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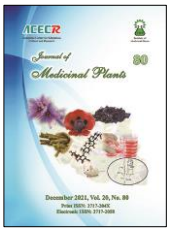

Review Article

Halocnemum strobilaceum (Pall.) M.Bieb.: a review of its botany, phytochemistry, pharmacology and ethnobotany

Fatemeh Nasernakhaei[1,*], Mahyar Zahraei[2]

[1] *Department of Plant Production Engineering and Genetics, Faculty of Agriculture, Shahid Chamran University of Ahvaz, Ahvaz, Iran*

[2] *Department of Biology, Faculty of Science, Shahid Chamran University of Ahvaz, Ahvaz, Iran*

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ABSTRACT

Background: *Halocnemum strobilaceum* (Pall.) M.Bieb. (Amaranthaceae) is a halophyte commonly used in traditional medicine to treat fever, jaundice, hair loss, dysmenorrhea, and headache. Other uses of *H. strobilaceum* include using its aerial parts extract as probiotics in aquaculture feed and a preservative in the food and beverage industries. **Objective:** This review will summarize the current state of knowledge available on this plant's botany, phytochemistry, pharmacology, and ethnobotany. **Methods:** The databases of Google Scholar, Web of Science, PubMed, Scopus, and SID were searched systematically, with no date limitation for articles published in English. **Results**: *H. strobilaceum* extracts are a rich source of anthocyanins, saponins, caffeic acid, flavonoids, coumarins, phenolic compounds, alkaloids, and fatty acids. The bioactivities ascribed to *H. strobilaceum* extracts are anticancer, antimicrobial, and antioxidant activities. They also can be used as insecticides against pests of stored products. **Conclusion:** Considering the different activities and many properties of *H. strobilaceum* it seems to be a suitable option for further experimental and clinical trial research.

1. Introduction

With increasing attention to herbal drug production with minimal adverse effects, there are higher possibilities to discover the medicinal and different physiological properties of formerly inaccessible herbal products. To

Abbreviations: TLC, Thin Layer Chromatography; PC, Paper Chromatography; UV, Ultraviolet; ^{1}H-NMR, Proton Nuclear Magnetic Resonance; MS, Mass Spectrometry; UPLC, Ultra Performance Liquid Chromatography; GC-MS, Gas Chromatography-Mass Spectrometry; GC-FID, Gas Chromatography-Flame Ionization Detection; TAC, Total Antioxidant Capacity; DPPH, 2,2-Diphenyl-1-Picrylhydrazyl; BCBT, *β*-Carotene Bleaching Test; GAE, Gallic Acid Equivalent; TGF, Transforming Growth Factor; IC_{50}, Median Inhibitory Concentration; EC_{50}, Median Effective Concentration; PC, Prostate Cancer; MTT, 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide; ROS, Reactive Oxygen Species; MIC, Minimum Inhibitory Concentration

*Corresponding author: f.nasernakhaei@scu.ac.ir

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confirm its benefit, it is necessary to recognize and identification of unused medicinal plants over the world [1]. Discovering these candidates, is nothing more than the process flow from a natural product screening to a novel isolate, which is complicated scientific work requiring skill and experience [1]. In essence, new drug development requires discovering new chemical entities, which can be synthesized or isolated from natural sources [2]. Traditional herbal remedies, which emphasize a holistic, patient-centered approach to disease treatment, are a promising place to start when it comes to finding novel immunomodulatory pharmaceuticals [3]. There are numerous examples of novel medications being developed from plant sources [2]. Due to the development of desertification and increasing saline lands in many parts of the world, such as Iran, the use of resistant plants that also have medicinal and therapeutic properties such as *Halocnemum strobilaceum* (Pall.) M.Bieb. seems necessary.

H. strobilaceum is one of the halophytic medicinal plants that grow in saline soils and has significant therapeutic and economic importance, such as its use in environmental restoration [4, 5]. Secondary metabolites of medicinal plants are the material basis of their clinically curative effects [6]. *H. strobilaceum* contains various phytochemicals, including saponins, flavonoids, alkaloids, anthocyanins, coumarins, and fatty acids [7, 8]. These compounds might display potent anticancer, antioxidant, anti-inflammation, and antimicrobial activities [9]. Because of the plant's distribution and its habitat in salt-affected lands, it can be a good option for halotechnologies [10]. This review will help to explore this plant's therapeutic potential and evaluate future research opportunities.

2. Methods

The databases of Google Scholar, Web of Science, PubMed, Scopus, and SID were searched systematically, with no date limitation up to April 2021 for articles published in English.

The utilized phrases were "phytochemical", "biological investigations", "traditional uses", "pharmacological activity", "anticancer activity", "antifungal activity", "antibacterial activity", "anti-inflammatory activity", "medicinal plants", "antioxidants", "toxicity", "commercial products", "ethnobotany", and "immunological activity" with "*Halocnemum strobilaceum*", reflecting subjects of interest.

3. Results

Between 120 articles, 82 were excluded due to being unrelated to the topic. In 38 papers, 12 were used to evaluate the plant's secondary metabolites composition, 23 for the plant's pharmacological activity, and 6 for ethnobotany and medicinal aspects. Due to the limited number of available articles and the importance of the topic, we considered two conference papers and abstracts.

3.1. Botanical description

H. strobilaceum is a succulent and glabrous shrub or subshrub (height 20-60 cm). The root system is superficial, with a poorly developed central pivot and a lateral superficial depth of 10-35 cm. Old stems are woody, intertwined with brownish bark; stems are jointed and succulent with many branches, and they stand erect to ascend with opposite orbicular buds. The hermaphrodite flowers are placed in inflorescences short, lateral, terminal, sessile, opposite, and cone-like or globular to oblong. The fruit is utricle and seeds are brown, compressed, and smooth to minutely tuberculate [11, 12].

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3.2. Taxonomic status

H. strobilaceum was formerly placed in the family Chenopodiaceae, but after the complete genome sequencing of its chloroplast and molecular-based APG system, it was transferred to the family Amaranthaceae. Here, the classification according to Cronquist's system has been mentioned (Table 1).

Table 1. Classification of *H. strobilaceum* [13]

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida (Dicotyledons)
Subclass	Caryophyllidae
Order	Caryophyllales
Family	Chenopodiaceae
Genus	*Halocnemum* M.Bieb.
Species	*Halocnemum strobilaceum* (Pall.) M.Bieb. (Synonym: *Salicornia strobilacea* Pall. [14])

3.3. Distribution

H. strobilaceum (with Persian name, Batlaghi shoor [15]) is distributed in the Mediterranean region, Central and West of Asia, Arabia, Iran, Pakistan, and Mongolia [12]. In Iran, this plant is found in vast areas of saline flats with high salinity and high ground water level [16] in Azerbaijan, Qom, Markazi, Fars, Boushehr, Isfahan, Khuzestan and Gorgan [14].

3.4. Phytochemistry

The phytochemistry of *H. strobilaceum* has been extensively studied since 1999. According to the studies, *H. strobilaceum* is rich in saponins, gallic acid, tannins, flavonoids, anthocyanins, coumarins, and alkaloids [7]. Today, over 177 compounds have been isolated and identified from this plant.

3.4.1. Saponins

Investigations show that *H. strobilaceum* is an excellent source of saponins [7]. Saponins are triterpene or steroid aglycone and one or more sugar chains [17].

3.4.2. Caffeic acid

Caffeic acid (3,4-dihydroxycinnamic acid) has been extracted from the halophytic plant *H. strobilaceum* [18].

3.4.3. Coumarins

Coumarins are bitter appetite suppressant compounds that many plants secrete as a defense. The studies show that coumarin and its derivatives can also be used as a safe and efficient pharmaceutical source [19]. Scopoletin [20], coumarin, 7-hydroxy-3-methylcoumarin, oreoselone, and heraclenin are the most common types of coumarins and are extracted from the aerial part of *H. strobilaceum* [21].

3.4.4. Flavonoids

The epigeal part of *H. strobilaceum* contains flavonoid composition (Table 2).

3.4.5. Fatty acid

Table 3 shows some fatty acids composition in *H. strobilaceum*.

3.4.6. Other compounds

Some relevant compounds isolated from *H. strobilaceum* including *p*-coumaric, rosmarinic, O-coumaric, 3,4-dimethoxybenzoic acids [8]. stigmasterol, α-amyrin, Campesterol, β-sitosterol [20], tannins [7], rutin hydrate [25], cromolyn, and astaxanthin [26].

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Table 2. Flavonoids extracted from *H. strobilaceum*

Compound name	Methods /Analysis	References
Chrysoeriol Luteolin 7-O-galactoside Quercetin 7-O-rhamnoside Luteolin	Melting point, TLC, PC, UV, ^{1}H-NMR and MS	[20]
Isoquercitrin Isorhamnetin 3-O-β-D-glucopyranoside Isorhamnetin Rhamnazin 3,4',5-trihydroxy-3'-methoxyflavone7-O-α-D-glucosaminopyranoside	Photoelectric colorimetric, Extraction, Melting point, Chromatography, UV and IR spectroscopies	[22]
Quercetin-O-glucoside Quercetin-O-gluc-O-rhamnose Quercetin rhamnoside Quercetin pentosyl-hexoside isomer Quercetin pentosyl-hexoside Rutin (Iso)rhemetin-O-hexoside (Iso)rhamnetin-3-O-rutinoside Demethylanhydroicaritin-3-Orha-(1–2)-glu Demethylanhydroicaritin-3-O-rha-(1–2)-rha Demethylanhydroicaritin-3-O-rha-(1–2)-OAc Demethylanhydroicaritin-3-O-rha-(1–2)-xyl Anhydroicaritin derivative Hydroxyicartine glycosides derivative	UPLC	[4]
Quercetin 3-glucoside Isorhamnetin-3-O-glucoside		[23]

3.5. Ethnobotany and medicinal uses

H. strobilaceum had been used in folk medicine for various medical conditions (Table 4). It is used to treat fever, jaundice, headache in region of Oued Righ in Algerian Sahara [27]; expectorants, and digestion in Fars province in Iran [28]; pregnancy difficulties, and dysmenorrhea in Arabian Peninsula [29]. Also it applied to hair loss in Libya [30]. Other uses of *H. strobilaceum* include using its aerial parts extract as probiotics in aquaculture feed [31]. *H. strobilaceum* is a good source of vitamins C and E (*α*-tocopherol, *β*-tocopherol, *δ*-tocopherol, & *γ*-tocopherol) as well as sodium, potassium, calcium, and magnesium. The green or red-violet shoots are consumed in Tunisia as gourmet vegetables due to their organoleptic properties and are used as preservative in the food and beverage industries [24].

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Table 3. Some fatty acids isolated from *H. strobilaceum*

Fatty acids	Methods	References
Lauric acid Myristic acid Stearic acid Behenic acid Oleic acid Linoleic acid	GC-MS GC-FID	[8, 24]
Hexadecenoic acid methyl ester 9-octadecenoic acid (Z)-methyl ester	GC-MS	[25]
3,4-secolanosta-4(28),8-diene-3-nitrile, 24-hydro	GC-MS	[26]
Capric acid Pentadecanoic acid Palmitoleic acid Heptadecanoic acid Arachidic acid δ -linolenic acid α-linolenicacid (ALA) Cis-11-eicosenoic acid Cis-11.14 eicosenoic acid Heneicosylic acid Dihomo- α-linolenic acid Arachidonic acid Eicosatrienoic acid Eicospentanoic acid Lignoceric acid Tricosanoic acid Linolelaidic acid SFA MUFA PUFA PUFA/SFA	GC-FID	[24]

Table 4. Summary of the traditional uses of *H. strobilaceum*

Traditional use	Part used	Area of study	Mode of application	References
Treatment of fever, jaundice, headache	Aerial parts	Region of Oued Righ in Algerian Sahara	-	[27]
Applied to hair loss	Seed oil	Libya	-	[30]
Treatment of pregnancy difficulties and dysmenorrhea	Plant extract	Arabian Peninsula	Tea	[29]
Treatment of headache, expectorant, and digestive	Aerial parts	Fars province in Iran	Decoction & Brew	[28]

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3.6. Pharmacological activity

H. strobilaceum could be a source of natural bioactive molecules with remarkable biological properties that could be used in pharmaceuticals, such as quercetin, isoquercitrin, luteolin, caffeic acid, heraclenin, scopoletin, isorhamnetin, lauric acid, octadecanoic acid methyl ester, and hexadecanoic acid methyl ester [8, 20-22, 25, 31].

3.6.1. Antioxidant and anti-inflammatory activity

Extracts of *H. strobilaceum* are rich sources of flavonoids and polyphenols, which gives them significant antioxidant properties [4, 31]. This antioxidant activity has been proven via various methods, such as TAC, DPPH radical scavenging activity, β-carotene bleaching ability, and ferric reducing powers [8] (Table 5). Handoussa et al. (2018) [4] separated total phenolics of *H. strobilaceum* using chromatographic analysis and found that of the three extracted solvent fractions, hexane, butanol, and ethyl acetate, the latter has considerable phenolic content (29.42 mg GAE/g DW) and significant antioxidant activity at 82.35 %. Another study, by Messina et al. (2019) [31] on the antioxidant activity of this plant also revealed that the polyphenol extract of *H. strobilaceum* has large amounts of polyphenol compounds and, consequently, significant antioxidant properties.

Other studies have suggested different properties for other compounds that have been identified and isolated from this plant, although they have not been explicitly studied regarding this plant. For example, various studies have shown that luteolin and isoquercitrin have anti-inflammatory properties and hepatoprotective properties, respectively [32, 33]. Isorhamnetin can potentially attenuate liver fibrosis by inhibiting TGF-β/Smad signaling and relieving oxidative stress [34].

Quercetin and isoquercitrin, some other compounds that have been identified in *H. strobilaceum*, have been reported by Rogerio et al. (2017) to be used for allergies via inhibiting eosinophilic inflammation [35]. Oleic acid is another essential compound with modulating effects on inflammatory conditions [36, 37].

Table 5. Antioxidant activity of *H. strobilaceum* extractions[1]

Assay	Extract/Fraction	IC_{50} (µg/ml)	EC_{50} (µg/ml)	mg of GAE/g DW	References
DPPH	Polar	107.5	-	-	[8]
	Apolar	61	-	-	[8]
	Ethyl acetate	-	-	-	[4]
	Ethyl acetate	-	-	-	[20]
	Butanol	-	-	-	[4]
	Water and n-hexane	-	-	-	[4]
	Polyophenol	-	6.9	-	[31]
Reducing power	Polar	-	4400	-	[8]
	Apolar	-	530	-	[8]
	Polyophenol	-	4.07	-	[31]
BCBT	Polar	3000	-	-	[8]
	Apolar	940	-	-	[8]
TAC	Polar	-	-	4.17	[8]
	Apolar	-	-	5.54	[8]

[1] All extractions are from aerial parts of the plant

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3.6.2. Anticancer and cytotoxic activity

H. strobilaceum root n-hexane extract has demonstrated strong cytotoxic activity against human cancer cell lines [25] (Table 6). Handoussa (2018) reported that the ethyl acetate fraction indicates its potential for anticancer activity against breast carcinoma (MCF-7), prostate carcinoma (PC-3), and lung carcinoma (A-549) [4]. According to Pourabdollah. (2021), the MTT-based cytotoxicity assay showed that the petroleum ether extract of *H. strobilaceum* has a higher cytotoxic effect than chloroform and methanol *H. strobilaceum* extractions against A-549 lung cancer [23]. Meanwhile, caffeic acid stimulates the immune system's function [38]. Rocha et al. (2012) accordingly reported that caffeic acid has a significant anticancer effect on the colon, gastric, liver, prostate, breast, skin, and lung cancer cell lines [39]. It can also act as an anticancer agent through decreasing cell proliferation, increasing intracellular ROS, altering mitochondrial membrane potential, lipid peroxidation, and apoptosis in HeLa and ME-180 cervical carcinoma cell lines and the human HT-1080 fibrosarcoma cell line [40, 41]. Heraclenin can improve the cytotoxic activity of some chemotherapeutic drugs as well [42]. On the other hand, scopoletin has been used to treat some autoimmune disorders, GvHD, pelvic organ prolapse, Sjögren's syndrome, and cystic fibrosis. The effects of scopoletin on phagocytosis and immunoregulation have been reported. Due to the prevention of metastasis, this compound is used in cancer treatment [43].

Manu et al. (2015) reported that the antitumor effects of capecitabine are enhanced by isorhamnetin in gastric cancer [44], which negatively regulates the signaling cascade of NF-κB. Lauric acid causes anticancer activity by inducing apoptosis [45].

Table 6. Anticancer and cytotoxic activities of *H. strobilaceum* extractions[1]

Cytotoxic activity against	Extract/Fraction	IC_{50} (µg/ml)[b]	References
MCF-7	Root n-hexane	341.98	[25]
	n-hexane	277.40	[25]
	Ethyl acetate [a]	43.1	[4]
	Butanol	> 200	[4]
Caco-2	Root n-hexane	226.87	[25]
	n-hexane	238.19	[25]
Hep-G2	Root n-hexane	423.45	[25]
	n-hexane	247.68	[25]
PC-3	Ethyl acetate	115	[25]
	Butanol	> 200	[4]
A-549	Ethyl acetate [a]	53.3	[4]
	Butanol	> 200	[4]
	Apolar	-	[23]
Ehrlich-ascites carcinoma	Volatile oil	-	[20]

[1] All extractions are from aerial parts of the plant unless specified
[a] Rich in flavonoid glycosides with quercetin, isorhamnetin, and icaritin moieties
[b] Cytotoxic activity of extracts were evaluated by MTT assay

3.6.3. Antimicrobial activity

The antimicrobial activity of *H. strobilaceum* have been summarized in Table 7. The evaluation of antibacterial activity of *H. strobilaceum* shoot fractions against five human pathogenic bacteria showed that it could inhibit bacterial proliferation [8]. In another antimicrobial assay, *H. strobilaceum* root and aerial part n-hexane extracts exhibited significant effect against *Bacillus subtilis* and *Staphylococcus aureus* [25]. Messina et al. (2019) have reported that aqueous polyphenol extracts of *H. strobilaceum* inhibit the growth of marine bacteria [31].

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Table 7. Antimicrobial activity of *H. strobilaceum* extractions[1]

Bacteria	Extract/Fraction	MIC value (µg/ml) / Inhibition zone	Assay	References
Escherichia coli	Apolar	9 mm inhibition zone (High antimicrobial activity)	Agar disk diffusion	[8]
Pseudomonas aeruginosa	Apolar	10 mm inhibition zone (Strong antimicrobial activity)	Agar disk diffusion	[8]
Staphylococcus aureus	Apolar	10 mm inhibition zone (Strong antimicrobial activity)	Agar disk diffusion	[8]
	Root n-hexane	50	Well diffusion	[25]
Enterococcus faecalis	Apolar	10 mm inhibition zone (Strong antimicrobial activity)	Agar disk diffusion	[8]
	Polar	8 mm inhibition zone (High antimicrobial activity)	Agar disk diffusion	[8]
Salmonella typhimurium	Apolar	11 mm inhibition zone (Strong antimicrobial activity)	Agar disk diffusion	[8]
Salmonella typhimurium	Apolar	11 mm inhibition zone (Strong antimicrobial activity)	Agar disk diffusion	[8]
Bacillus subtilis	Root n-hexane	6.25	Well diffusion	[25]
	n-hexane	200	Well diffusion	[25]
Polaribacter irgensii	Polyphenol	>10	Microplate method	[31]
Halomonas aquamarina	Polyphenol	0.0001	Microplate method	[31]
Pseudoalteromonas elyakovii	Polyphenol	0.00001	Microplate method	[31]
Roseobacter litoralis	Polyphenol	0.0001	Microplate method	[31]
Shewanella putrefaciens	Polyphenol	>10	Microplate method	[31]
Vibrio aesturianus	Polyphenol	0.01	Microplate method	[31]
Vibrio carchariae	Polyphenol	>10	Microplate method	[31]
Vibrio harveyi	Polyphenol	>10	Microplate method	[31]
Vibrio natriegens	Polyphenol	>10	Microplate method	[31]
Vibrio proteolyticus	Polyphenol	0.01	Microplate method	[31]

[1] All extractions are from aerial parts of the plant unless specified

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3.6.4. Insecticide and Enzyme inhibitory activity

The crude ethanolic extract of *H. strobilaceum* showed significant effects against the red flour beetle, *Tribolium castaneum*, due to its acetylcholinesterase inhibition activity [7].

4. Discussion

As previously described, *H. strobilaceum* could be a source of some compounds with remarkable biological properties (Tables 2 and 3) that could be used in pharmaceuticals (Tables 4, 5, and 6).

5. Conclusion

The present review included the phytochemical, ethnobotanical, antioxidant, antimicrobial, and anticancer potential of *H. strobilaceum*. This review intimates the traditional uses of the plant and its constituents in treating fever, jaundice, hair loss, dysmenorrhea, and headache. The various extracts of this plant might have anticancer, anti-inflammatory, antimicrobial, and antioxidant activities. They also can be used as insecticides against pests of stored products. Considering the different activities and many properties of this plant and also that this is a halophytic plant that easily grows in salt and drought conditions, which are problems in many countries today, especially in the Middle East and Iran it seems to be a suitable option for further experimental and clinical trial research. At the same time, it can be economically viable for countries with low water conditions and saline soils.

Author contributions

F.N: writing and editing the article; M.Z: collecting the articles and writing the manuscript.

Conflict of interest

The authors declare that there is no conflict of interest.

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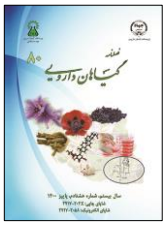

مقاله مروری

مروری بر گیاهشناسی، فیتوشیمی، فارماکولوژی و اتنوبوتانی گیاه باتلاقی شور *Halocnemum strobilaceum* (Pall.) M.Bieb.

فاطمه ناصرنخعی[۱،*]، مهیار زهرایی[۲]

[۱] گروه مهندسی تولید و ژنتیک گیاهی، دانشکده کشاورزی، دانشگاه شهید چمران اهواز، اهواز، ایران

[۲] گروه زیست‌شناسی، دانشکده علوم، دانشگاه شهید چمران اهواز، اهواز، ایران

اطلاعات مقاله

گل‌واژگان:
باتلاقی شور
ضدسرطان
ضدمیکروبی
آنتی‌اکسیدان
شورپسند
تاج خروسیان

چکیده

مقدمه: استفاده از گیاه هالوفیت باتلاقی شور *Halocnemum strobilaceum* (Pall.) M.Bieb. (از تیره تاج خروسیان) برای درمان تب، زردی، مشکلات گوارشی، سردرد و کچلی گزارش شده است. از دیگر کاربردهای این گیاه می‌توان به استفاده از عصاره اندام هوایی آن به عنوان پروبیوتیک در خوراک آبزیان و نیز نگهدارنده در صنایع غذایی و نوشیدنی اشاره کرد. **هدف:** در این مقاله اطلاعات و یافته‌های موجود در خصوص گیاه‌شناسی، فیتوشیمی، فارماکولوژی و اتنوبوتانی گیاه مذکور جمع‌آوری و خلاصه شده است. **روش بررسی:** مقالات موجود در پایگاه‌های Google Scholar، Scopus، Web of Science، PubMed و SID بدون توجه به زمان انتشارشان مورد بررسی قرار گرفت. **نتایج:** عصاره‌های *H. strobilaceum* دارای مقادیر زیاد ترکیباتی از قبیل آنتوسیانین‌ها، ساپونین‌ها، کافئیک اسید، فلاونوئیدها، کومارین‌ها، ترکیبات فنولی، آلکالوئیدها و اسیدهای چرب می‌باشد. این مواد دارای خواص بیولوژیک زیادی همچون خاصیت ضد سرطانی، ضد میکروبی و آنتی‌اکسیدان هستند. **نتیجه‌گیری:** بررسی‌های صورت گرفته نشان داد به دلیل وجود ترکیبات مختلف در *H. strobilaceum* و ویژگی‌های آن‌ها، این گیاه می‌تواند گزینه مناسبی برای تحقیقات بیشتر آزمایشگاهی و بالینی باشد.

مخففها: TLC، کروماتوگرافی لایه نازک؛ PC، کروماتوگرافی کاغذی؛ UV، فرابنفش؛ ^{1}H-NMR، رزونانس مغناطیسی هسته‌ای پروتون؛ MS، طیف سنجی جرمی؛ UPLC، کروماتوگرافی مایع با فشار فوق‌العاده بالا؛ GC-MS، کروماتوگرافی گازی متصل به طیف‌سنج جرمی؛ GC-FID، کروماتوگرافی گازی متصل به آشکارساز یونش شعله‌ای ؛ TAC، ظرفیت آنتی‌اکسیدانی تام؛ DPPH، ۲،۲- دی فنیل-۱- پیکریل هیدرازیل؛ BCBT، آزمون رنگبری بتاکاروتن؛ GAE، معادل گالیک اسید؛ TGF، فاکتور رشد تغییر دهنده؛ IC_{50}، میانگین غلظت مهارکننده؛ EC_{50}، میانگین غلظت موثر؛ PC، سرطان پروستات؛ MTT، ۳- (۵،۴- دی متیل تیازول-۲- ایل)-۵،۲- دی فنیل تترازولیوم برماید؛ ROS، گونه‌های فعال اکسیژن؛ MIC، حداقل غلظت مهارکنندگی

* نویسنده مسؤول: f.nasernakhaei@scu.ac.ir

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