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Phytochemical and Biological Studies of some Marines from Iran and Thailand

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Phytochemical and Biological Studies of some Marines from Iran and Thailand

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Introduction: Marine compounds are among the most important natural products. In this study, the phytochemical investigation of 8 seaweeds, *Cystoseira indica*, *C. merica*, *Sargassum angostifolium*, *S. oligocystum*, *S. boveanum*, *Padina australis*, *Gracilaria corticata* and *G. salicornia* was performed. Besides, antimalarial, atituberculosis, acetyl choline esterase inhibitor and cytotoxic activities of them were evaluated. The sponge *Myrmekioderma* spp. As well as a soft coral from Thailand were phytochemically analyzed and their pure compounds were elucidated.

Methods: Marine organisms were collected by diving, dried and powdered. MeOH: EtOAc (1:1) extracts of seaweeds were subjected to antituberculosis, antimalaria, ACEI and cytotoxic tests by Microculture radioisotope technique, GFPMA, microplate assay methods and Sulphorodamin. Seaweeds *S. angostifolium* and *S. oligocystum* were partitioned in solvents with different polarities and subjected to cytotoxic tests. All marines were extracted and chromatographed using Flash chromatography, MPLC and HPLC. Interested fractions were selected based on preliminary ¹H-NMR analysis and TLC profile in each step. Isolated compounds were elucidated using ¹H-NMR, ¹³C-NMR, 2D NMR (¹H-¹H COSY, HMBC, HMQC), IR and MS spectra. At last antiproliferative activity of the isolated compounds from seaweeds and sponge were analyzed.

Result: From *C.indica*, a cyclic depsipeptide with new skeleton, fatty acids such as palmitic and oleic acid and steroids including fucosterol and 24-ethylcholest-5-en-3-ol were isolated. The depsipeptide showed cytotoxic activity on HeLa cell line ($IC_{50}=0.286\pm 0.018$). Six pure compounds were isolated from the sponge *Myrmekioderma* sp., Out of which, there were Three new sesquiterpenes, 10-Oxoabolene, 12-oxocurcuphenol and 10-hydroxyabolene, together with curcuphenol, curcodiol and Indole-3-carbaldehyde. The antiproliferative activity of these compounds determined to show an interesting selectivity; i.e., a remarkable susceptibility in HT-29 cells. Five cembrane diterpenes, (+) sarcophine along with its hydroxyl derivatives were isolated from soft coral. It was the first time that 9 α -hydroxysarcophine, 9 β -hydroxysarcophine, 10 β -hydroxysarcophine and 10 α -hydroxysarcophine were isolated from nature.

Discussion: Isolating new compounds with significant structures from investigated marines besides their biological activities from one side and rich sources of marines in our country from the other side, indicates the necessity of the marines. Full biological and phytochemical analyzing will lead to find newer compounds with better activity.

Keywords: Seaweed, Sponge, Soft coral, Cembrane diterpene, Sesquiterpene, Depsipeptide

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Abbreviation

TCE: TriChloroEthane

DCM: DiChloroMethane

MeOH: Methanol

EtOAc: Ethyl Acetate

Hex: Hexane

CH₂Cl₂: Dichloromethane

BuOH: Buthanol

ACEI: Angiotensine Converting Enzyme Inhibitor

GFPMA: Green Fluorescent Protein Reporter Microplate Assay

NMR: Nuclear Magnetic Resonance

EIMS: Electron Impact Mass Spectroscopy

ESIMS: ElectroSpray Ionization Mass Spectroscopy

FABMS: Fast Atomic Bombardment Mass Spectroscopy

DEPT: Distortionless Enhancement by Polarization Transfer

COSY: COrrelation Spectroscopy

HMBC: Heteronuclear Multiple Bond Coherence

HMQC: Heteronuclear Multiple Quantum Coherence

NOESY: Nuclear Overhauser Effect Spectroscopy

CC: Column Chromatography

MPLC: Medium Pressure Liquid Chromatography

HPLC: High Pressure Liquid Chromatography

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بررسی فیتوشیمیایی و بیولوژیک برخی از موجودات دریایی ایران و تایلند

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مقدمه: موجودات دریایی از مهمترین منابع ترکیبات طبیعی میباشند. در این مطالعه ۸ جلبک دریایی به نامهای *S. boveanum*، *S. oligocystum*، *Sargassum angostifolium*، *C. merica*، *Cystoseira indica*، *Padina australis*، *Gracilaria corticata* و *G. salicornia* از نظر فیتوشیمیایی بررسی شدند. به علاوه آثار ضد سل، ضد مالاریا، مهار کننده استیل کولین و سایتوتوکسیک این گیاهان نیز ارزیابی شد. اسفنج *Myrmekioderma* و گونه ای مرجان نرم از کشور تایلند نیز مورد بررسی فیتوشیمیایی قرار گرفتند و ترکیبات جدا شده از آنها شناسایی و تعیین ساختار شدند.

روش ها: گیاهان و جانوران دریایی مورد نظر پس از جمع آوری از طریق غواصی، خشک و آسیاب شدند. عصاره متانول- اتیل استاتی (۱:۱) جلبکها با استفاده از متدهای *GFPMA*، *Microculture radioisotope technique*، *Sulphorodamin* و *microplate assay method* از نظر فعالیت ضد سل، ضد مالاریا، مهار کننده استیل کولین و سایتوتوکسیک بررسی شدند. جلبکهای *S. oligocystum* و *S. angostifolium* در حلالهای با پلاریته مختلف توزیع شد و فعالیت سایتوتوکسیک عصاره های حاصله بررسی شد. عصاره گیری از گیاهان و جانوران دریایی انجام شد و عصاره های حاصله به کمک روشهای *MPLC*، *Flash Chromatography* و در پایان *HPLC* جداسازی شدند. انتخاب فراکسیونها در هر مرحله از طریق بررسی طیف $^1\text{H-NMR}$ انجام شد. ساختار شیمیایی ترکیبات خالص به دست آمده با بررسی طیف های $^1\text{H-NMR}$ ، $^{13}\text{C-NMR}$ ، $^1\text{H-NMR}$ (2D NMR ($^1\text{H-}^1\text{H-COSY}$, HMBC , HMQC))، IR و MS آنها تعیین گردید. در نهایت فعالیت سایتوتوکسیک ترکیبات استخراج شده از جلبکها و اسفنج مورد بررسی قرار گرفت.

نتایج: از جلبک *C. indica* یک دپسی پپتید حلقوی با ساختار جدید همراه اسیدهای چرب مانند پالمیتیک اسید و اولنیک اسید و استروئیدهایی مانند فوکوسترول و 24-ethylcholest-5-en-3-ol استخراج شد. دپسی پپتید حاصله فعالیت سایتوتوکسیک خوبی بر رده سلولی HeLa داشت. از اسفنج مورد بررسی ۶ ترکیب حاصل شد که شامل ۳ سزکونی

ترین جدید 10-Oxoabolene ، 12-oxocurcuphenol و 10-hydroxyabolene همراه با curcuphenol ، curcodiol و ایندول الکلونید Indole-3-carbaldehyde میباشند. ترکیبات حاصله اثر سایتوتوکسیک خوبی بر روی رده سلولی HT-29 نشان دادند. ۵ دی ترپنویید از نوع سمبران شامل sarcophine (+) و مشتقات هیدروکسیله آن از مرجان جدا شدند. ترکیبات 9 β -Hydroxysarcophine ، 9 α -Hydroxysarcophine ، 10 α -Hydroxysarcophine ، 10 β -Hydroxysarcophine برای اولین بار از طبیعت استخراج شدند. جلبکهای مورد مطالعه اثر ضد سل و ضد مالاریا نشان ندادند در حالیکه اثر سایتوتوکسیک قابل توجهی داشتند. جلبک *S. boveanum* بیشترین اثر مهار کنندگی استیل کولین استراز را نشان داد.

بحث: با توجه به شناسایی ترکیبات جدید با ساختارهای قابل توجه در موجودات دریایی مورد بررسی و آثار بیولوژیک عصاره ها و ترکیبات جدا شده و مطالعات بسیار کم در این زمینه در ایران از یکطرف و منابع غنی کشورمان از سوی دیگر، لزوم ارزیابی گیاهان و جانوران دریایی موجود مورد تأیید قرار می گیرد. بدیهی است این ارزیابی میتواند به افزایش تعداد ساختارهای جدید با آثار درمانی مطلوب منجر شود.

کلید واژه ها: جلبک، اسفنج، مرجان نرم، دپسی پپتید، سزکونی ترین، سمبران دی ترین