oxide 2 induces apoptosis in skin epidermoid cancer cells (Pavithra et al. 2018). (E)- $\beta$ -Farnesene has been studied for its application in neurodegenerative diseases as an alarm pheromone (Russo and Marcu 2017). Limonen-6-ol, pivalate has been reported to have antioxidant, anti-inflammatory, and insect-repellent activity (Mohammad et al. 2016). Bicyclo [4.4.0]dec-2-ene-4-ol, 2-methyl-9-(prop-1-en-3-ol-2-yl)- has local anesthetic and anti-inflammatory properties (Shareef et al. 2016). From these data, we can confirm that *C. simplex* possesses myriad compounds with pharmaceutical properties.

In conclusion, the Mauritian soft corals *S. polydactyla* and *C. simplex* have potential medical value, particularly high antibacterial properties against various pathogenic bacteria. The qualitative biochemical test showed the presence of various bioactive compounds such as terpenoids, steroids, and coumarins which can be responsible for the antibacterial activities. Moreover, the

GCMS-MS analysis identified important compounds which possess vital biological properties. Therefore, identifying biologically important compounds from the soft corals from Mauritius may be harnessed for future pharmaceutical exploration. Future studies should include testing different soft coral species' solvent extracts, such as methanol, and a wider range of bacteria. Furthermore, with the emergence of various deadly diseases and viruses, anticancer and antiviral properties can also be tested to study the effectiveness of these crude extracts.

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## REFERENCES

- Abdelkarem FM, Desoky EK, Nafady AM, Allam AE, Mahdy A, Ashour A, Mohamed GA, Miyamoto T, Shimizu K. 2021. Two new polyhydroxylated steroids from Egyptian soft coral *Heteroxenia fuscescens* (Fam.: Xeniidae). *J Nat Prod* 35 (2): 236-243. DOI: 10.1080/14786419.2019.1624958.
- Abubakar M, Majinda R. 2016. GC-MS Analysis and preliminary antimicrobial activity of *Albizia adianthifolia* (Schumacher) and *Pterocarpus angolensis* (DC). *Medicines* 3 (1): 3. DOI: 10.3390/medicines3010003.
- Afifi R, Abdel-Nabi IM, El-Shaikh K. 2016. Antibacterial activity from soft corals of the Red Sea, Saudi Arabia. *J Taibah Univ Sci* 10 (6): 887-895. DOI: 10.1016/j.jtusci.2016.03.006.
- Aggarwal BB, Yuan W, Li S, Gupta SC. 2013. Curcumin-free turmeric exhibits anti-inflammatory and anticancer activities: Identification of novel components of turmeric. *Mol Nutr Food Res* 57 (9): 1529-42. DOI: 10.1002/mnfr.201200838.
- Ahmed AF, Su JH, Shiue RT, Pan XJ, Dai CF, Kuo YH, Sheu JH. 2004. New beta-caryophyllene-derived terpenoids from the soft coral *Sinularia nanolobata*. *J Nat Prod* 67 (4): 592-597. DOI: 10.1021/np030286w.
- Alotaibi AA, Bepari A, Bassiri RA. 2021. *Saussurea Lappa* exhibits anti-oncogenic effect in Hepatocellular Carcinoma, HepG2 Cancer Cell Line by Bcl-2 mediated apoptotic pathway and mitochondrial cytochrome C release. *Curr Issues Mol Biol* 43 (2): 1114-1132. DOI: 10.3390/cimb43020079.
- Altameme H, Hameed I, Idan S. 2016. *Artemisia annua*: Biochemical products analysis of methanolic aerial parts extract and antimicrobial capacity. *RJPBCS* 7 (2): 1843-1868.
- Aparna V, Dileep KV, Mandal PK, Karthe P, Sadasivan C, Haridas M. 2012. Anti-inflammatory property of *n*-hexadecanoic acid: structural evidence and kinetic assessment. *Chem Biol Drug Des* 80 (3): 434-439. DOI: 10.1111/j.1747-0285.2012.01418.x.
- Arancibia LA, Naspi CV, Pucci GN, Arce ME, Colloca CB. 2016. Biological activity of 1-heneicosanol isolated from *Senecio coluhuapiensis*, an endemic species from Patagonia, Argentina. *The Pharm Chem J* 3 (4): 73-77.
- Aratake S, Tomura T, Saitoh S. 2012. Soft coral Sarcophyton (Cnidaria: Anthozoa: Octocorallia) species diversity and chemotypes. *PLoS One* 7 (1): e30410. DOI: 10.1371/journal.pone.0030410.
- Beechan CM, Djerassi C, Eggert H. 1978. Terpenoids-LXXIV: The sesquiterpenoids from the soft coral *Sinularia mayi*. *Tetrahedron Lett* 34 (16): 2503-2508. DOI: 10.1016/0040-4020(78)88378-1.
- Bernardini G, Minetti M, Polizzotto G, Biazzo M, Santucci A. 2018. Pro-apoptotic activity of french polynesian *Padina pavonica* extract on human osteosarcoma cells. *Mar Drug* 16 (12): 504. DOI: 10.3390/md16120504.
- Blunt J, Copp B, Keyzers R, Munro M, Prinsep M. 2017. Marine natural products. *Nat Prod Rep* 34: 235-294. DOI: 10.1039/C6NP00124F.
- Brahmachari G. 2017. Andrographolide: A molecule of antidiabetic promise. In: Brahmachari G (eds). *Discovery and Development of Antidiabetic Agents from Natural Products*. Elsevier. Amsterdam, Netherlands. DOI: 10.1016/B978-0-12-809450-1.00001-6.
- Breijyeh Z, Jubeh B, Karaman R. 2020. Resistance of Gram-negative bacteria to current antibacterial agents and approaches to resolve it. *Molecules* 25 (6): 1340. DOI: 10.3390/molecules25061340.
- Burgos RA, Alarcón P, Quiroga J, Manosalva C, Hancke J. 2020. Andrographolide, an anti-inflammatory multitarget drug: all roads lead to cellular metabolism. *Molecule* 26 (1): 5. DOI: 10.3390/molecules26010005.
- Cai DY, Gao X, Wu XH, Hong TT. 2013. Synergistic effect of beta-elemene injection combined paclitaxel injection on human breast cancer MB-468 cells: an in vitro study. *Chin J Integr Med* 33 (7): 978-982.
- Carroll AR, Copp BR, Davis RA, Keyzers RA, Prinsep MR. 2020. Marine natural products. *Nat Prod Rep* 39: 1122-1171. DOI: 10.1039/D0NP00089B.
- Carvalho AMS, Heimfarth L, Pereira EWM. 2020. Phytol, a chlorophyll component, produces anti-hyperalgesic, anti-inflammatory, and antiarthritic effects: possible NFκB pathway involvement and reduced levels of the proinflammatory cytokines TNF-α and IL-6. *J Nat Prod* 83 (4): 1107-1117. DOI: 10.1021/acs.jnatprod.9b01116.
- Chan WK, Tan LT, Chan KG, Lee LH, Goh BH. 2016. Nerolidol: A sesquiterpene alcohol with multi-faceted pharmacological and biological activities. *Molecules* 21 (5): 529. DOI: 10.3390/molecules21050529.
- Chang HT, Cheng YH, Wu CL, Chang ST, Chang TT, Su YC. 2008. Antifungal activity of essential oil and its constituents from *Calocedrus macrolepis* var. *formosana* Florin leaf against plant pathogenic fungi. *Bioresour Technol* 99 (14): 6266-6270. DOI: 10.1016/j.biortech.2007.12.005.
- Chen S, Ahmed A, Dai CF, Lu CK, Hu W, Wang J, Shu JH. 2006. Sinugibberosides A-E, new terpenoids with cyclic peroxyhemiketal from the soft coral *Sinularia gibberosa*. *Tetrahedron Lett* 62 (29): 6802-6807. DOI: 10.1016/j.tet.2006.04.088.
- Chen W, Li Y, Guo Y. 2012. Terpenoids of *Sinularia* soft corals: Chemistry and bioactivity. *APSB* 2 (3): 227-237. DOI: 10.1016/j.apsb.2012.04.004.
- Choudhary A, Naughton LM, Montánchez I, Dobson A, Rai DK. 2017. Current status and future prospects of marine natural products (MNP) as antimicrobials. *Mar Drugs* 15 (9): 272. DOI: 10.3390/md15090272.
- CLSI. 2018. Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals. In: *Clinical and Laboratory Standards Institute, 4th edn VET08*. Wayne, PA.
- Coll JC, Bowden BF, Tapiolas DM, Willis RH, Djura P, Streamer M, Trott L. 1985. Studies of Australian soft corals—XXXV: The terpenoid chemistry of soft corals and its implications. *Tetrahedron Lett* 41 (6): 1085-1092. DOI: 10.1016/S0040-4020(01)96476-2.
- Da Silva TBC, Alves VL, Mendonça LVH, Conserva LM, da Rocha EMM, Andrade EHA, Lemos RPL. 2004. Chemical constituents and preliminary antimalarial activity of *Humiria balsamifera*. *Pharm Biol* 42 (2): 94-97. DOI: 10.1080/13880200490510702.
- Dahham SS, Tabana YM, Iqbal MA, Ahamed MB, Ezzat MO, Majid AS, Majid A. 2015. The anticancer, antioxidant and antimicrobial properties of the sesquiterpene β-caryophyllene from the essential oil of *Aquilaria crassna*. *Molecules* 20 (7): 11808-11829. DOI: 10.3390/molecules200711808.
- Dayab M, Elkaton T, Ward F. 2016. Qualitative and quantitative analysis of phytochemical studies on brown seaweed, *Dictyota dichotoma*. *Intl J Eng Dev Res* 4: 674-678.
- Dineshkumar G, Karthik M, Rajakumar R. 2018. GC-MS analysis of bioactive compounds from ethanolic leaves extract of *Eichhornia crassipes* (Mart) Solms. and their pharmacological activities. *J Pharm Innov* 7: 459-462.
- Eloff JN. 1998. A sensitive and quick microplate method to determine the minimal inhibitory concentration of plant extracts for bacteria. *Planta Med* 64 (8): 711-713. DOI: 10.1055/s-2006-957563.



- Ermolenko EV, Imbs AB, Gloriovova TA, Poroikov VV, Sikorskaya TV, Dembitsky VM. 2020. Chemical diversity of soft coral steroids and their pharmacological activities. *Mar Drugs* 18 (12): 613. DOI: 10.3390/md18120613.
- Fidyat K, Fiedorowicz A, Strzdała L, Szumny A. 2016.  $\beta$ -caryophyllene and  $\beta$ -caryophyllene oxide-natural compounds of anticancer and analgesic properties. *Cancer Med* 5 (10): 3007-3017. DOI: 10.1002/cam4.816.
- Girish C, Pradhan SC. 2017. Herbal drugs on the liver. In: Muriel P (eds). *Liver Pathophysiology: Therapies and Antioxidants*. Academic Press, Boston, MA, USA. DOI: 10.1016/B978-0-12-804274-8.00044-8.
- Godin PJ, Stevenson JH, Sawicki RM. 1965. The insecticidal activity of jasmolin II and its isolation from pyrethrum (*Chrysanthemum cinerariaefolium* Vis.). *J Econ Entomol* 58 (3): 548-551. DOI: 10.1093/jee/58.3.548.
- Goud T, Reddy N, Krishnaiah P, Venkateswarlu Y. 2002. Spathulenol: A rare sesquiterpene from soft coral *Sinularia kavarattiensis*. *Biochem Syst Ecol* 30 (5): 493-495. DOI: 10.1016/S0305-1978(01)00094-1.
- Gumgumjee NM, Hajar AS. 2015. Antibacterial activities and GC-MS analysis of phytocomponents of *Ehretia abyssinica* R. Br. ex Fresen. *Intl J Appl Biol* 6 (2): 236-241.
- Hameed I, Mohammad G, Jawad M. 2016. In vitro antibacterial, antifungal and phytochemical analysis of methanolic fruit extract of *Cassia fistula*. *Orient J Chem* 32 (3): 1-18. DOI: 10.13005/ojc/320307.
- Hassan A, Mohammad R, Hetta M, Mohamed T, El-Gendy O, Sleim A. 2016. Biological and chemical investigation of the soft coral *Lobophytum pauciflorum* collected from the Egyptian Red Sea. *Intl J Pharmacogn Phytochem Res* 8 (6): 906-911.
- Hooijerink D, Schilt R, Hoogenboom R, Huveneers-Oorsprong M. 1999. Identification of metabolites of the anabolic steroid methandienone formed by bovine hepatocytes in vitro. *Analyst* 123 (12): 2637-2641. DOI: 10.1039/A805132A.
- Huong NT, Ngoc NT, Hanh TTH, Quang TH, Cuong NX, Nam NH, Van Minh C. 2019. Chemical constituents from the soft coral *Sinularia digitata*. *VJCH* 57 (5): 636-640. DOI: 10.1002/vjch.201900112.
- Jahajeeah D, Bhoyroo V, Ranghoo-Sanmukhiya M. 2021. An assessment of soft coral community (Octocorallia; Alcyonacea) around Mauritius and Rodrigues Islands — New records of soft corals. *Reg Stud Mar Sci* 47: 101976. DOI: 10.1016/j.rsma.2021.101976.
- Jenecius A, Uthayakumari F, Mohan V. 2012. Gc-ms determination of bioactive components of *Sauropus Bacciformis* blume (Euphorbiaceae). *J Chem Pharm Sci* 2 (4): 347-358.
- Jiang Z, Jacob JA, Loganathachetti DS, Nainangu P, Chen B. 2017.  $\beta$ -Elemene: Mechanistic studies on cancer cell interaction and its chemosensitization effect. *Front Pharmacol* 9 (8): 105. DOI: 10.3389/fphar.2017.00105.
- Joshi A, Krishnan GS, Kaushik V. 2020. Molecular docking and simulation investigation: Effect of beta-sesquiphellandrene with ionic integration on SARS-CoV2 and SFTS viruses. *J Genet Eng Biotechnol* 18: 78. DOI: 10.1186/s43141-020-00095-x.
- Junwei L, Juntao C, Changyu N, Peng W. 2018. Molecules and functions of rosewood: *Pterocarpus cambodianus*. *Arab J Chem* 11 (6): 763-770. DOI: 10.1016/j.arabjc.2017.12.030.
- Kamatou GP, Viljoen A. 2009. A review of the application and pharmacological properties of  $\alpha$ -bisabolol and  $\alpha$ -bisabolol-rich oils. *J Am Oil Chem Soc* 87: 1-7. DOI: 10.1007/s11746-009-1483-3.
- Kavčič S, Knez Ž, Leitgeb M. 2013. Antimicrobial activity of n-butyl lactate obtained via enzymatic esterification of lactic acid with n-butanol in supercritical trifluoromethane. *J Supercrit Fluids* 85: 143-150. DOI: 10.1016/j.supflu.2013.11.003.
- Khalesi MK, Beefink RH, Wijffels RH. 2008. The soft corals *Sinularia flexibilis*: potential for the drug development. In: Leewis RJ, Janse M (eds). *Advances in coral Husbandry in Public Aquariums*. Arnhem, Netherlands.
- Kim DH, Park MH, Choi YJ. 2013. Molecular study of dietary heptadecane for the anti-inflammatory modulation of NF- $\kappa$ B in the aged kidney. *PLoS One* 8 (3): e59316. DOI: 10.1371/journal.pone.0059316.
- Kohlmeier M. 2013. Chapter 5 - How does nutrigenetics influence long-term health? In: Kohlmeier M (eds). *Nutrigenetics*. Academic Press, San Diego. DOI: 10.1016/B978-0-12-385900-6.00005-8.
- Kusmita L, Nuryadi H, Widyananto PA, Muchlissin S, Sabdono A, Trianto A, Radjasa OK. 2021. Bioactivity of carotenoid produced by soft coral symbiotic microorganisms from Panjang and Karimunjawa Island, Central Java, Indonesia. *Biodiversitas* 22: 732-740. DOI: 10.13057/biodiv/d220226.
- Lee GH, Hyun KY. 2018. 2-nonadecanone alleviates depression through inflammation relief in sd rat. *Biomed Sci Letters* 24: 206-212. DOI: 10.15616/BSL.2018.24.3.206.
- Legault J, Côté PA, Ouellet S, Simard S, Pichette A. 2013. Isocaryophyllene cytotoxicity induced by lipid peroxidation and membrane permeabilization in L-929 cells. *J App Pharm Sci* 3 (8): 25-31. DOI: 10.7324/JAPS.2013.3805.
- Li G, Li P, Tang X. 2019. Natural products from corals. In: Li Z (eds). *Symbiotic Microbiomes of Coral Reefs Sponges and Corals*. Springer, Dordrecht, The Netherlands. DOI: 10.1007/978-94-024-1612-1.
- Madigan MT, Martinko JM, Parker J, Brock TD. 2000. *Biology of Microorganisms*. Prentice-Hall, Inc, New Jersey, USA.
- Malarvili T, Velavan S, Parthasarathy R. 2015. GC-MS analysis of bioactive compounds in *Bryonopsis laciniosa* fruit extract. *Intl J Pharm Sci* 6 (8): 3375-3379. DOI: 10.13040/IJPSR.0975-8232.
- Mitić ZS, Jovanović B, Jovanović SC, Stojanović-Radić ZZ, Mihajilov-Krsteš T, Jovanović NM, Stojanović GS. 2019. Essential oils of *Pinus halepensis* and *P. heldreichii*: Chemical composition, antimicrobial and insect larvicidal activity. *Ind Crops Prod* 140 (1): 111702. DOI: 10.1016/j.indcrop.2019.111702.
- MNAP. 2017. Republic of Mauritius National Action Plan on Antimicrobial Resistance 2017-2021. Ministry of Health and Quality of Life, Mauritius.
- Mohammad G, Omran AM, Hussein H. 2016. Antibacterial and phytochemical analysis of *Piper nigrum* using gas chromatography – mass spectrum and fourier-transform infrared spectroscopy. *Intl J Pharmacogn Phytochem Res* 8 (6): 977-996.
- Mukda J, Mansuang W, Wandee G. 2013. Antidermatophytic properties of ar-turmerone, turmeric oil, and curcuma longa preparations. *Intl Sch Res Notices* 2013: 250597. DOI: 10.1155/2013/250597.
- Narayanasamy RR, Ramalakshmi S, Muthuchelian K. 2011. GC-MS analysis of bioactive components from the ethanolic leaf extract of *Canthium dicoccum* (Gaertn.) Teijsm & Binn. *J Chem Pharm Res* 3 (3): 792-798.
- Nurrachma MY, Sakaraga D, Nugraha AY. 2021. Cembranoids of soft corals: Recent updates and their biological activities. *Nat Prod Bioprospect* 11: 243-306. DOI: 10.1007/s13659-021-00303-2.
- Olaoye SB, Olukayode SA, Ayansola JA. 2017. Hexahydrofarnesyl acetone-rich extracts from *Hildebrandia barteri*. *J Herbs Spices Med Plants* 23 (4): 393-400. DOI: 10.1080/10496475.2017.1350614.
- Pavithra PS, Mehta A, Verma R. 2018. Aromadendrene oxide 2, induces apoptosis in skin epidermoid cancer cells through ROS mediated mitochondrial pathway. *Life Sci* 197: 19-29. DOI: 10.1016/j.lfs.2018.01.029.
- Pechère M, Pechère J, Siegenthaler G, Germanier L, Saurat JH. 1999. Antibacterial activity of retinaldehyde against propionibacterium acnes. *J Dermatol* 205 (2): 153-158. DOI: 10.1159/000051375.
- Peng Z, Wang Y, Fan J. 2017. Costunolide and dehydrocostuslactone combination treatment inhibit breast cancer by inducing cell cycle arrest and apoptosis through c-Myc/p53 and AKT/14-3-3 pathway. *Sci Rep* 7: 41254. DOI: 10.1038/srep41254.
- Rahman MM, Ahmad SH, Mohamed MT, Ab Rahman MZ. 2014. Antimicrobial compounds from leaf extracts of *Jatropha curcas*, *Psidium guajava*, and *Andrographis paniculata*. *Sci World J* 2014: 635240. DOI: 10.1155/2014/635240.
- Rodríguez-Chaves D, Bagnarello-Madriral V, Alpizar-Cordero J. 2018. Actividad in vitro anti-leishmania (Trypanosomatidae) del epóxido trans-Z- $\alpha$ -bisaboleno y del Saffrol, en frutos de *Piper auritum* (Piperaceae). *Rev Biol Trop* 66 (2): 826-835. DOI: 10.15517/rbt.v66i2.33412.
- Rosselli S, Maggio A, Formisano C, Napolitano F, Senatore F, Spadaro V, Bruno M. 2007. Chemical composition and antibacterial activity of extracts of *Helleborus bocconei* Ten. subsp. *intermedius*. *Nat Prod Commun* 2 (6): 675-679. DOI: 10.1177/1934578X0700200611.
- Rozirwan R, Bengen DG, Zamani NP, Effendi H, Chaidir C. 2014. Screening on the potential bioactive compounds of antibacterial activity in soft coral collected from South Bangka Island Waters and Lampung Bay. *JITKT* 6 (2): 83-295. DOI: 10.29244/jitkt.v6i2.9005.
- Russo EB, Marcu J. 2017. Cannabin Pharmacology: The usual suspects and a few promising leads. *Adv Pharmacol* 80: 67-134. DOI: 10.1016/bs.apha.2017.03.004.
- Saga Y, Hatakenaka Y, Matsumoto M, Yoshioka Y, Matsumura S, Zaima N, Konishi Y. 2020. Neuroprotective effects of aromatic turmerone

- on activity deprivation-induced apoptosis in cerebellar granule neurons. *NeuroRep* 1 (18): 1302-1307. DOI: 10.1097/WNR.0000000000001551.
- Sain S, Naoghare PK, Devi SS, Daiwile A, Krishnamurthi K, Arrigo P, Chakrabarti T. 2014. Beta caryophyllene and caryophyllene oxide, isolated from *Aegle marmelos*, as the potent anti-inflammatory agents against lymphoma and neuroblastoma cells. *Antiallergy Agents Med Chem* 13 (1): 45-55. DOI: 10.2174/18715230113129990016.
- Saleem M. 2009. Lupeol, a novel anti-inflammatory and anticancer dietary triterpene. *Cancer Lett* 285 (2): 109-115. DOI: 10.1016/j.canlet.2009.04.033.
- Salem MZM, Ali HM, Basalah MO. 2014. Essential oils from wood, bark, and needles of *Pinus roxburghii* Sarg. From Alexandria, Egypt: antibacterial and antioxidant activities. *BioResour* 9 (4): 7454-7466. DOI: 10.15376/biores.9.4.7454-7466.
- Sammarco PW, Coll JC. 1992. Chemical adaptations in the Octocorallia: Evolutionary considerations. *Mar Ecol Prog Ser* 88: 93-104. DOI: 10.3354/meps088093.
- Saravanan R, Raja K, Shanthi D. 2021. GC-MS analysis, molecular docking and pharmacokinetic properties of phytocompounds from *Solanum torvum* unripe fruits and its effect on breast cancer target protein. *Appl Biochem Biotechnol* 194 (1): 529-555. DOI: 10.1007/s12010-021-03698-3.
- Shaaban M, Shaaban K, Ghani M. 2013. Hurgadacin: A new steroid from *Sinularia polydactyla*. *Steroids* 78 (9): 866-873. DOI: 10.1016/j.steroids.2013.05.006.
- Shareef H, Haidar J, Hussein H, Hameed I. 2016. Antibacterial effect of ginger (*Zingiber officinale*) roscoe and bioactive chemical analysis using gas chromatography mass spectrum. *Orient J Chem* 32 (2): 817-837. DOI: 10.13005/ojc/320207.
- Soares GM, Figueiredo LC, Faveri M, Cortelli SC, Duarte PM, Feres M. 2012. Mechanisms of action of systemic antibiotics used in periodontal treatment and mechanisms of bacterial resistance to these drugs. *J Appl Oral Sci* 20 (3): 295-309. DOI: 10.1590/s1678-77572012000300002.
- Tammam MA, Rárová L, Kvasnicová M. 2020. Bioactive steroids from the red sea soft coral *Sinularia polydactyla*. *Mar Drugs* 18 (12): 632. DOI: 10.3390/md18120632.
- Tan N, Satana D, Sem B, Tan E, Altan HB, Demirci B. 2016. Antimycobacterial and antifungal activities of selected four *Salvia* species. *Rec Nat Prod* 10 (5): 593-603.
- Tanod W, Aristawati A, Putra M, Muliadin M. 2018. Soft coral (*Sinularia* sp.) extracts with antibacterial activity. *Omni-Akuatika* 14 (1): 108-117. DOI: 10.20884/1.oa.2018.14.1.375.
- Tanod W, Dewanto D, Ndobe S, Riyadi P, Putra M. 2019. Screening of antibacterial and Antioxidant activity of soft corals *Sinularia* sp. and *Sarcophyton* sp. from Palu Bay Central Sulawesi, Indonesia. *Squalen Bull Mar Fish Postharvest Biotech* 14 (2): 73-83. DOI: 10.15578/squalen.v14i2.394.
- Thao NP, Thanh NV, Nam NH, Cuong NX, Kim YH, Kiem PV, Minh CV. 2015. Steroid constituents from *Lobophytum crassum*. *VJOC* 53 (2e): 1-4. DOI: 10.15625/0866-7144.2015-2e-001.
- Trevizan L, Nascimento K, Santos JA. 2016. Anti-inflammatory, Antioxidant and anti-Mycobacterium tuberculosis activity of viridiflorol: The major constituent of *Allophylus edulis* (A. St-Hil., A. Juss. & Cambess.) Radlk. *J Ethnopharmacol* 192: 510-515. DOI: 10.1016/j.jep.2016.08.053.
- Tsai YC, Hsu HC, Yang WC, Tsai WJ, Chen CC, Watanabe T. 2007. Alpha-bulnesene, a PAF inhibitor isolated from the essential oil of *Pogostemon cablin*. *Fitoterapia* 78 (1): 7-11. DOI: 10.1016/j.fitote.2006.09.016.
- Venkata Raman B, La S, Pardha Saradhi M, Narashimha Rao B, Naga Vamsi Krishna A, Sudhakar M, Radhakrishna TM. 2012. Antibacterial, Antioxidant activity and GC-MS analysis of *Eupatorium odoratum*. *Asian J Pharm Clin Res* 5 (2): 99-106.
- Willie P, Uyoh EA, Aikpokpodion PO. 2021. Gas Chromatography-Mass Spectrometry (GC-MS) assay of bio-active compounds and phytochemical analyses in three species of Apocynaceae. *Pharmacog J* 13 (2): 383-392. DOI: 10.5530/pj.2021.13.49.
- Xia B, Tong Y, Xia C, Chen C, Shan X. 2020.  $\alpha$ -Cyperone confers antidepressant-like effects in mice via neuroplasticity enhancement by sirt3/ros mediated nlrp3 inflammasome deactivation. *Front Pharmacol* 11: 577062. DOI: 10.3389/fphar.2020.577062.
- Xie Q, Li F, Fang L, Liu W, Gu C. 2020. The antitumor efficacy of  $\beta$ -elemene by changing tumor inflammatory environment and tumor microenvironment. *Biomed Res Intl* 2020: 6892961. DOI: 10.1155/2020/6892961.
- Yan X, Liu J, Leng X, Ouyang H. 2021. Chemical diversity and biological activity of secondary metabolites from soft coral genus *Sinularia* since 2013. *Mar Drugs* 19 (6): 335. DOI: 10.3390/md19060335.
- Yeo SK, Ali AY, Hayward OA, Turnham D, Jackson T, Bowen I D, Clarkson R. 2016.  $\beta$ -Bisabolene, a sesquiterpene from the essential oil extract of *oponox* (*Commiphora guidottii*), exhibits cytotoxicity in breast cancer cell lines. *Phytotherapy* 30 (3): 418-425. DOI: 10.1002/ptr.5543.
- Yu Z, Wang R, Xu L, Xie S, Dong J, Jing Y. 2011.  $\beta$ -elemene piperazine derivatives induce apoptosis in human leukemia cells through downregulation of c-FLIP and generation of ROS. *PLoS One* 6 (1): e15843. DOI: 10.1371/journal.pone.0015843.
- Yuan L, Zhang F, Shen M, Jia S, Xie J. 2019. Phytosterols suppress phagocytosis and inhibit inflammatory mediators via ERK pathway on LPS-triggered inflammatory responses in RAW264.7 macrophages and the correlation with their structure. *Foods* 8 (11): 582. DOI: 10.3390/foods8110582.
- Zhu TZ, Li XM, Luo LH, Xu YH, Cao P, Liu Y. 2014. beta-Elemene inhibits proliferation through crosstalk between glia maturation factor beta and extracellular signal regulated kinase 1/2 and impairs drug resistance to temozolomide in glioblastoma cells. *Mol Med Rep* 10 (2): 1122-1128. DOI: 10.3892/mmr.2014.2273.
- Ziaei A, Ramezani M, Wright L, Paetz C, Schneider B, Amirghofran Z. 2011. Identification of spathulenol in *Salvia mirzayanii* and the immunomodulatory effects. *Phytother Res* 25 (4): 557-62. DOI: 10.1002/ptr.3289.
- Zu S, Deng YQ, Zhou C. 2020. 25-Hydroxycholesterol is a potent SARS-CoV-2 inhibitor. *Cell Res* 30 (11): 1043-1045. DOI: 10.1038/s41422-020-00398-1.