An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

IN SILICO PREDICTION OF SKIN COSMECEUTICAL PROPERTIES OF RED MACROALGAE GRATELOUPIA FILICINA

Nikunj Patel[1], Virendra Yadav[2], Lensi Patel[3], Nayan Prajapati[4], Haresh Kalasariya[*]

[1,3,4,*]Smt. S. S. Patel Nootan Science & Commerce College,Sankalchand Patel University, Visnagar-384 315

[2]Department of Microbiology, School of Life Sciences, Jaipur National University, SIILAS, Campus- Jaipur

*Corresponding author E-mail: hareshahir22@gmail.com

ARTICLE INFO

Key Words

G. filicina, GC-MS Characterization, In Silico study, Lazar, Pass Predictor

Access this article online

Website: https://www.jgtps.com/

Quick Response Code:

ABSTRACT

In the present study, the phycochemical characterization analysis of the marine algae extract of *Grateloupia filicina* was done using the GCMS method at SAIF – IIT Bombay and 14 compounds were identified. The objective of this study was to predict compounds with high activity and low toxicity by using In silico web tools. The 2D structures were downloaded by using the PubChem database. Endpoint value of carcinogenicity, MRDD and mutagenicity predicted by the lazar web tool. The ProTox-II was used for the prediction of LD50 and Toxicity class. Whereas Pass webserver used to predict different biological activities that are helpful to predict skin cosmeceutical properties such as skin irritative effect, anti-infective, antimycobacterial, wound healing agent, antioxidant, skin whitener, Melanin inhibitor, Collagenase inhibitor, MMP9 expression inhibitor, Hyaluronic acid agonist, etc. These studied activities are helpful to predict phycocomponents for the natural formulation of skin.

INTRODUCTION

Marine algae are similarly known as seaweed, macroscopic multicellular photosynthetic organisms. [1,2,3] It can be differentiated from most algae that are microscopic size.[4] Marine macroalgae are members of the kingdom Protista. Meaning they do not belong to the plant category.[5,6] Based on photosynthetic pigment, it can be classified into different types such as Brown algae (Phaeophyta), Green algae (Chlorophyta) and Red algae (Rhodophyta).[7] Some species of seaweeds/marine algae are perennial whereas some species are annual.[8] But the best Growth of marine algae can be seen in November to march.[9,10] Marine macroalgae possess many biologically active phycocompounds such as pigments (chlorophyll, carotenoids, phycocyanin, phycoerythrin, fucoxanthin, flavonoids, phenolic compounds, vitamins, lipids, polysaccharides, alkaloids, etc.)[11, 12] This types of phycoconstitutes revealed many potential benefits/biological properties such as antioxidant, antimicrobial, antiviral, anti-inflammatory, antioxidant, anti-tumor and anticonvulsant activities.[13, 14, 15, 16, 17] Due to a rich source of structurally diversified metabolites, it is widely used in pharmacological and medical development.[18, 19] It can be used in various industries such as the food industry, dairy industry, textile industry,

pharmaceutical industry, etc.[20, 21, 22] It has great attention in skin cosmetic benefits because nowadays cosmetic products contain many harmful/toxic substances such as much harmful toxic substance such as parabens, BHAV, BHT, SLS, SLES, Triclosan, Oxybenzone, Dibutylphthalate, etc.[23] This chemical components accumulates in skin layers and cause harmful effects such as to darken the skin, discoloration of the skin, skin dehydration, skin scarring, wrinkles, dark spot, blotches, patchiness of skin, etc.[24,v 25] recently, this becoming a mounting issue confronting public health.The best way to avoid this harmful effect by reducing the use of chemical cosmetics or switching to an alternative natural way.[26, 27] Hence, at present many natural resources like plants, marine algae, etc. widely used as a whole or its products as an ingredient of cosmetic formulation.[28, 29, 30, 31, 32]. The present study aims to characterize the collected alga H3 by GCMS analysis and investigate its various toxicity effects of obtained phycocompounds by its using Drulito, LAZAR, ProTox-II, and PASS webserver. This study is used to predict compounds with potential skin beneficiary properties by *In silico* means. It is similarly known to the computational study of biology performed on a computer or via computer simulation. This study is helpful to fulfill the gap between experimental and computational biology.

MATERIALS AND METHODOLOGY:

Sample Collection: The algal sample was collected from the site of beyt Dwarka, Okha, Gujarat, India. Location of the site is Lat Ref: North Long Ref: East, Coordinates: 22° 28' 32.69" N, 69° 8' 38.14" E. Beyt Dwarka site is occupied at the mouth of the Gulf of Kutch arranged 3 km off the shore of Okha.

Storage, transportation & its identification: The algal sample was collected in the month of March-2019 during low tide conditions. The collected sample was washed with distilled water to remove impurities and macroscopic epiphytes and then placed on absorbent paper to remove excess water and stored at a low temperature until analyses.[33, 34]

GCMS analysis: GCMS analysis was carried out by using a methanolic extract of selected alga *Grateloupia filicina* at Sophisticated Analytical Instrument Facility (SAIF) at IIT Bombay A chromatogram was obtained and its identification of compounds was done using NIST (National Institute of Standard) library.[35, 36, 37, 38]

PubChem study:

Pubchem is an open chemistry database. It is a collection of details for a huge number of chemical molecules and their activities against biological assay. This database maintained by NCBI, a component of NLM. By using the name of phycocompounds, CAS, EC no., NIST ID, SMILE structure can be retrieved from this database. SMILE(Simplified Molecular Input Line Entry System), a line notation that is the prime requisite for each compound as an input for further prediction in different tools[39, 40, 41, 42, 43, 44]

DruLito:

It is a virtual screening web tool to evaluate drug-likeness (such as Lipinski's rule MDDR-like rule, Veber rule, Ghose filter, BBR rule, CMC-50 like rule) or to determine compound with a certain pharmacological or biological activity. [45, 46, 47] Lipinski's Rule of 5 similarly known as Pfizer's rule of five or RO5 that is helpful to check orally active drug-like or nota drug-like molecule.[48]

Lazar: Lazar(Lazy Structure-Activity Relationship) is a virtual web tool to provide predictions for a variety of toxic properties such as Carcinogenicity (Rat), Carcinogenicity (Mouse), MRDD, Mutagenicity (*Salmonella typhimurium*), etc for each phycocompound by using SMILE structure as an input.[49]

Table 1: Data obtained from PubChem Database.

Compound Code	Name Of Phcocompounds	Cas	Nist	Id	Smile Structure
C1	Hydroxylamine,O-(3-methylbutyl)-	19411-65-5	1243	1754	CC(C)CCON
C2	Butane,1-(ethenyloxy)-3-methyl-	39782-38-2	46352	8026	CC(C)CCOC=C
C3	Hexadecane	544-76-3	62249	5554	CCCCCCCCCCCCCCCC
C4	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	102608-53-7	114703	43206	CC(C)CCCC(C)CCCC(C)CCCC(=CCO)C
C5	11-Tridecen-1-ol	___	130968	6574	CC=CCCCCCCCCCO
C6	Hexadecanoic acid,methyl ester	112-39-0	79124	9050	CCCCCCCCCCCCCCCC(=O)OC
C7	Phthalic acid,monoamide, N ethyl-N-(3-methylphenyl)-,undecyl ester	___	309865	109620	CCCCCCCCCCCOC(=O)C1=CC=CC=C1C(=O)N(CC)C2=CC=CC(=C2)C
C8	n-Hexadecanoic acid	57-10-3	151973	8479	CCCCCCCCCCCCCCCC(=O)O
C9	9-Dodecenoic acid,methyl ester,(E)-	55030-26-7	9816	2639	CC/C=C/CCCCCCCC(=O)OC
C10	Cyclopentaneundecanoic acid,methyl ester	25779-85-5	12997	3327	COC(=O)CCCCCCCCCC1CCCC1
C11	1,3-Propanediol,2-dodecyl	10395-09-2	197467	2227	CCCCCCCCCCCCC(CO)CO
C12	ZZZ-1,4,6,9-Nonadecatetraene	___	131116	2298	CCCCCCCCCC=CCC=CC=CCC=C
C13	2-Acetylamino-3-hydroxy-propionic acid	___	190204	6417	CC(=O)NC(CO)C(=O)O
C14	(2S,3S)-(-)-3-Propyloxiranemethanol	89321-71-1	1083485	17776	CCCC1C(O1)CO

Figure: 01 Image of red alga *Grateloupia filicina*

Table 2: Lipinski's rule of 5 predictions by Drulito.

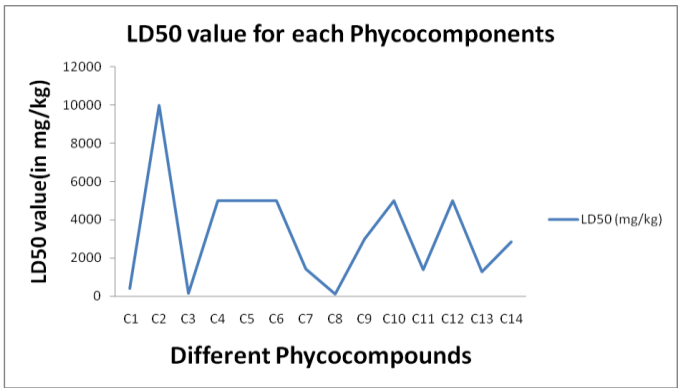
No.	Molecular Weight	Logp	Hba	Hbd	Total No Of Molecules Violated The Rule
C1	103.1	0.849	0	1	0
C2	114.1	2.682	1	1	0
C3	226.3	9.444	0	0	1
C4	296.3	8.949	1	1	1
C5	198.2	5.561	1	1	1
C6	270.3	7.891	2	0	1
C7	437.3	7.601	4	0	1
C8	256.2	7.57	2	1	1
C9	212.2	5.099	2	0	1
C10	268.2	7.49	2	0	1
C11	244.2	5.706	2	2	1
C12	260.3	9.687	0	0	1
C13	147.1	-1.514	5	3	0
C14	116.1	0.525	2	1	0

Table 3: Toxicity prediction by using LAZAR

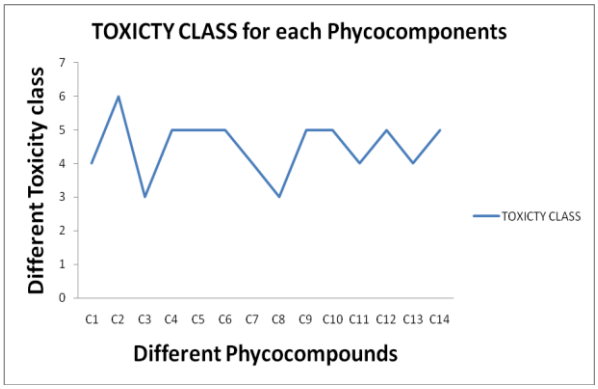
NC-No Carcinogenicity, NM-Non Mutagenic, C-Carcinogenic, M-Mutagenic

	Carcinogenicity (Rat)	Carcinogenicity(Mouse)	Mutagenicity(Salmonella Typhimurium)
C1	NC	C	NM
C2	C		NM
C3	NC	C	NM
C4	NC	NC	NM
C5	NC	NC	NM
C6	NC	C	NM
C7	NC	NC	NM
C8	NC	NC	NM
C9	NC	NC	NM
C10	NC	NC	NM
C11	NC	C	NM
C12	NC	C	NM
C13	NC	C	M
C14	NC	C	NM

Graph: 1 LD50 Value obtained by using ProTox-II



Graph:2 Toxicity class prediction by using ProTox-II



Graph: 3 MRDD data retrieved by LAZAR

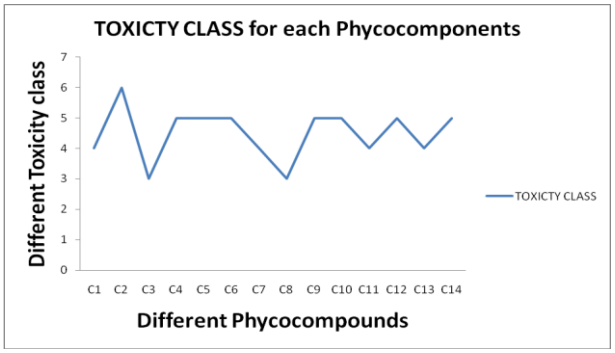
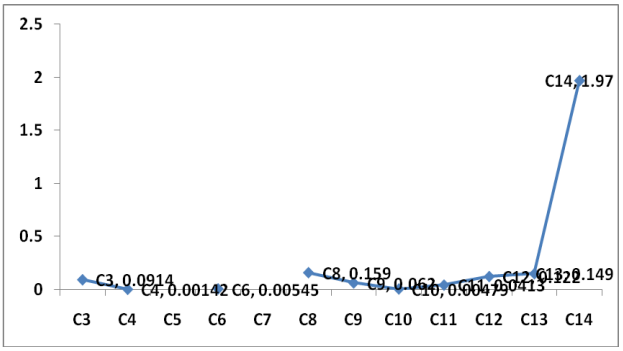
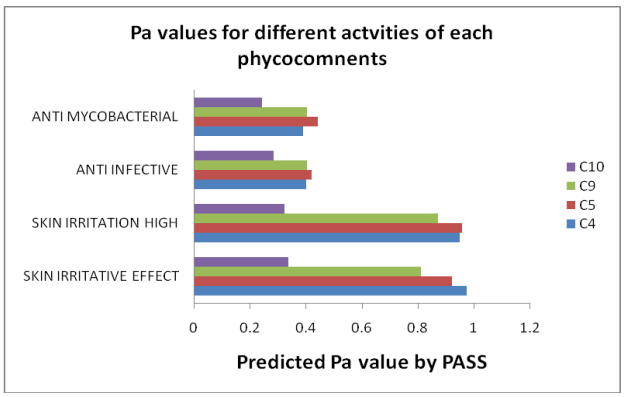


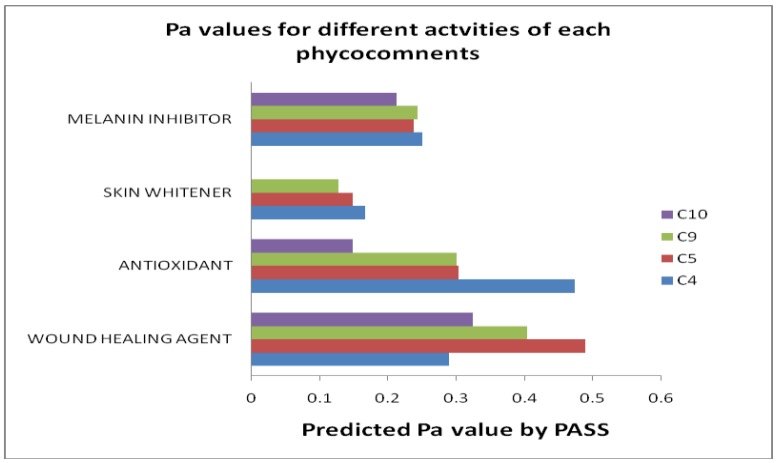
Table 3: Toxicity prediction by using LAZAR



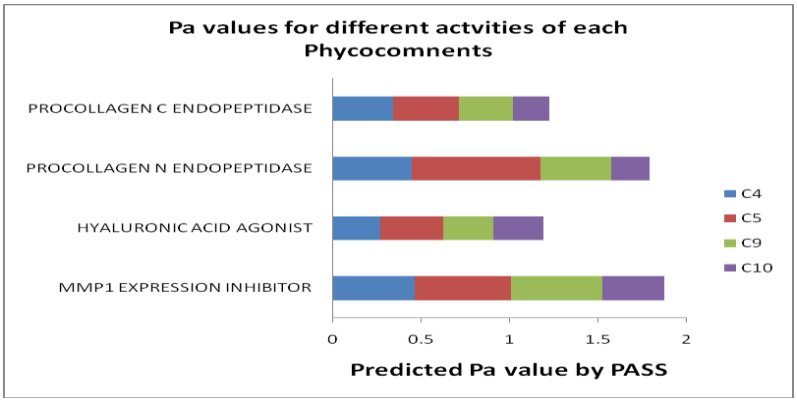
Graph:4: Pa value prediction for each phycocomponents by PASS webserver



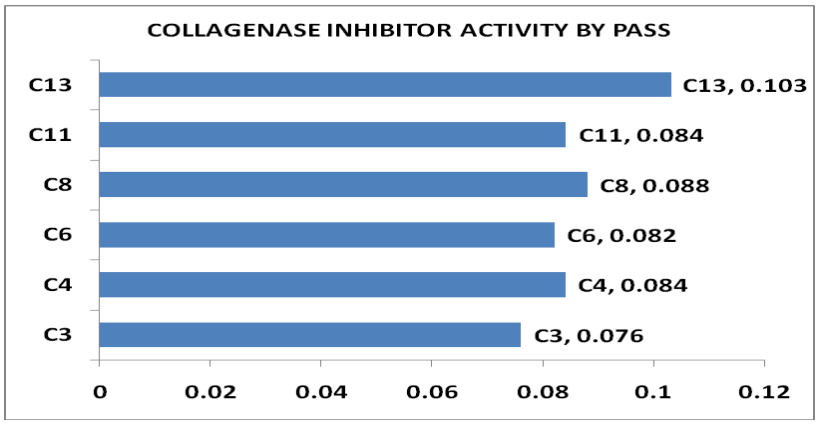
Graph 5: Pa value prediction for each phycocomponents by PASS webserver



Graph 6: Pa value prediction for each phycocomponents by PASS webserver



Graph: 7 Collagenase inhibitor activity prediction by using PASS



ProTox-II: It is a web server useful to predict toxicity parameters such as toxicity class, LD 50 value, toxicity target as well as other toxicity effects such as the Hepatotoxicity model, Carcinogenicity model, Immunotoxicity model, Mutagenicity model, Cytotoxicity model, Androgen receptor and Estrogen receptor model of any chemical compound by using SMILE structure as an input for prediction.[50, 51, 52]

LD50: It is the lethal dose meaning the dose at which 50% of test subjects die upon exposure to a compound. It is often given in mg/kg body weight.

PASS webserver: Prediction of biological activities for each phycocompounds carried out by using PASS***(Prediction of Activity Spectra for Substances)*** web tool. Various biological activities such as skin irritative effect, skin irritation high, Anti-infective, Antimycobacterial, Wound healing effect, Antioxidant, Skin whitener, Melanin inhibitor, Procollagen C and N endopeptidase, Hyaluronic acid agonist, and MMP1 expression inhibitor, etc. predicted by using this webtool.Only activities with Pa > Pi are considered as possible for a particular compound. It is useful to evaluate the general biological potential of a drug like chemical compounds. Searched output produced Pa & Pi value for each query. Pa is known as probability "to be active" whereas Pi stands Probability "to be inactive". PASS webserver use .sdf file (structural data file) required as an input. Based on predicted Pa value, the pharmacological or medical testing can be performed to verify the results from the information by the PASS tool.[53, 54, 55, 56]

RESULT AND DISCUSSION:

In silico prediction helpful to fulfill the gap between experimental and via computer simulation. Drulito, ProTox-II and LAZAR tools are useful to screen compounds with no toxicity or toxic effects. It will needful further pharmacological evaluation as well as drug development. It also saves time, money, refinement of the protocol as well as several animals used in the study. Besides, PASS justified replacement, reduction, and refinement ethics for an animal used in research. A replacement will help initial screening of phycocompounds to replace the unnecessary animal studies or avoids animal studies. The reduction will use to reduce the number of animals used in research. And the third, refinement will help to improve the process for animal study. All in all, it can also help the researchers to decide and to prepare a protocol for testing a new phycocompouns for specific biological effects as well as to check pre-reported activities and effects.

Acknowledgments: I am very much grateful to the other co-authors for contributing and sharing their knowledge. As well as I am thankful to SAIF Laboratory, IIT Bombay to carry out GCMS forthe submitted sample. I am also thankful to the Department of Microbiology and Sankalchand Patel University, Visnagar for providing facilities to complete this work.

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