



Volatile bioactive compounds from marine macro-algae and their pharmacological properties

R Vijayaraj, K Altaff*, N Sri Kumaran & Swarnakala

Department of Marine Biotechnology, AMET University, Chennai, Tamil Nadu – 603 112, India

*[E-mail: kaltaff@gmail.com]

Received 07 September 2020; revised 04 September 2022

The present study is aimed at identification of bioactive compounds and their pharmacological properties of four macro-algae (*Hydropuntia edulis*, *Halymenia venusta*, *Ulva lactuca* and *Padina gymnospora*) from the Hare Island, Tuticorin district of Tamil Nadu, India. The characterization of ethanol extracted compounds was done using GC-MS techniques. The major secondary metabolites such as alkaloids, phenol, saponins, flavonoids, steroids, terpenoids and tannins were recorded from all the algal samples. The numbers of major volatile compounds recorded in the GC-MS analysis are 32, 19, 8 and 14 in *H. edulis*, *H. venusta*, *U. lactuca* and *P. gymnospora*, respectively. All these identified compounds could be of therapeutic values for many acute and chronic diseases and disorders. These secondary metabolites belong to alkanes, aliphatic amines, aromatics, aldehydes, 1°, 2° amines and ketone groups. Many of these characterized compounds could be used for therapeutic purposes.

[**Keywords:** Bioactive compounds, Marine macro-algae, Pharmacological properties, Secondary metabolites, Therapeutic values]

Introduction

The marine organisms especially the marine macro algae are rich in structurally new bioactive compounds with great biomedical and pharmacological applications. Recently, the bioactive compounds from marine macro algae are found to be responsible for the treatment of several acute and chronic diseases and disorders such as antimicrobial, anti-inflammatory, anticancer, antifungal, anti-diabetic, etc.¹. Since several decades, people from Asian and European countries utilize bioactive compounds and biopolymers from macro-algae as a source of food and pharmaceuticals. The primary and secondary metabolites produced by marine macro-algae are potential bioactive compounds which generated interest in the pharmaceutical industry to develop novel drug against diseases requiring short term and long term treatment. Marine macro algae are pools of bioactive compounds such as polysaccharids, carotenoids, pigments, enzymes and polyphenols as well as vital water soluble and fat soluble vitamins².

Currently, marine macro-algae are used worldwide for many different purposes such as human consumption, improving nutrients in animal feeds, cosmetics, medicine, fertilizer, etc. and they have shown non-toxic nature which apart from regulation of metabolism in human beings and animals also

protect from various diseases³. The macro-algae develop many innovatory physiological and biochemical system in marine environment resulting in the production of several biologically active metabolites which are characterized by several biological activities such as anti-diabetic⁴, antiviral⁵, antifungal⁶, anticoagulant⁷, antitumor⁸ and anti-inflammatory activities⁹. The biopolymers (alginate, carrageenan and agar) from marine macro-algae have been used in medicine and food¹. Based on above rationale, the bioactive compounds from marine macro-algae are considered as a potent therapeutic agent. Hence, the present study is focused at extraction and characterization of bioactive compounds from marine macro algae (*H. edulis*, *H. venusta*, *U. lactuca* and *P. gymnospora*).

Materials and Methods

Macro-algae sampling and identification

Bulk samples (7±1 kg) of marine macroalgae were sampled from intertidal waters of coastal region of Tuticorin, Tamil Nadu coast (Lat. 8°48'36" N; Long. 78°8'24" E), by hand picking in shallow water and also from a depth ranging between 1 and 3 m. Altogether, four different seaweed samples (*Hydropuntia edulis* (S. G. Gmelin) Gurgel & Fredericq, 2004; *Halymenia venusta* Børgesen, 1932;

Ulva lactuca Linnaeus, 1753 and *Padina gymnospora* (Kützinger) Sonder, 1871) were collected from different locations and morphological characterization and identification was carried out by following the descriptions from standard literature¹⁰.

Extraction of crude bioactive compound

The different powder samples were soaked in ethanol solvent and resulted extract was concentrated at room temperature and stored for further studies.

Investigation of primary phytoconstituents

The crude extract of marine macroalgae were subjected to qualitative phytochemical analysis using stranded procedure to detect major phytoconstituents such as alkaloids, phenol, saponins, flavonoids, steroids, phytosterol, glycosidase, carbohydrates, protein and lipid¹¹.

Identification of bioactive compounds

Separation and characterization of bioactive compounds

The identification of bioactive compounds from different crude extract of marine macroalgae was performed using GC (GC-7890A/MS-5975C) from Agilent Technologies, USA with column size 30 m in length \times 250 μ m in diameter \times 0.25 μ m in thickness of film. For mass spectroscopic detection, high energy of 70 eV was used for electron ionization. The 99.95 % of pure helium gas with initial temperature (50 to 150 °C) and final temperature (300 °C) with increasing rate 3 °C per min to 10 °C per min are used, respectively. 1 μ L of crude extract dilute with respective solvent (ethanol) was injected in splitless mode. The relative quantities of the bioactive compounds present in each crude extracts were expressed as percentage peak in GC chromatogram. The identification of bioactive components was based on National Institute of Standards and Technology (NIST) libraries using Retention Time (RT). The constituents were identified after comparison with those available in the computer library (NIST and Willey) attached to the GC-MS instrument and the results obtained have been tabulated.

Results

Phytochemical compounds

The results of the phytochemical analysis show the occurrence of compounds like alkaloids, phenol, saponins, flavonoids, steroids, terpenoids and tannins in the crude extracts of the algal species (Table 1). Number of compounds recorded in the four macro-

Table 1 — Phytochemical compounds from crude extract of marine macro-algae

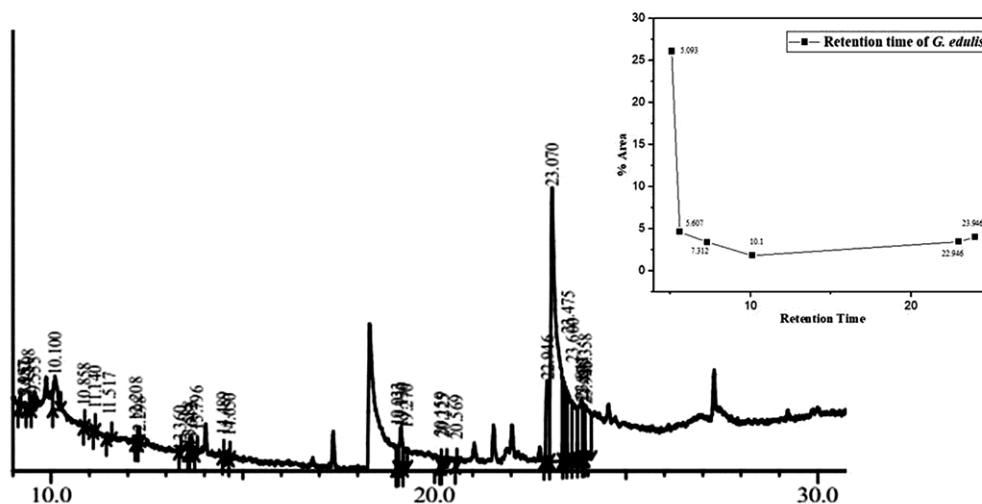
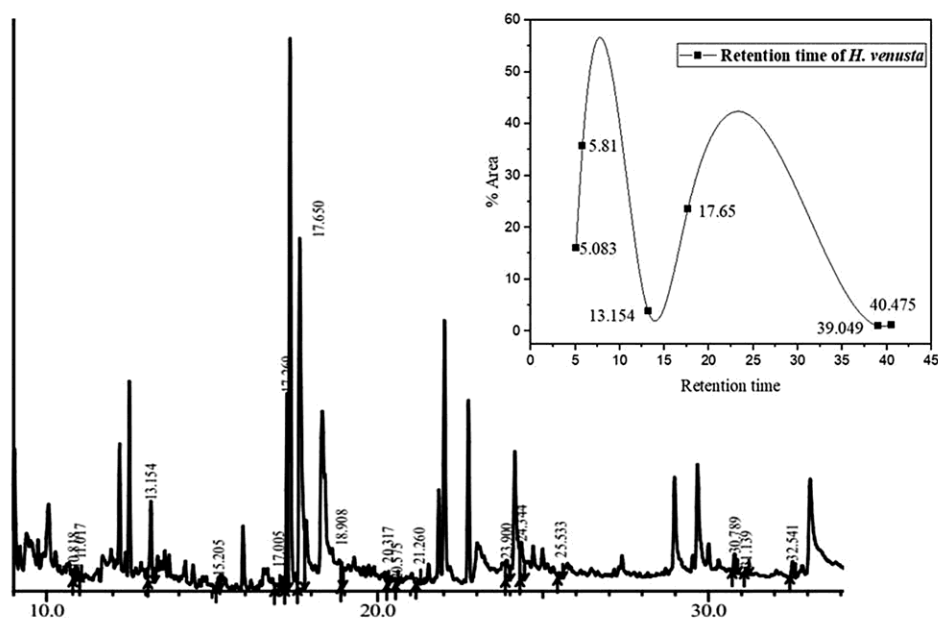
Phytochemicals	<i>H. edulis</i>	<i>H. venusta</i>	<i>U. lactuca</i>	<i>P. gymnospora</i>
Alkaloids	+	+	-	-
Phenol	+	+	+	+
Saponins	+	-	-	+
Flavonoids	+	+	+	+
Steroids	+	+	+	+
Phytosterol	-	+	+	+
Glycosidase	+	+	+	-
Carbohydrates	+	+	+	-
Protein	+	+	+	+
Lipid	+	+	+	-

(+ Presence; - Absence)

algal species ranged between five and nine. Maximum of nine compounds were extracted from *H. edulis* and *H. venusta* while eight and six compounds were resulted from *U. lactuca* and *P. gymnospora*, respectively. Phenol, flavonoids and steroids occurred in the extracts of all the four species of macroalgae. Number of other phytochemicals showed variations pertaining to their occurrence in the four species of macro-algae.

GC-MS analysis

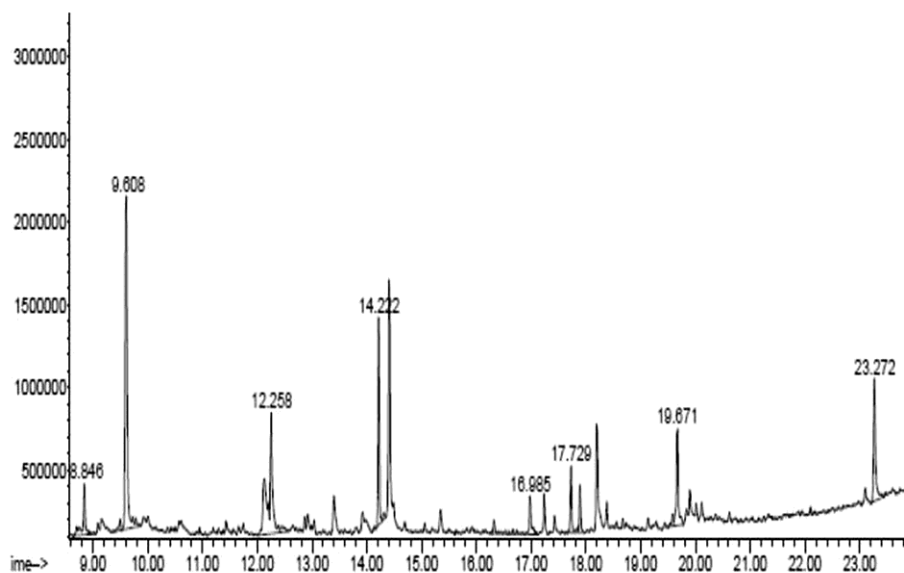
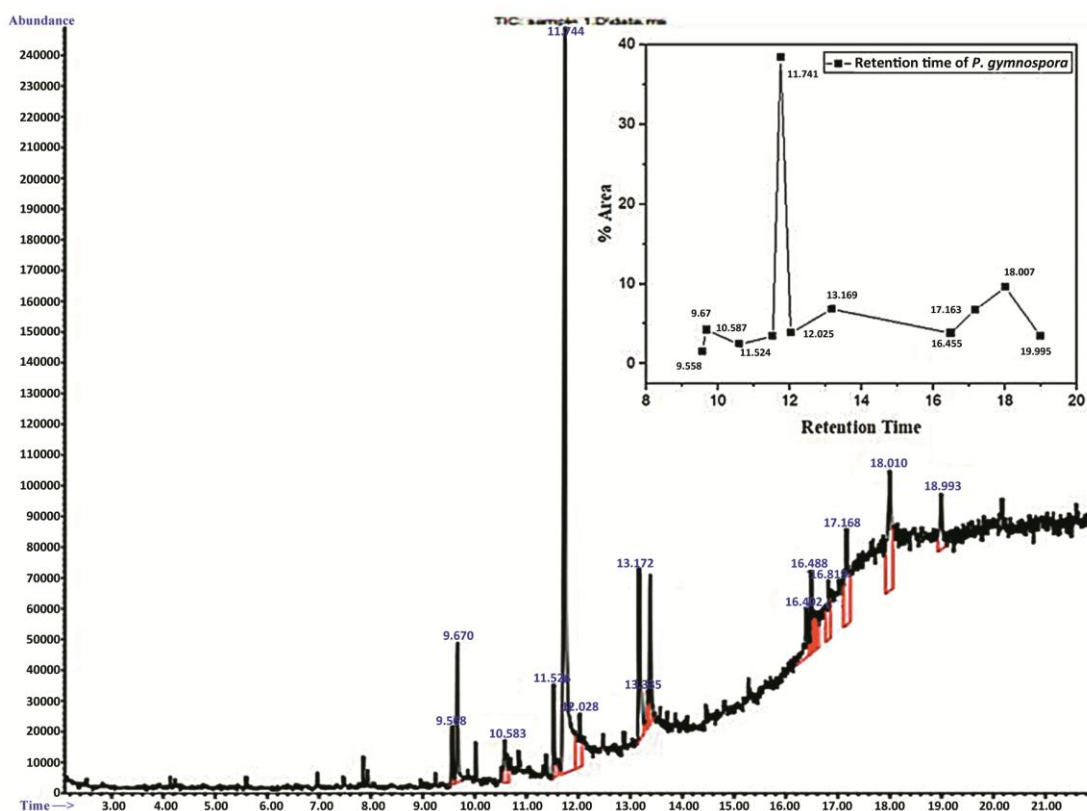
GC-MS analysis results of four marine macro-algal species recorded totally 72 volatile compounds. The number of compounds recorded in *G. edulis*, *H. venusta*, *U. lactuca* and *P. gymnospora* are 32, 19, 8 and 14, respectively (Figs. 1 – 4 & Tables 2 – 5). Of these compounds, L-alanine is the only compound occurred from the extracts of *H. edulis* and *H. venusta*. The molecular weight of compounds from *H. edulis* ranged between 32.046 g/mol (Hydrazine-H₂N-NH₂) and 604.466 (3-d-ribofuranosyl-C₂₁H₂₉N₆O₁₃P) g/Mol. Most of the bioactive compounds of *H. edulis* are antioxidant, antiviral, anti-inflammatory, antibacterial, antifungal, antiprotozoal, antidepressants, antineoplastic, antiherpes, antidiabetic, anticoagulant and anticancer. Some of the compounds of this species also exhibit cytotoxic activity, cardioprotective, hepatoprotective and neuroprotective properties. The molecular weight of compounds from *H. venusta* ranged between 59.068 g/mol (Acetamide-C₂H₅NO) and 346.47 (Diisopropylidene-C₂₄H₂₆O₂) g/mol. The bioactive compounds of this species mostly act as antiarrhythmic, inhibitor of Bloom's syndrome, hypocholesterolemic, anticancer, HCV antidiabetic and immunomodulatory agents. The molecular weight of compounds from *U. lactuca* ranged between

Fig. 1 — GC Chromatogram of bioactive compounds of *H. edulis*Fig. 2 — GC chromatogram of bioactive compounds of *H. venusta*

74.079 g/mol (Propanoic acid - $C_3H_6O_2$) and 390.564 g/mol (Isooctyl Phthalate- $C_{24}H_{38}O_4$). The bioactive compounds of this species apart from common activities like anti-inflammatory, antimicrobial and cytotoxic activity, they are antirheumatic, anti-androgenic and antitubercular agents. Similarly, the molecular weight of compounds from *P. gymnospora* ranged between 110.2 g/mol (3-Octyne - C_8H_{14}) and 607.3 g/mol (Octasiloxane- $C_{18}H_{54}O_7Si_8$). In addition to anti-inflammatory and antimicrobial activity, the bioactive compounds of this species perform antiobesity, antihyperlipidemic and hepatoprotective activities.

Discussion

The phytochemicals occur naturally in the seaweeds. These phytochemicals are biologically significant and play an essential role in defending seaweeds against various pathogenic microbial invasion and acute and chronic disorders. There is evidence of phytochemicals from marine macroalgae possessing anticancer activity due to producing high amount of dietary fiber and polyphenol compound, which act against free radical scavenging activity and anti-inflammatory effects¹⁻². The research approach on phytochemicals is considered effective in discovering bioactive profile of the marine algae of

Fig. 3 — GC Chromatogram of bioactive compounds of *U. lactuca*Fig. 4 — GC Chromatogram of bioactive compounds of *P. gymnospora*

therapeutic importance. Screening and evaluation of bioactive compounds revealed occurrence of a wide range of secondary metabolites (alkaloids, phenol, saponins, flavonoids, steroids, terpenoids, tannins,

carbohydrates, protein and lipid) which could be nutraceutical as well as of pharmaceutical importance. Preliminary phytochemical screening is a part of chemical evaluation. In the present study, presence

Table 2 — GC MS analysis of bioactive compounds from *H. edulis*

Peak No.	Retention time	Name	Molecular formula	Molecular weight (g/mol)
1.	5.093	N-(cyclohexylcarbonyl)-	C ₁₄ H ₁₇ NO ₂	231.295
2.	5.607	Glycine	C ₁₀ H ₁₅ NO ₄	213.2304
3.	5.658	Nitro-L-arginine	C ₆ H ₁₃ N ₅ O ₄	219.2
4.	6.493	dl-Phenylephrine	C ₉ H ₁₃ NO ₂	167.208
5.	7.312	Actinobolin	C ₁₃ H ₂₀ N ₂ O ₆	300.311
6.	7.515	Hydrazine	H ₂ N-NH ₂	32.046
7.	7.599	3-d-ribofuranosyl	C ₂₁ H ₂₉ N ₆ O ₁₃ P	604.466
8.	8.339	Pyrido[3,4-d]imidazole	C ₈ H ₆ N ₃ O ₄	211.177
9.	8.633	Cyanoacetylurea	C ₄ H ₅ N ₃ O ₂	127.103
10.	8.957	17-Octadecen-14-ynoic acid	C ₁₉ H ₃₂ O ₂	292.463
11.	9.398	2-Hydrazinopyridine	C ₅ H ₇ N ₃	109.132
12.	9.555	Norephedrine	C ₉ H ₁₃ NO	151.209
13.	10.1	2(1H)-Pyridone	C ₅ H ₅ NO	95.101
14.	10.858	3-Hydroxypiperidine	C ₅ H ₁₁ NO	101.149
15.	11.14	2-Pyrroline, 1,2-dimethyl-	C ₆ H ₁₁ N	97.161
16.	11.517	1-Methyldecylamine	C ₁₃ H ₂₈ N ₂ O	228.38
17.	12.208	Akuammilan-17-ol	C ₂₀ H ₂₄ N ₂ O ₂	324.424
18.	12.298	l-Guanidinosuccinimide	C ₅ H ₇ N ₃ O ₂	141.13
19.	13.36	(2-Aziridinylethyl)amine	C ₄ H ₁₀ N ₂	86.138
20.	13.588	Actinobolin	C ₁₃ H ₂₀ NO ₆	300.311
21.	13.642	Piperidine, 3-methyl-	C ₁₃ H ₁₉ N	189.302
22.	13.796	dl-Alanyl-dl-leucine	C ₉ H ₁₈ N ₂ O ₃	202.254
23.	14.65	N-dl-Alanylglycine	C ₅ H ₁₀ N ₂ O ₃	146.146
24.	19.13	Thiophene-3-ol	C ₄ H ₄ OS	100.135
25.	19.27	Glutaraldehyde	C ₅ H ₈ O ₂	100.117
26.	20.159	dl-Alanyl-l-alanine	C ₆ H ₁₂ N ₂ O ₃	160.173
27.	20.225	L-alanine	C ₃ H ₇ NO ₂	89.094
28.	20.569	N-Methylglucamine	C ₇ H ₁₇ NO ₅	195.215
29.	22.946	1-Propanone	C ₆ H ₇ NO ₂	125.127
30.	23.475	2-Piperidinone	C ₅ H ₉ NO	99.133
31.	23.6	Benzenemethanol	C ₇ H ₈ O	108.14
32.	23.946	5-Aminoisoxazole	C ₃ H ₄ N ₂ O	84.078

Table 3 — GC Chromatogram of bioactive compound of *H. venusta*

Peak No	Retention time	Name	Molecular formula	Molecular weight (g/mol)
1.	5.083	Adenosine	C ₁₀ H ₁₃ N ₅ O ₄	267.245
2.	5.81	Acetamide	C ₂ H ₅ NO	59.068
3.	10.818	Phenyl 3-pyridyl ketone	C ₁₂ H ₉ NO	183.21
4.	13.154	Eicosane	C ₂₀ H ₄₂	282.556
5.	17.65	2-Mercaptobenzothiazole	C ₇ H ₅ NS ₂	167.244
6.	18.908	m-Tolyl isothiocyanate	C ₈ H ₇ NS	149.211
7.	20.317	5-Nitro-3-cyano-2	C ₆ H ₃ N ₃ O ₃	165.108
8.	20.575	L-Leucine	C ₆ H ₁₃ NO ₂	131.175
9.	21.26	4-Piperidinecarboxamide	C ₆ H ₁₂ N ₂ O	128.175
10.	23.9	5,5-Dibutylnonane	C ₁₇ H ₃₆	240.475
11.	24.344	n-Butyl myristate	C ₁₈ H ₃₆ O ₂	284.484
12.	25.533	Pyrrolidine	C ₄ H ₉ N	71.123
13.	31.139	Fumaric acid	C ₄ H ₄ O ₄	116.072
14.	32.541	Trifluoroacetate	C ₂ F ₃ O ₂	113.015
15.	36.742	L-Alanine	C ₃ H ₇ NO ₂	89.094
16.	37.282	N-cyclobutylcarbonyl	C ₇ H ₁₁ NO ₃	157.169
17.	38.384	Benzenesulfonate	C ₁₂ H ₁₆ O ₈ S	320.312
18.	39.049	Diisopropylidene	C ₂₄ H ₂₆ O ₂	346.47
19.	40.475	Bupropion	C ₁₃ H ₁₈ ClNO	239.743

Table 4 — GC- MS analysis of bioactive compound of *U. lactuca*

Peak No	Retention time	Name	Molecular formula	Molecular weight (g/mol)
1.	8.846	Methyl salicylate	C ₈ H ₈ O ₃	152.149
2.	9.608	Propanoic acid	C ₃ H ₆ O ₂	74.079
3.	12.258	2, 1, 3-Benzothiadiazole	C ₆ H ₄ N ₂ S	136.172
4.	14.222	Diethyl Phthalate	C ₁₂ H ₁₄ O ₄	222.24
5.	16.985	Ethylene Bromohydrin	C ₂ H ₅ BrO	124.965
6.	17.729	Dibutyl phthalate	C ₁₆ H ₂₂ O ₄	278.348
7.	19.671	Phytol	C ₂₀ H ₄₀ O	296.539
8.	23.272	Isooctyl Phthalate	C ₂₄ H ₃₈ O ₄	390.564

Table 5 — GC-MS analysis of bioactive compounds of *P. gymnospora*

Peak Number	Retention time	Compound name	Molecular formula	Molecular weight (g/mol)
1.	9.568	1,2,4-Triazolo[4,3-b]pyridazin-8-ol	C ₆ H ₇ N ₅ O	165.15
2.	9.670	Tetradecanoic acid	C ₂₈ H ₅₆ O ₄	456.7
3.	10.583	3-Octyne	C ₈ H ₁₄	110.2
4.	11.524	9-octadecenoic acid	C ₁₈ H ₃₄ O ₂	282.5
5.	11.744	<i>n</i> -Hexadecanoic acid	C ₁₆ H ₃₂ O ₂	256.43
6.	12.028	Octadecyl ester	C ₃₂ H ₆₄ O ₂	480.8
7.	13.172	Citronellyl isobutyrate	C ₁₄ H ₂₆ O ₂	226.35
8.	13.335	9,12-Octadecadien-1-ol	C ₁₈ H ₃₄ O	266.5
9.	16.402	Octasiloxane	C ₁₈ H ₅₄ O ₇ Si ₈	607.3
10.	16.488	Methyltris(trimethylsiloxy)silane	C ₁₀ H ₃₀ O ₃ Si ₄	310.68
11.	16.819	4-(1,1-Dimethylpropyl)phenol	C ₁₁ H ₁₆ O	164.24
12.	17.168	2-Ethylacridine	C ₁₅ H ₁₃ N	207.27
13.	18.010	Cyclotrisiloxane	H ₆ O ₃ Si ₃	138.3
14.	18.993	1H-Indole	C ₈ H ₇ N	117.15

of phytoconstituents such as alkaloids, phenol, saponins, flavonoids, steroids, terpenoids, tannins, carbohydrates, protein and lipid were recorded.

Normally, the phenolic compounds are involved in several biological activities especially for antioxidant properties due to their interaction with phenolic hydroxyl group in π -electrons benzene ring which is also responsible for the antimicrobial, anti-inflammatory, anti-feedant, anti-viral, anticancer and vasodilatory actions¹². Alkaloids exhibit cytotoxic activity against cancer cell line due to the presence of microtubule interfering agent which bind to the β -tubulin, thus inhibiting the formation of the mitotic spindle fiber required for cell division¹³. Saponins are considered as a major phytoconstituents used for several biological properties especially for reduced acute and chronic inflammation and it is also used to develop several commercialized product and as a dietary supplement in various industries¹⁴. Steroids of macro-algae are considered as insecticidal, antiparasitic and cardiotoxic drug as it plays an important role for nutrition, medicine and cosmetics in human and animals¹⁵. Tannins are used as a therapeutic product *i.e.* antiviral, antibacterial, antiulcer and antioxidant agents. In recent years it has

been used also to treat piles, inflammation, burns and as astringent¹⁴.

The occurrence varied types of such phytochemical compounds in all the four macro-algal species obviously indicate their utility value in multiple pharmacological applications. In GC-MS analysis, numbers of volatile compounds are recorded from *H. edulis*, *H. venusta*, *U. lactuca* and *P. gymnospora*. All these identified compounds could be of therapeutic values for several acute and chronic diseases and disorders. The pharmaceutical applications of these compounds are wide and have been summarized in Tables 6 – 9. Occurrence of these compounds in marine macroalgae could be addition of new sources to the pharmaceutical industry. Majority of these compounds possess high bioactive potentials to prevent pathogenicity as well as regulation of many physiological processes⁸¹. There is expanding perception towards bioactive compounds related to their different biological activities. Though all the four species of macro-algae inhabited in the same habitat, GC-MS screening of their extracts showed considerable variations with regard to number of phytochemical compounds they possess. Similar to present study, Cyril *et al.*⁸² reported rich content of

Table 6 — Pharmacological properties of bioactive compounds from *H. edulis*

Peak No.	Name	Pharmacological properties	Reference
1.	N-(cyclohexylcarbonyl)	Cytotoxic Activity	16
2.	Glycine	Neuroprotective Effects	17
3.	Nitro-L-arginine	Antioxidant and Cytotoxic Properties	18
4.	dl-Phenylephrine	Septic shock	19
5.	Actinobolin	Antiviral and Antimicrobial activity	20
6.	Hydrazine	Antidepressants and Antineoplastic Agents	21
7.	[3-d-ribofuranosyl]	Antiviral & Antimicrobial activity	22
8.	1,6-dicarboxylic acid	Antidiabetic Compounds	23
9.	Cyanoacetyurea	Antiviral and Anticancer activity	24
10.	17-Octadecen-14-ynoic	Antibacterial activity	25
11.	2-Hydrazinopyridine	Antimicrobial and Anticancer activity	26
12.	Norephedrine	Antiinflammatory and Anticancer properties	27
13.	2(1H)-Pyridone	Antifungal, Antimicrobial and Antioxidant activity	28
14.	3-Hydroxypiperidine	Antimicrobial, Anticancer activity	29
15.	2-Pyrroline, 1,2-dimethyl-	Antitumour properties	30
16.	1-Methyldecylamine	Antimicrobial, Anticancer activity	31
17.	Akuammilan-17-ol	Cytotoxic Properties	32
18.	1-Guanidinosuccinimide	Antiinflammatory and Anticancer activity	33
19.	(2-Aziridinylethyl)amine	Antiviral Properties	34
20.	Actinobolin	Antiherpes activity	35
21.	Piperidine, 3-methyl-	Anticoagulant activity	36
22.	dl-leucine	Anticancer Activity	37
23.	N-dl-Alanylglycine	Anticancer activity	38
24.	Thiophene-3-ol	Anticancer, Antioxidant	39
25.	Glutaraldehyde	Food Ulcer, Antimicrobial	40
26.	dl-Alanyl-l-alanine	Antibacterial and Cytotoxic Properties	41
27.	l-alanine	Antidiabetic, cardioprotective activity	42
28.	N-Methylglucamine	Antidiabetic activity, Inhibition of Alpha Amylase	43
29.	1-Propanone	AntiDiabetic Activity	44
30.	2-Piperidinone	Hepatoprotective, Anticancer Activity	45
31.	Benzenemethanol	Antibacterial and Cytotoxic Properties	46
32.	5-Aminoisoxazole	Antiprotozoal and cytotoxic agents	47

Table 7 — Pharmacological properties of bioactive compounds from *H. venusta*

Peak No	Name	Pharmacological properties	Reference
1.	Adenosine	Antiarrhythmic Activity,	48
2.	Acetamide	Inhibition of Bloom's syndrome	49
3.	Phenyl 3-pyridyl ketone	Hypocholesteremic activity	50
4.	Eicosane	Anticancer Properties	51
5.	2-Mercaptobenzothiazole	Antiinflammatory	52
6.	m-Tolyl isothiocyanate	Antiinflammatory	53
7.	5-Nitro-3-cyano-2	Unidentified	-
8.	L-Leucine	Unidentified	-
9.	4-Piperidinecarboxamide	Unidentified	-
10.	5,5-Dibutylnonane	Unidentified	-
11.	n-Butyl myristate	Antifungal Activity	54
12.	Pyrrolidine	HCV and Antiviral activity	55
13.	Fumaric acid	Immunomodulatory effect	56
14.	Trifluoroacetate	Antioxidant Activity	57
15.	L-Alanine	Antidiabetic, cardioprotective activity	58
16.	N-cyclobutylcarbonyl	Unidentified	-
17.	Benzenesulfonate	Unidentified	-
18.	Diisopropylidene	Unidentified	-
19.	Bupropion	Antidepressant and Antioxidant	59

Table 8 — Pharmacological properties of bioactive compounds from *U. lactuca*

Peak No	Name	Pharmacological properties	Reference
1.	Methyl salicylate	Antirheumatic Agents, Antiinflammatory activity	60
2.	Propanoic acid	Antiinflammatory and Anticancer	61
3.	2, 1, 3-Benzothiadiazole	Antiinflammatory	62
4.	Diethyl Phthalate	Antimicrobial, Antiinflammatory and Anticancer activity	63
5.	Ethylene Bromohydrin	Antifungal and Antiinflammatory and Cytotoxic Activity	64
6.	Dibutyl phthalate	Anti-androgenic, Anticancer activity	65
7.	Phytol	Antitubercular, Antimycobacterial and Antiviral Activity	66
8.	Isooctyl Phthalate	Antimicrobial and Cytotoxic Activity	67

Table 9 — Pharmacological Properties of *P. gymnospora*

Peak No	Compound name	Biological properties	References
1.	1,2,4-Triazolo[4,3-b]pyridazin-8-ol	-Unidentified- Anticancer	68
2.	Tetradecanoic acid	Anti obesity	69
3.	3-Octyne	Antioxidant activity Antimicrobial activity	70 71
4.	9-octadecenoic acid	Antihyperlipidemic and hepatoprotective activity Anticancer activity	72 73
5.	<i>n</i> -Hexadecanoic acid	Anti-inflammatory Antioxidant activity	74
6.	Octadecyl ester	Antioxidant and Anti malaria	75
7.	Citronellyl isobutyrate	Antimicrobial activity	76
8.	9,12-Octadecadien-1-ol	Antioxidant activity	77
9.	Octasiloxane	-Unidentified-	
10.	Methyltris(trimethylsiloxy)silane	-Unidentified-	
11.	4-(1,1-Dimethylpropyl)phenol	-Unidentified-	
12.	2-Ethylacridine	Hepatoprotective activity and Anticancer Activity	78
13.	Cyclotrisiloxane	Anticancer activity	79
14.	¹ H-Indole	Antimicrobial activity	80

secondary metabolites and variation pertaining to their number in two other marine macroalgae, namely, *Sargassum wightii* and *Gracilaria verrucosa*. Bioactive compounds from the seaweed *Caulerpara cernosa* is believed to possess high medicinal property especially in treating diabetes and rheumatoid arthritis⁸³. Applications of bioactive compounds from seaweeds in controlling pathogenicity of aquaculture organisms will lead to eco-friendly economic activity⁸³⁻⁸⁴. Recent report on pro-mineralogenic compounds from two green macroalgae *Codium fragile* and *Cladophora rupestris* exhibited mineralogenic and osteogenic activities. The quantitative analysis of operculum formation in zebrafish larvae further established mineralogenic activity of bioactive compounds from seaweeds⁸⁵. Due to the rich content of vital bioactive compounds there should be more investigations on utilization of bioactive compounds of seaweeds in human health and other related applications.

Conclusion

Present study enumerates new secondary metabolites from marine macroalgae using phytochemical and GC-MS analysis. These secondary metabolites from natural sources could be effective compounds in the pharmaceutical applications. The compounds such as 1,6-dicarboxylic acid, adenosine, propanoic acid, and tetradecanoic acid could be alternative to synthetic compounds used for metabolic disorders. Further usage of these compounds in therapeutics will have minimum side effects.

Acknowledgments

The authors express their gratitude to the Management of AMET University for providing research facilities to carry out this work. R.V. acknowledges with Gratitude University Research Fellowship and Financial Assistance granted by the AMET University to carry out this research work. The authors are thankful to the Dr. M. Jayaprakashvel,

Professor - Marine Biotechnology, AMET and Dr. R. Mutheshilan, Professor - Marine Biotechnology, AMET for their support and valuable suggestions to successfully complete this work.

Conflict of Interest

The authors have no conflict of interest.

Ethical Statement

Not applicable for this study.

Author Contributions

All the authors contributed equally to this research work.

Reference

- Mohapatra L, Pati P, Panigrahy R & Bhattamisra S K, Therapeutic health booster: seaweeds against several maladies, *Indian J Geo-Mar Sci*, 42 (5) (2013) 538-546.
- Mariya V & Ravindran V S, Biomedical and Pharmacological significance of marine macro - algae-review, *Indian J Geo-Mar Sci*, 42 (5) (2013) 527-537.
- Rani S & Usha R, Utilization of seaweeds in enhancing the biochemicals and productivity of *Cassia angustifolia* Vahl, *Indian J Geo-Mar Sci*, 4 (2) (2013) 184-188.
- Vijayaraj R, Sri Kumaran N, Altaff K, Ramadevi S & Sherlin Rosita A, *In Silico* Pharmacokinetics and Molecular Docking of Novel Bioactive Compound (11-Methoxy-2-Methyltridecane-4-OL) for Inhibiting Carbohydrates Hydrolyzing Enzyme, *J Biol Act Prod Nat*, 9 (6) (2019) 445-456.
- Richards J T, Kern E R, Glasgow L A, Overall J C, Deign E F, *et al.*, Antiviral activity of extracts from marine algae, *Antimicrob Agents Chemother*, 14 (1) (1978) 24-30.
- Oumaskour K, Boujaber M, Etahiri S & Assobhei O, Screening of antibacterial and antifungal activities in green and brown algae from the coast of Sidi Bouzid (El Jadida, Morocco), *Afri J Biotech*, 11 (104) (2012) 16831-16837.
- Athukorala Y, Lee K W, Kim S K & Jeon Y J, Anticoagulant activity of marine green and brown algae collected from Jeju Island in Korea, *Bioresour Technol*, 98 (9) (2007) 1711-1716.
- Abirami R G & Kowsalya S, Anticancer Activity of Methanolic and Aqueous Extract of *Ulva Fasciata* in Albino Mice, *Int J Pharm Pharm Sci*, 4 (2) (2012) 681-684.
- Boonchum W, Peerapornpisal Y, Kanjanapothi D, Pekkoh J, Amornlerdpison D, *et al.*, Antimicrobial and anti-inflammatory properties of various seaweeds from the gulf of Thailand, *Int J Agric Biol*, 13 (1) (2011) 100-104.
- Manisseri M K, Geetha A & Syda R G, *Common Seaweeds and Seagrasses of India Herbarium*, (Central Marine Fisheries Research Institute, Kochi), Vol 2, 2012, pp. 41. <http://eprints.cmfri.org.in/id/eprint/8948>
- Harborne J B, *Methods of extraction and isolation*, In: *Phytochemical methods*, 3rd edn, (Chapman & Hall, an imprint of Thomson Science, UK), 1998, pp. 60-66.
- Aliyu A B, Ibrahim H, Musa A M, Ibrahim M A, Oyewale A O, *et al.*, *In vitro* evaluation of antioxidant activity of *Anisopus mannii* NE Br, *Afri J Biotech*, 9 (16) (2010) 2437-2441.
- Solanki R, Gupta A, Tripathy A, Soni D & Jana G K, Pharmacognostic, phytochemical and physicochemical studies of *Atrocarpus hetrophyllus* leaf (Moraceae), *J Nat Prod Plant Resour*, 1 (4) (2011) 20-26.
- Mandal P, Sinha S P & Mandal N C, Antimicrobial activity of Saponins from *Acacia auriculiformis*, *Fitoterapia*, 76 (5) (2005) 462-565.
- Kolodziej H, Kayser O, Radtke O A, Kiderlen A F & Koch E, Pharmacological profile of extracts of *Pelargonium sidoides* and their constituents, *Phytomedicine*, 10 (2003) 18-24.
- Boge T C, Himes R H, Vander Velde D G & Georg G I, The effect of the aromatic rings of taxol on biological activity and solution conformation: synthesis and evaluation of saturated taxol and taxotere analogs, *J Med Chem*, 37 (20) (1994) 3337-3343.
- Viu E, Zapata A, Capdevila J L, Fossom L H, Skolnick P, *et al.*, Glycine site antagonists and partial agonists inhibit N-methyl-D-aspartate receptor-mediated [3H] arachidonic acid release in cerebellar granule cells, *J Pharmacol Exp Ther*, 285 (2) (1998) 527-532.
- Pânzariu A T, Apotrosoaei M, Vasincu I M, Drăgan M, Constantin S, *et al.*, Synthesis and biological evaluation of new 1, 3-thiazolidine-4-one derivatives of nitro-L-arginine methyl ester, *Chem Cent J*, 10 (1) (2016) p. 6.
- Gregory J S, Bonfiglio M F, Dasta J F, Reilley T E, Townsend M C, *et al.*, Experience with phenylephrine as a component of the pharmacologic support of septic shock, *Crit Care Medi*, 19 (11) (1991) 1395-1400.
- Armstrong J & Hunt D E, *In vitro* antimicrobial activity of actinobolin applied to tooth surfaces, *J Period Res*, 8 (6) (1973) 404-405.
- Tweedie D J, Erikson J M & Prough R A, Metabolism of hydrazine anti-cancer agents, *Pharm Therap*, 34 (1) (1987) 111-127.
- Kim H M, Shim I S, Baek Y W, Han H J, Kim P J, *et al.*, Investigation of disinfectants for foot-and-mouth disease in the Republic of Korea, *J Infect Public Health*, 6 (5) (2013) 331-338.
- Sivajothi V & Dakappa S S, *In vitro* and *in silico* antidiabetic activity of pyran ester derivative isolated from *Tragiacannabina*, *Asi Pac J Tro Biomed*, 4 (2014) S455-S459.
- O'Callaghan C N, Anticancer Agents: VIII. Synthesis of Substituted Benzopyranom-[2, 3-d] Pyrimidines from 3-Carbamoyl-2-Iminochromens, In: *Proceedings of the Royal Irish Academy, Section B: Bio, Geo Chemi Sci*, 1973, pp. 291-297.
- Idan S A, Al-Marzoqi A H & Hameed I H, Spectral analysis and anti-bacterial activity of methanolic fruit extract of *Citrullus Colocynthis* using Gas Chromatography- Mass Spectrometry, *Afr J Biotechnol*, 14 (46) (2015) 3131-3158.
- Chee D N A, Rodis M L, Saat N, Ngaini Z & Halim A N A, Synthesis and Antibacterial Study Of Organotin(IV) Complexes Containing Hydrazinopyridine Ligand, *Malaysian J Anal Sci*, 21 (5) (2017) 1143 - 1150.
- Ghorab M M, Alqasoumi S I, Abdel-Kader M S & Alsaid M S, Utility of L-Norephedrine in the semisynthesis of novel thiourea and thiazolidine derivatives as a new class of anticancer agents, *Acta Pol Pharm*, 71 (2014) 615-623.
- Xuan T D, Minh T N & Khanh T D, Isolation and biological activities of 3-hydroxy-4 (1H)-pyridone, *J Pla Intera*, 11 (1) (2016) 94-100.

- 29 Xu G P, Wang H B & Wu Z L, Efficient bioreductive production of (S)-N-Boc-3-hydroxypiperidine using ketoreductase ChKRED03, *Pro Biochem*, 51 (7) (2016) 881-885.
- 30 Guo L, Wu J Z, Han T, Cao T, Rahman K, *et al.*, Chemical composition, antifungal and antitumor properties of ether extracts of *Scapania Verrucosa* Heeg and its endophytic fungus *Chaetomium fusiforme*, *Molecules*, 13 (9) (2008) 2114-2125.
- 31 Rajini A, Nookaraju M, Reddy I A K & Venkatathri N, Synthesis, characterization, antimicrobial and cytotoxicity studies of a novel titanium dodecylamino phosphate, *J Saudi Chem Soc*, 21 (2017) S77-S85.
- 32 Wei S, Quanquan Q, Peiyuan L, Xiaolin L, Qi X, *et al.*, Synthesis, Characterization, and Anticancer Activity of a Series of Ketone-N4-Substituted Thiosemicarbazones and Their Ruthenium(II) Arene Complexes, *Inorg Chem*, 52 (21) (2013) 12440-12449.
- 33 Bass P D, Gubler D A, Judd T C & Williams R M, Mitomycinoid alkaloids: mechanism of action, biosynthesis, total syntheses, and synthetic approaches, *Chem Revi*, 113 (8) (2013) 6816-6863.
- 34 Efimova M A, Ivanov A V, GaffarovKh Z & Moskvichev O V, Immunobiological Properties of Reovirus Type I, *Russ Agric Sci*, 40 (2) (2014) 153-156.
- 35 Alarcón B, Lacal J C, Fernández-Sousa J & Carrasco L, Screening for new compounds with antiherpes activity, *Antiviral Res*, 4 (5) (1984) 231-244.
- 36 Mochizuki A, Nakamoto Y, Naito H, Uoto K & Ohta T, Design, synthesis, and biological activity of piperidine diamine derivatives as factor Xa inhibitor, *Bioorg Med Chem Lett*, 18 (2) (2008) 782-787.
- 37 Ishiwata S, Itoh K, Yamaguchi T, Ishida N & Mizugaki M, Comparison of serum and urinary levels of modified nucleoside, 1- methyladenosine, in cancer patients using a monoclonal antibody based inhibition ELISA Tohoku, *J Exp Med*, 176 (1) (1995) 61-8.
- 38 Cheng Y, Xie G, Chen T, Qiu Y, Zou X, *et al.*, Distinct urinary metabolic profile of human colorectal cancer, *J Proteome Res*, 11 (2) (2012) 1354-63.
- 39 Ahmed S A, Ahmed O M & Elgendy H S, Novel Synthesis of Purine Analogues and Thieno [2, 3-b] pyridine derivatives with anticancer and antioxidant activity, *J Pharm Res*, 8 (9) (2014) 1303-1313.
- 40 Kim S H, Bartholomew D G, Allen L B, Robins R K & Revankar G R, Imidazo [1,2-a]-s-triazine nucleosides, Synthesis and antiviral activity of the N-bridgehead guanine, guanosine, and guanosine monophosphate analogues of imidazo[1,2-a]-s-triazine, *J Med Chem*, 21 (9) (1978) 883-889.
- 41 Javid S, Chaudhari S K, Munir I, Amjad M S, Akbar K F, *et al.*, Plant Metabolites and Pharmacological Activities of *Leptadenia Pyrotechnica* (Forssk.) Decne, *Nat Bioact Compd*, (2019) 551-560.
- 42 Kolodziej H, Traditionally used *Pelargonium* species: Chemistry and biological activity of umckaloabo extracts and their constituents, *Curr Topics Phytochem*, 3 (2000) 77-93.
- 43 Maleki M, Karimi G, Tafaghodi M, Raftari S & Nahidi Y, Comparison of intralesional two percent zinc sulfate and glucantime injection in treatment of acute cutaneous leishmaniasis, *Indian J Dermat*, 57 (2) (2012) 118-122.
- 44 Mishra R, Jha K K, Kumar S & Tomer I, Synthesis, properties and biological activity of thiophene: A review, *Der Pharma Chemica*, 3 (4) (2011) 38-54.
- 45 Naito H, Ohsuki S, Sugimori M, Atsumi R, Minami M, *et al.*, Synthesis and antitumor activity of novel pyrimidinylpyrazole derivatives. II. Optimization of the phenylpiperazine moiety of 1-[5-methyl-1-(2-pyrimidinyl)-4-pyrazolyl]-3-phenylpiperazinyl-1-trans-propenes, *Chem Pharma Bull*, 50 (4) (2002) 453-462.
- 46 Lucchini JJ, Corre J & Cremieux A, Antibacterial activity of phenolic compounds and aromatic alcohols, *Res Microbiol*, 141 (4) (1990) 499-510.
- 47 Liu T, Dong X, Xue N, Wu R, He Q, *et al.*, Synthesis and biological evaluation of 3, 4-diaryl-5-aminoisoxazole derivatives, *Bioorganic Med Chem*, 17 (17) (2009) 6279-6285.
- 48 La Verne D, Harry R, Peter U, Nwangwu T, Holcslaw, *et al.*, Partial synthesis of 6'-hydroxycinchonine and its antiarrhythmic activity in mice, *J Med Chem*, 22 (8) (1979) 1014-1016.
- 49 Özkay Y, Işıkdağ İ, İncesu Z & Akalın G, Synthesis of 2-substituted-N-[4-(1-methyl-4, 5-diphenyl-1H-imidazole-2-yl) phenyl] acetamide derivatives and evaluation of their anticancer activity, *Euro J Med Chem*, 45 (8) (2010) 3320-3328.
- 50 Wright H B, Dunnigan D A & Biermacher U, Hypocholesteremic Agents. I. Pyridyl Carbinols, *J Med Chem*, 7 (1) (1964) 113-115.
- 51 Kazemi M, Phenolic profile, antioxidant capacity and anti-inflammatory activity of *Anethumgraveolens* L. essential oil, *Nat Prod Res*, 29 (6) (2015) 551-553.
- 52 Kumar P, Chandak N, Kaushik P, Sharma C, Kaushik D, *et al.*, Benzenesulfonamide bearing pyrazolylpyrazolines: synthesis and evaluation as anti-inflammatory-antimicrobial agents, *Med Chem Res*, 23 (2) (2014) 882-895.
- 53 Giri R S, Thaker H M, Giordano T, Williams J, Rogers D, *et al.*, Design, synthesis and characterization of novel 2-(2, 4-disubstituted-thiazole-5-yl)-3-aryl-3H-quinazoline-4-one derivatives as inhibitors of NF-κB and AP-1 mediated transcription activation and as potential anti-inflammatory agents, *Euro J Med Chem*, 44 (5) (2009) 2184-2189.
- 54 Bergaoui A, Boughalleb N, Ben Jannet H, Harzallah-Shiric F, El Mahjoub M, *et al.*, Chemical composition and antifungal activity of volatiles from three *Opuntia* species growing in Tunisia, *Pak J Biol Sci*, 10 (15) (2007) 2485-2489.
- 55 Cuzzocrea S, Chatterjee P K, Mazzon E, Dugo L, Serraino I, *et al.*, Pyrrolidine dithiocarbamate attenuates the development of acute and chronic inflammation, *British J Pharma*, 135 (2) (2002) 496-510.
- 56 Stangel M, Moharreggh-Khiabani D, Linker R A & Gold R, Fumaric acid and its esters in the treatment of multiple sclerosis: studies and effects, *Nervenarzt*, 79 (2) (2008) 212-217.
- 57 Bernini R, Barontini M, Cis V, Carastro I, Tofani D, *et al.*, Synthesis and Evaluation of the Antioxidant Activity of *Lipophilic Phenethyl* Trifluoroacetate Esters by *In Vitro* ABTS, DPPH and in Cell- Culture DCF Assays, *Molecules*, 23 (1) (2018) p. E208.
- 58 Kendziorek M, Paszkowski A & Zagdańska B, Biochemical characterization and kinetic properties of alanine aminotransferase homologues partially purified from wheat (*Triticum aestivum* L.), *Phytochemistry*, 82 (2012) 7-14.

- 59 Hadizadeh F, Ebrahimzadeh M A, Hosseinzadeh H, Motamed-Shariaty V, Salami S *et al.*, Antidepressant and antioxidant activities of some 2-benzoxazolinone derivatives as Bupropion analogues, *Pharmacologyonline*, 1 (2009) 331-335.
- 60 Zhang X, Lei P, Sun T, Jin X, Yang X, *et al.*, Design, Synthesis, and Fungicidal Activity of Novel Thiosemicarbazide Derivatives Containing Piperidine Fragments, *Molecules*, 22 (12) (2017) p. 2085.
- 61 Pantelić N, Stanojković T P, Zmejovski B B, Sabo T J & Kaluđerović G N, *In vitro* anticancer activity of gold (III) complexes with some esters of (S, S)-ethylenediamine-N, N'-di-2-propanoic acid, *Eur J Med Chem*, 90 (2015) 766-774.
- 62 Jain N K, Kulkarni S K & Singh A, Modulation of NSAID-induced antinociceptive and anti-inflammatory effects by α -adrenoceptor agonists with gastroprotective effects, *Life Sci*, 70 (24) (2002) 2857-2869.
- 63 Kamata R, Nakajima D & Shiraishi F, Agonistic effects of diverse xenobiotics on the constitutive androstane receptor as detected in a recombinant yeast-cell assay, *In Vitro Toxicol*, 46 (2018) 335-349.
- 64 Manirarora J N, Parnell S A, Hu Y H, Kosiewicz M M & Alard P, NOD dendritic cells stimulated with *Lactobacilli* preferentially produce IL-10 versus IL-12 and decrease diabetes incidence, *Clin Dev Immunol*, 2011 (2011) p. 630187.
- 65 Van Vugt-Lussenburg B M, Van der Lee R B, Man H Y, Middelhof I, Brouwer A, *et al.*, Incorporation of metabolic enzymes to improve predictivity of reporter gene assay results for estrogenic and anti-androgenic activity, *Reprodu Toxic*, 75 (2018) 40-48.
- 66 Saludes J P, Garson M J, Franzblau S G & Aguinaldo A M, Antitubercular constituents from the hexane fraction of *Morinda citrifolia* Linn. (Rubiaceae), *Phytother Res*, 16 (7) (2002) 683-685.
- 67 Srinivasan G V, Sharanappa P, Leela N K, Sadashiva C T & Vijayan K K, Chemical composition and antimicrobial activity of the essential oil of *Leea indica* (Burm. f.) Merr. Flowers, *Nat Prod Radiance*, 8 (5) (2009) 488-493.
- 68 Chang Y, Lathrop R, Bohm E, Gander-Meisterernst I, Greger R, *et al.*, Medicament for the treatment of viral skin and tumour diseases, *United States Patent* (US9770406), 2017, p. 1.
- 69 Jehoshua K, Berry E, Avraham Y, Najajreh Y, Saidian M, *et al.*, Compounds and methods of treating obesity, *United States Patent* (US2011178151), 2011, p. 1.
- 70 Chung E Y, Byun Y H, Shin E J, Chung H S, Lee Y H, *et al.*, Antibacterial effects of vulgarone B from *Artemisia iwayomogi* alone and in combination with oxacillin, *Arch Pharm Res*, 32 (12) (2009) 1711-1719.
- 71 Perestrelo R, Silva C L, Rodrigues F, Caldeira M & Câmara J S, A powerful approach to explore the potential of medicinal plants as a natural source of odor and antioxidant compounds, *J Food Sci Technol*, 53 (1) (2016) 132-144.
- 72 Toppo E, Darvin S S, Esakkimuthu S, Stalin A, Balakrishna K, *et al.*, Antihyperlipidemic and hepatoprotective effects of Gardenin A in cellular and high fat diet fed rodent models, *Chem Biol Interact*, 269 (2017) 9-17.
- 73 Ismail A M, In L L, Tasyriq M, Syamsir D R, Awang K, *et al.*, Extra virgin olive oil potentiates the effects of aromatase inhibitors via glutathione depletion in estrogen receptor-positive human breast cancer (MCF-7) cells, *Food Chem Toxicol*, 62 (2013) 817-824.
- 74 Jeong S O, Son Y, Lee J H, Cheong Y, Park S H, *et al.*, Resveratrol analog piceatannol restores the palmitic acid - induced impairment of insulin signaling and production of endothelial nitric oxide via activation of anti-inflammatory and antioxidative heme oxygenase-1 in human endothelial cells, *Mol Med Rep*, 12 (1) (2015) 937-944.
- 75 Sharma K R, Seenivasagan T, Rao A N, Ganesan K, Agrawal O P, *et al.*, Mediation of oviposition responses in the malaria mosquito *Anopheles stephensi* Liston by certain fatty acid esters, *Parasitol Res*, 104 (2) (2009) 281-286.
- 76 Sestraş R E, Jäntschi L & Bolboacă S D, Poisson parameters of antimicrobial activity: A quantitative structure-activity approach, *Int J Mol Sci*, 13 (4) (2012) 5207-5229.
- 77 Kharchenko O V, Kharitonenko A I, Vovk A I, Babii L V, Khil'chevskii A N, *et al.*, Inhibiting properties of stable nitroxyl radicals in reactions of linoleic acid and linoleyl alcohol oxidation catalyzed by 5-lipoxygenase, *Ukr Biokhim Zh*, 77 (1) (1999) 52-57.
- 78 Musini A, Rao J P & Giri A, Phytochemicals of *Salacia oblonga* responsible for free radical scavenging and antiproliferative activity against breast cancer cell lines (MDA-MB-231), *Physiol Mol Biol Plants*, 21 (4) (2015) 583-590.
- 79 Bouabdallah S, Sghaier R M, Selmi S, Khelifi D, Laouini D, *et al.*, Current approaches and challenges for chemical characterization of inhibitory effect against cancer cell line isolated from *Gokshur* extract, *J Chromatogr B Analyt Technol Biomed Life Sci*, 1026 (2016) 279-285.
- 80 Lee J H, Kim Y G, Kim C J, Lee J C, Cho M H, *et al.*, Indole-3-acetaldehyde from *Rhodococcus* sp. BFI 332 inhibits *Escherichia coli* O157: H7 biofilm formation, *Appl Microbiol Biotechnol*, 96 (4) (2012) 1071-1078.
- 81 Cyril R, Lakshmanan R & Thiyagarajan A, *In vitro* bioactivity and phytochemical analysis of two marine macroalgae, *J Coast Life Med*, 5 (10) (2017) 427-432.
- 82 Dhevika S & Deivasigamani B, Phytochemical profiling and GC-MS analysis of *Caulerpa racemosa*, *Res J Life Sci Bioinform Pharma Chem Sci*, 4 (5) (2018) 155 - 165.
- 83 Sujatha R, Siva D & Nawas P, Screening of phytochemical profile and antibacterial activity of various solvent extracts of marine algae *Sargassum swartzii*, *World Sci News*, 115 (2019) 27-40.
- 84 Ravi S, Banu V H & Nawas P M A, Profiling of phytochemical, antioxidant properties and antimicrobial activity of marine red seaweed *Jania rubens*, *Pharma Inno J*, 8 (4) (2019) 445-452.
- 85 Gwladys S, Vania R P, Klervi L L, Sara M, Fabienne G, *et al.*, Marine green macroalgae: a source of natural compounds with mineralogenic and antioxidant activities, *J Appl Phys*, 29 (1) (2017) 575-584.