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Biological activities, chemical and bioactive compounds of Echinophora platyloba DC: A systematic review

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ABSTRACT

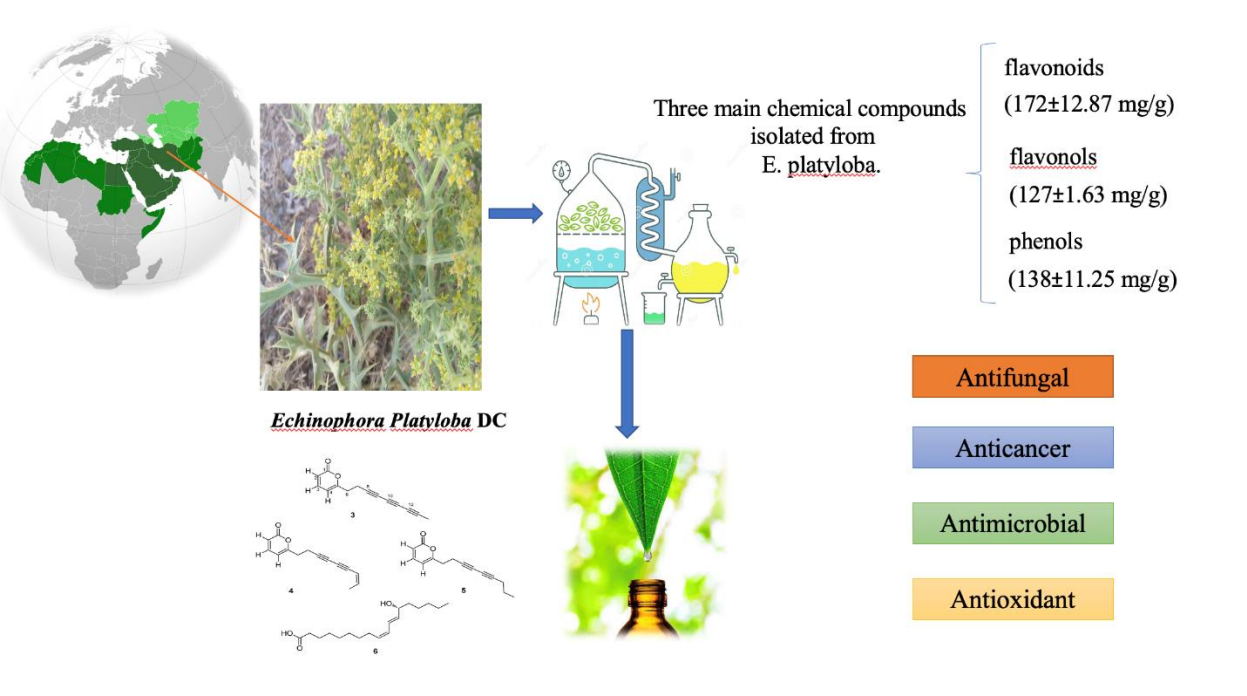
Echinophora platyloba DC has been recognized for its therapeutic potential due to the presence of antioxidant and antimicrobial compounds. This study aims to conduct a systematic investigation into the chemical composition and biological activities of this plant.

A comprehensive review of English research articles published within the last 15 years was conducted using relevant terms in databases such as PubMed, Cochrane Library, Web of Science, and CINAHL. The search strategy employed specific keywords, and the findings were collected based on the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines.

A total of thirty-seven articles were included in the study. Among the reviewed articles, nine studies focused on the antifungal effects of *Echinophora platyloba* DC, while four studies examined its antimicrobial compounds. Three studies provided evidence for joint antimicrobial and antifungal properties. Additionally, four studies confirmed the plant's potential anticancer properties, three studies explored its antioxidant effects, and two studies demonstrated its combined antimicrobial and antioxidant properties. Furthermore, six studies reported various effects, including anti-cholesterol properties, pain relief, skin burn repair, and reduction of menopausal symptoms. The most abundant compounds identified in the extract and essential oil were β-ocimene, followed by α-phellandrene.

Echinophora platyloba DC was shown to have optimal antifungal, antimicrobial, anticancer, and antioxidant effects. Moreover, the clinical effects of this plant have been deemed acceptable.

Keywords: *Echinophora platyloba* DC, antioxidant activity, antibacterial activity, antioxidant properties, anticancer effects.



INTRODUCTION

Essential oils and extracts derived from medicinal plants have gained significant attention due to their potential benefits in both food preservation and health promotion. These natural substances are known to possess a wide range of biological activities, such as antioxidant and antibacterial properties [1-2]. Medicinal plants are rich in sources of various secondary metabolites, which are bioactive compounds responsible for their therapeutic effects. These metabolites include phenolic compounds, flavanols, flavonoids, glycosides, alkaloids, and polyacetylenes. Phenolic compounds, in particular, are known for their potent antioxidant properties, which enable them to eliminate harmful free radicals and protect cells from oxidative damage [3-4]. In terms of antibacterial activity, essential oils and extracts from medicinal plants have demonstrated effectiveness against a broad spectrum of pathogenic bacteria [3, 5]. These compounds have varietal antibacterial mechanisms such as disrupting the cytoplasmic membrane of bacterial cells, compromising their integrity and leading to cell death [6]. Additionally, certain compounds can interfere with proton movement and electric currents across bacterial membranes, leading to cellular dysfunction. Furthermore, coagulation of cellular contents within microorganisms can occur, which counts as another antibacterial mechanism of these compounds [6]. However, the potency and specific mechanisms of action can vary depending on the plant species, the composition of the essential oil or extract, and the target bacteria. Therefore, extensive research is conducted to identify and understand the bioactive

compounds present in medicinal plants, as well as their effects on different bacterial strains [6]. Overall, the rich chemical composition of essential oils and extracts from medicinal plants offers promising opportunities for the development of natural food preservatives and health-enhancing drugs. Their antioxidant and antibacterial properties make them valuable resources in various industries, including food and pharmaceuticals, with ongoing research aiming to explore their full potential and applications [7-9]. Due to the side effects of chemical and synthetic antimicrobial agents and increasing bacterial resistance to current antibiotics and other antimicrobial agents, more studies have recently focused on identifying potential natural antimicrobial agents from plant, animal, and microbial sources [10-11].

Echinophora platyloba DC is an herbaceous, annual plant known for its aromatic properties. This plant is rich in a wide range of secondary metabolites such as tannins, terpenoids, alkaloids and flavonoids, which are known for their good biological properties in laboratory conditions. The most extracted part of this plant is the essential oil found in its seeds. Essential oils and their components are gaining popularity due to their relatively safe status, their widespread acceptance by consumers, and their exploitation for potential multifunctional use [12-13]. The plant typically grows to a height of 30 to 100 cm and is primarily found in Mediterranean areas, particularly in sandy coastal regions. In Iran, it is abundant in mountains such as Ashtrankoh, Koh Kola, SabzKoh, and Sefid Koh [6]. This plant has an extensive underground rhizome system, and its above-ground stem is densely branched. The leaves of *E. platyloba* DC end in thorns. Its growth period spans from June to September. In Iranian cuisine, both the fresh and dried aerial parts of certain *Echinophora* species are commonly used to add flavor to cheese and yogurt. Moreover, *Echinophora* species have been traditionally employed in Iranian traditional medicine for their healing properties, particularly in the treatment of stomach ulcers, attributed to their antifungal effects [6]. Recently, scientists paid more attention to *E*. *Platyloba* DC because of its digestive properties, as well as potential antimicrobial and anticancer effects. It has been utilized as a stomach stimulant and tonic due to the mentioned properties. The unique combination of antimicrobial, digestive, and potential anticancer effects associated with *E. platyloba* DC has led to its exploration and utilization in various domains, including traditional medicine and culinary applications. Potentially, this plant is considered as a promising source for development of new therapeutic interventions [14-16]. *E. platyloba* DC has been used for a long time in Iranian traditional medicine as an effective antifungal agent, particularly in preventing fungal contamination of dairy products and food [6]. Antifungal activity, particularly in synergy with azole drugs, against *Candida albicans* infections, make this plant interesting for scientists to investigate more about the effects of its secondary metabolites [6]. *In vivo* and *in vitro* antifungal properties of *E. platyloba* have been studied in detail and therefore, this plant is a promising candidate for treatment of infections caused by *Candida albicans* [6]. Its potential as a therapeutic agent against such infections highlights the possibility of utilizing it as a novel approach in the management and treatment of *Candida albicans* infections. However, further research and clinical studies are needed to be done to understand possible mechanisms and efficiency of *E. platyloba* DC secondary metabolites against infections by *Candida albicans* as well as determining safety levels and optimal usage of this plant's metabolites as a part of antifungal therapies [17]. Studies have shown that essential oil compounds from *E. platyloba* DC, particularly its phenolic and flavonoid compounds, possess antimicrobial, antifungal and antioxidant properties [17]. These compounds can inhibit the growth

of both Gram-positive and Gram-negative bacteria by targeting essential cellular processes and structures [17]. The broad-spectrum antimicrobial activity of these compounds highlights their potential as natural alternatives to conventional antibiotics. Further research is needed to identify specific compounds and understand their mechanisms of action, as well as explore potential synergies with existing antibiotics [18-19].

In addition to antimicrobial properties, antioxidant properties of this plant extract have been identified by inhibiting free radicals. The phenolic and flavonoid compounds present in this plant reduce percentage of oxidants through chemical reactions as hydrogen donors [20-21]. Several studies have emphasized the importance of healing properties of *E. platyloba* DC [20- 21]. This plant has shown therapeutic potential in traditional medicine, particularly in wound healing and treatment of stomach ulcers. Further research in this area could lead to the development of new treatments and interventions. The presence of biologically active compounds in this plant has established it as an effective therapeutic supplement [19, 21].

To enhance our understanding and ensure the coherence of information regarding this plant, a systematic study has been undertaken to investigate its chemical composition and biological activities. The aim of this study is to explore the extract characteristics and broaden our knowledge in this field.

Research strategy and study selection: Research articles published in the last fifteen years in English were analyzed using relevant key terms in Google Scholar, PubMed, EMBASE, Cochrane Library, Web of Science, and CINAHL databases. Terms for screening articles included "*Echinophora platyloba*", "biological activities", "chemical composition", "chemical", "antioxidant activity", "antioxidant", "extract", "antibacterial activity", "antibacterial", "antifungal", "chemical". The combination of these words with the operators "and" and "or" was also searched and investigated.

Inclusion and Exclusion criteria: The inclusion criteria for this systematic study encompassed articles that examined *E. platyloba* DC and its extract parameters, without restrictions on properties. Studies investigating compounds, antimicrobial, antifungal, and other properties related to *E. platyloba* DC were included. Articles that explored *E. platyloba* DC alongside other plant species without restrictions were also considered. Exclusion criteria included studies on plants other than *E. platyloba* DC, unavailable full texts, and irrelevant or invalid manuscripts. The aim was to gather coherent and relevant information on the chemical composition and biological activities of *E. platyloba* DC.

Protocol for selection of articles and screening: Two authors conducted search strategies and independently screened the titles and abstracts of articles based on the review article objectives, inclusion and exclusion criteria, and quality. Abstracts of all articles were reviewed, and in cases where the title and abstract provided incomplete information, the full text of the article was retrieved for evaluation. To avoid duplication, articles obtained from the initial search were checked for repetition. Articles that did not meet the inclusion criteria or were unrelated to the topic were excluded. The full texts of the remaining articles were retrieved for detailed review and analysis. The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines were followed for analysis and interpretation of the findings, as illustrated in Figure 1. The quality of the final selected articles was assessed by an experienced researcher in the field of systematic reviews and biological research.

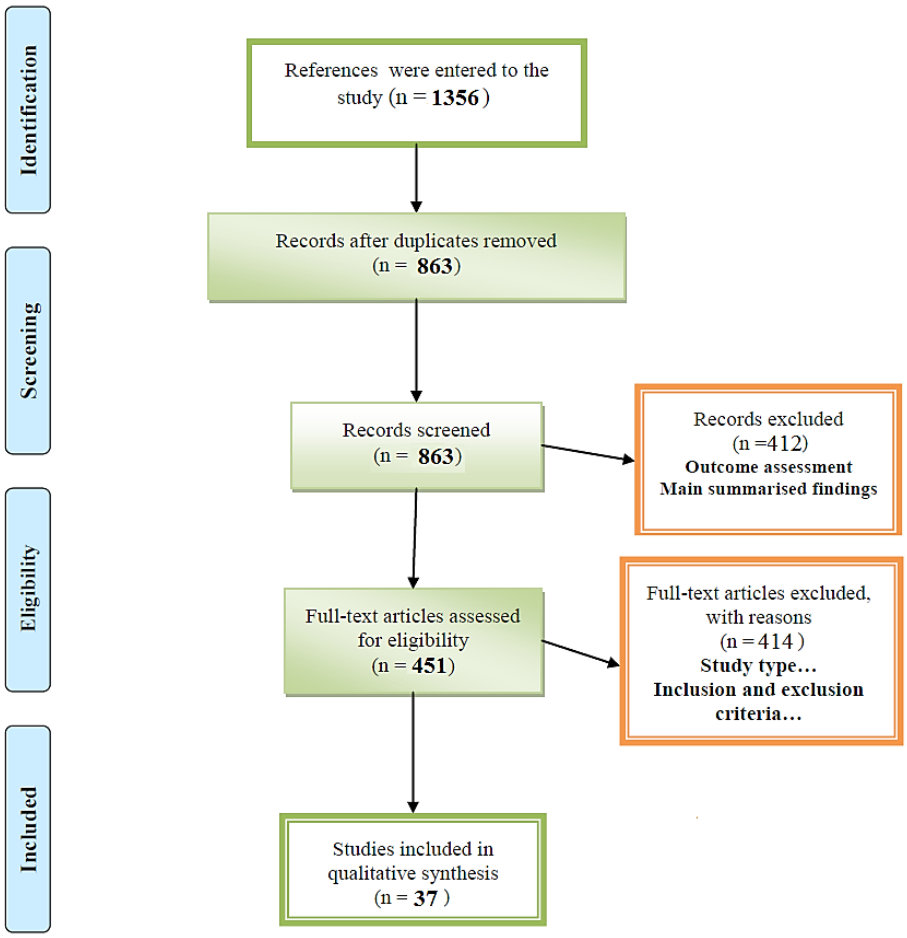


Figure 1. Diagram of articles based on Prisma selection.

Selection of main articles and variables: Our initial literature search obtained 1356 records. Of those, 493 articles were initially excluded as duplicates. By examining articles text, inclusion and exclusion criteria and topic relevance, a total of thirty-seven articles were included in the systematic study (Figure 1). Of those, twenty-six articles evaluated biological activity, 6 articles examined chemical composition [22-27], and 5 articles examined chemical composition and biological activities together [8, 28-31].

Regarding biological activity, among reviewed articles, four out of nine studies related to antifungal effects [32-40] also confirmed antimicrobial effects [41-44], and three studies showed a combination of antimicrobial and antifungal properties. According to our evaluations, four studies focused on anti-cancer properties of *E. platyloba* DC, 3 studies focused on antioxidant effects, two studies investigated both antimicrobial and antioxidant properties, and six studies focused on other properties of plant extract, such as anti-cholesterol properties, pain relief, skin burn repair, and reduction of menopausal symptoms [45-50] (Table 1). Since *E. platyloba* DC is a native plant species of Iran, all studies were conducted in Iran. *Echinophora platyloba* plants are typically found growing in their natural habitat, which includes arid and semi-arid regions such as mountainous areas, rocky slopes, and dry lands. These plants are well-adapted to the harsh conditions of these environments and are often not cultivated as traditional field crops. Instead, they are found growing in their native habitats, where they have evolved to thrive [6].

Table 1. Biological activity (BA) mentioned in articles for *E. platyloba* DC.

First Author, Year (Ref)	Type of BA	Type of study	Location	Main results
Hasanvand, 2016 [32]	AF	Experimental	Iran	All concentrations of the extract had an inhibitory effect on growth of *Aspergillus flavus*, and the highest effect was observed at 2000 ppm
Sepehri , 2016 [33]	//	Interventional	Iran	Antifungal effects were reported at an optimal level
Khajeh, 2016 [34]	//	//	Iran	mRNA levels of CDR1 and CDR2 genes were significantly decreased after incubation with *E. Platyloba*
Hashemi, 2016 [35]	//	Experimental	Iran	Crude extract was effective in inhibiting growth of *Aspergillus flavus, Penicillium expansum* and *Fusarium graminearum*
Aslani, 2014 [36]	//	//	Iran	The extract inhibited the expression of *mdr* one and *erg* genes in mushrooms
Avijgan, 2014 [37]	//	//	Iran	Ethanolic extract was effective against clinical isolates of *Candida albicans* isolated from women suffering from chronic recurrent vaginitis
Avijgan, 2012 [38]	//	//	Iran	Hydroalcoholic extract of *E. platyloba* inhibited the growth of *Candida albicans*
Youse, 2012 [39]	//	//	Iran	Hydroalcoholic extract was effective in inhibiting the growth of *Trichomonas* (a type of parasite)
Mahboubi, 2009 [40]	//	//	Iran	Hydroalcoholic extract of *E. platyloba* inhibited the growth of *Candida albicans*
Nasri, 2021 [41]	AM	Interventional	Iran	Results showed a significant antimicrobial activity of *E. platyloba* powder
Pilevar, 2017 [42]	//	Experimental	Iran	The essential oil was acceptable in terms of taste and had a good antimicrobial effect on *Staphylococcus aureus*
Bazvandi, 2017 [43]	//	//	Iran	The extract had a significant inhibitory effect on three pathogenic gram-negative bacteria and gram-positive bacteria
Ranjbar, 2016 [44]	//	//	Iran	Concentration of 150 mg/ml had a germicidal effect on *Salmonella enteritidis* and *Salmonella typhi* bacteria and that 250 mg/ml had a bactericidal effect on *Salmonella choleraesuis*
Ehsani, 2016 [51]	AM, AF	Interventional	Iran	Adding the extract to the pasteurized cream increased antifungal and antibacterial properties
Hashem, 2013 [8]	//	//	Iran	The essential oil showed strong antimicrobial activity against the tested bacteria, while the methanolic extract remained almost inactive against Gram-negative bacteria

First Author, Year (Ref)	Type of BA	Type of study	Location	Main results
Entezari, 2009 [12]	//	//	Iran	The extract reduced the growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa* to zero and was effective in inhibiting two pathogenic fungi
Kalantari, 2021 [52]	AC	Experimental	Iran	*E. platyloba* DC affected cancer cells by regulating apoptotic genes
Entezari, 2014 [53]	//	//	Iran	The extract was effective in reducing the proliferation of leukemia cancer cells
Shahneh, 2014 [54]	//	//	Iran	*E. platyloba* DC (*Apiaceae*) crude extract induced apoptosis in human prostate adenocarcinoma cells
Shahneh, 2013 [55]	//	//	Iran	Fibrosarcoma cell lines underwent apoptosis after being treated with *E. platyloba*
Soleimani, 2022 [28]	AO	//	Iran	*E. platyloba* contained significant antioxidant properties
Gholivand, 2011 [29]	//	Interventional	Iran	The highest radical-scavenging activity was shown by the polar sub-fraction of methanol extract
Khazai, 2011 [30]	//	//	Iran	Antioxidant activity of *E. platyloba* extract was confirmed
Sharafati, 2012 [31]	AM, AO	//	Iran	*E. platyloba* extract had a positive effect on reducing antioxidant capacity and appropriate microbial inhibition was observed
Saei-Dehkordi, 2012 [56]	//	experimental	Iran	Antimicrobial effects on gram-positive and gram-negative bacteria were observed, and antioxidant properties were optimal
Khosravizad, 2017 [45]	lipid profile	//	Iran	*E. platyloba* extract had a positive effect on improving the lipid profile
Sokhandani, 2016 [46]	Gonadal function	//	Iran	Alcoholic extract was effective in improving the activity of the hypothalamus-pituitary-gonadal axis
Nematian, 2015 [47]	analgesic effect	//	Iran	*E. platyloba* could produce analgesic effect
Asghari, 2014 [48]	skin wound	//	Iran	Skin wound in rats improved after treatment with *E. platyloba* extract
Delaram, 2011 [49]	PC	Clinical trial	Iran	The extract could reduce premenstrual syndrome in women
Delaram, 2011 [50]	//	Clinical trial	Iran	*E. platyloba* reduced the severity of dysmenorrhea

Abbreviations: Anti-oxidative (AO), Antimicrobial (AM), Anti-fungal (AF), Anti-cancer (AC), Premenstrual Syndrome (PC)

Chemical compounds of *E. platyloba* are listed in Table 2. In 2 studies, the number of secondary metabolites of the plant such as phenol, flavonoid and flavanone were measured [30-31]. In 1 study, fatty acids such as Stigmasterol, Sitosterol and Stigmasterol-β-D-glycoside were investigated [22]. In two studies, flavonoids such as Myricetin, Myrcene, Quercetin and luteolin were identified [23-24]. In one study, the amount

of phenol in alcoholic extract and in essential oil were 67.5 and 83.3, respectively [29]. In six studies, terpenoid compounds were evaluated [8, 24-28]. The largest number of compounds obtained from extracts and essential oils was β-ocimene (28.16-38.52%), followed by α-phellandrene (11.84-24.33%) [29].

Table 2. Chemical composition of *E. platyloba* DC according to the previously mentioned studies

First Author, Year	Chemical composition (Value)		Mean ± SD
Sharafati, 2012 [31]	Secondary metabolites (mg/g)	phenols	138±11.25
		flavonoids	172±12.87
Khazai, 2011 [30]		flavanols	127±1.63
Valizadeh, 2014 [22]	Fatty Acid (g/100 g)	Stigmasterol	1.37±0.16
		Sitosterol	0.75±0.30
		Stigmasterol-β-D-glycoside	0.39±0.09
Hadjmohammadi, 2013 [23]	Flavonoids (mg/g)	Myricetin	0.71 ± 0.02
		Myrcene	3.34 ± 0.01
		Quercetin	0.15 ± 0.02
Rahimi-Nasrabadi, 2010 [24]			
		luteolin	0.025 ± 0.01
Gholivand, 2011 [29]	phenol components [57]	methanolic extract	67.5 ± 0.48
		In essential oil	83.3 ± 0.24
Hassanpouraghdam [25]	Excellent compounds (monotripene)	β-ocimene	28.16-38.52%
		α-phellandrene	11.84-24.33%
		γ-decalactone	8.16-16.06%
Abdossi, 2021[26]		Limonene	6.56-18.23%
		cis-ocimene	4.63-17.29%
Moghaddam, 2014 [27]		*b*-phellandrene	3.16-7.23%
		α-pinene	2.32-18.52%
Hashem, 2013 [8]		Carene	1.16-16.23%
Rahimi-Nasrabadi, 2010 [24]		(E)-sesquilavandulol	0.76-0.47%
Soleimani Shadvar, 2022 [28]		*β-pinene*	0.19-2.52%
Valizadeh, 2014 [22]	Sugar composition	Saccharose	--

CONCLUSION

The essential oil of *E. platyloba* DC has antibacterial and antifungal properties, making it beneficial for human health. This is attributed to its content of phenolic, flavonoid, and other secondary metabolites. In Iranian medicine, *E. platyloba* DC is traditionally used as a stimulant and improves digestion by boosting stomach function [14-16, 35]. Due to the importance of this plant's secondary metabolites and essential oil and their beneficial properties, multiple studies have focused on its

biological activities and chemical compounds. The examination of propolis by Majiene et al. (2007) reveals its potent antimicrobial properties against a spectrum of pathogens [57] . This study serves as a comparative framework for assessing the antimicrobial activity of *E. platyloba* DC, suggesting the need for dedicated research to explore its specific bioactive components and their antimicrobial mechanisms. The parallel between propolis and *E. platyloba* DC enriches our understanding of natural antimicrobials and underscores the importance of such plants in developing new antimicrobial therapies.

In this article, we summarized antifungal, antimicrobial, anticancer, and antioxidant effects of *E. platyloba* DC from different recent studies. According to many studies, it has been found that antibacterial and antifungal effects of this plant are probably due to saponin compounds as well as the presence ofalkaloids and flavonoids [12]. The antibacterial effects of essential oil from *E. platyloba* DC can be attributed to the presence of substances such as carvacrol, linalool, p-cymene, alpha-pinene, and terpinene. These compounds have been identified as having antimicrobial properties and are likely responsible for the plant's ability to inhibit bacterial growth [58]. According to Hashemi et al. (2013), antibacterial activity of *E. platyloba* DC essential oil was related to ocimene, α-pinene, myrcene and α-phellandrene [8]. Based on a laboratory study, the main components of *E. platyloba* DC essential oil are 2-furanone, myrcene, linalool, cis-β-ocimene, trans-β-ocimene with impressive antibacterial effects [59]. According to another study by Fayyaz et al. (2015), asarone, anethole, dimethyl styrene, eugenol, dimethyl styrene isomer, nuciferol, cedran, and isofol are antibacterial compounds of *E. platyloba* DC [60].

Nasri et al. (2020) reported that the powder extract of *E. platyloba* DC has antibacterial effect [41]. According to Bazvandi et al. (2017), *E. platyloba* DC extract has a significant inhibitory effect on three Gram-negative bacteria (*Escherichia coli*, *Shigella flexner*, *Acinetobacter baumannii*) and two Gram-positive bacteria (*Staphylococcus aureus*, *Enterococcus faecalis*) [59]. The inhibitory effect was greater on Gram-positive bacteria compare to Gram-negative bacteria, which is due to the existence of the hydrophilic lipopolysaccharides (LPS) present in the outer membrane of Gram-negative as a barrier against hydrophobic compounds, including those found in essential oils. As a result, Gram-negative bacteria generally had a higher tolerance to hydrophobic antimicrobial agents than Gram-positive bacteria [59]. However, minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values of *E. platyloba* DC essential oil demonstrated significant sensitivity in Gram-positive bacteria and relative sensitivity in Gram-negative bacteria [59]. This suggested that the essential oil exhibits stronger antimicrobial activity against Gram-positive bacteria than Gram-negative bacteria [18-19]. Research studies have not consistently demonstrated a significant difference between the efficacy of essential oil and alcoholic extract of *E. platyloba* DC. However, according to one particular study [59], methanolic extracts had good antimicrobial effects. The essential oil generally had strong antimicrobial activity against bacteria, while the methanolic extract showed limited activity against Gram-negative bacteria [59]. This suggested that the essential oil may be more effective against a broader range of bacteria, while the methanolic extract may have specific limitations in its activity against Gram-negative bacteria [8].

In the current systematic review, the effectiveness of *E. platyloba* DC in inhibiting the growth of pathogenic fungi was extensively examined. According to Abdossi et al. (2021), the essential oil of *E. platyloba* DC had strong antifungal activity by inhibiting the growth of mycelium in plant pathogenic fungi. However, it should be noted that the antifungal activity of the essential oil may vary depending on the screening methods used in different studies [26]. The study by Avijgan et al. (2013) was conducted to evaluate the antifungal effect of ethanolic

extracts of *E. platyloba* DC against clinical isolates of *Candida albicans*. The strain being used in the trial was obtained from women with chronic recurrent vaginitis. The results demonstrated that the ethanolic extract had significant antifungal activity against *Candida albicans*. The findings suggested that in addition to conventional antifungal drugs, the administration of *E. platyloba* DC extract could potentially enhance the effectiveness of treatment for vaginal candidiasis[38]. In other studies, the antifungal effect of *E. platyloba* DC was investigated at the molecular level [12, 34-35]. According to Aslani et al. (2014) studies, chemical compounds in *E. platyloba* DC affected resistant genes of *Candida albicans* [36]. The study by Khajeh et al. (2016) reported that mRNA levels of *CDR1* and *CDR2* genes in *Candida albicans* decreased significantly after incubation with *E. Platyloba* DC extracts [34].

In various evaluations, the antioxidant role of *E. Platyloba* DC was shown to be adequate [28-29, 56]. Numerous studies indicated that the *Echinophora* genus is a rich source of phenolic compounds and flavonoids, which exhibit potent antioxidant activity [29-31]. It is known that phenolic compounds can effectively inhibit lipid oxidation reactions due to the ability of phenolic hydroxyl groups to scavenge free radicals and to react with oxygen, thereby preventing oxidative damage [29-31]. These phenolic compounds found in *Echinophora* species play a crucial role against free radicals [29-31]. Dehkordi et al. (2012) reported that thymol, trans-osimen, carvacrol, and (E)-sesqui-lavandulol are the main components in *E. Platyloba* DC extracts. Free radical inhibition was optimal and showed relative antioxidant activity. They also reported that *E. platyloba* DC extracts had good antimicrobial activity against *L. monocytogenes*, *B. cereus*, *B. subtilis*, *S. aureus*, *S. typhimurium*, *E. coli* O157:H7, *P. aeruginosa, C. albicans, C. tropicalis, R. rubra*, *and R. mucilaginosa*. Among the mentioned microorganisms, *R. mucilaginosa* and *P. aeruginosa* were the most sensitive and resistant organisms, respectively [56].

In the systematic review presented here, we did research on cholesterol manging properties, pain relief, skin burn repair, and menopausal side effects reduction of *E. Platyloba* DC extracts. Khosravizad et al. (2017) reported that the extract of this plant, by improving lipid profiles, has a positive effect on decreasing LDL, cholesterol, and TG, and increasing HDL, TSH, and T4 in hyperlipidemia patients [45]. Sokhandani et al. (2016) reported a positive effect of alcoholic extracts on gonads of hyperlipidemic rats [46]. In another study, the analgesic effect of *E. Platyloba* DC extract was determined [47]. In relation to the biological activity of this extract, an effect on healing skin burns was shown to be significant [48]. In addition, research has shown that consumption of *E. platyloba* DC extracts and essential oil can be effective in improving premenstrual syndromes [49-50]. According to Kalantari et al. (2021), the apoptotic genes *Bax*, *Bad*, *Bcl2*, and *P53* were investigated in A549 Lung Cancer Cells, and the results showed that the effect of *E. platyloba* extracts on genes involved in carcinogenesis was greater than that of anticancer drugs [52].

In the present systematic study, the most abundant compound obtained from extracts and essential oil was β-ocimene, followed by α-phellandrene. Abdossi et al (2021) reported that the most abundant compounds obtained from *E. platyloba* DC extracts and essential oil are related to monotrypene β-ocimene (34.16-57.52% of total) [26]. According to the study by Asghari et al. (2003), the main components of *E. platyloba* DC essential oil are trans-beta-vacimene, 2-furanone, myrcene, linalool, cis-β-vacimene [59]. In a preliminary investigation conducted by Moghaddam et al. (2015), 29 compounds were identified, of which p-cymene (22.15%), α-pinene (18.52%), β-phellandrene (14.40%), α-phellandrene (9.69%) were the most abundant ones [27]. However, the findings also show that essential oil content and chemical

compounds of *E. platyloba* DC change during three different stages of growth and development [61].

Recent studies have highlighted the critical role of dietary modulation of the gut microbiome in managing metabolic syndrome, emphasizing the transformative potential of diet in altering gut flora to enhance metabolic health [62]. This dovetails with the growing body of evidence that bioactive compounds in plants like *E. platyloba* DC can similarly affect the gut microbiota, presenting a natural approach to metabolic syndrome management. Investigating *E. platyloba* DC's bioactive compounds could thus inform the development of functional foods targeting metabolic syndrome. Moreover, research into probiotics illustrates the gut microbiota's significant influence on mental health, broadening the scope of bioactive compounds' applications [63] . This underscores *E. platyloba* DC compounds' potential capacity to impact metabolic and mental health, advocating for deeper research into their effects within the gut-brain axis framework. In addition, Nikolaevsky et al. (2014) identified the hepatoprotective, antioxidant, and antitoxic properties of amaranth oil, which also present a promising frontier for metabolic and liver health management. Overall after incorporating insights from the field of functional food science,this analysis calls for detailed scientific research to delve into the broad spectrum of bioactive effects offered by *E. platyloba* DC, extending beyond its known antimicrobial, antifungal, and antioxidant capabilities [64] . This endeavor is crucial for leveraging its full potential in crafting novel dietary solutions aimed at enhancing human health, aligning with contemporary research trends in functional food science.

In terms of drug safety, studies have indicated that *E. platyloba* DC extracts do not exhibit any significant adverse side effects on body organs [65]. Furthermore, active compounds present in *E. platyloba* DC essential oil make it a suitable candidate for natural antioxidant and antimicrobial applications in food preservation. Its biologically active compounds contribute to its potential as a natural and organic alternative for food preservation and safety [56].

Based on our findings in terms of focusing on available research and studies on *E. platyloba* DC properties, there is a lack of studies on the clinical aspect of this topic. Additionally, there is not enough specific information about the percentage or average content of secondary metabolites and other biological compounds of this plant. However, researchers attempted to provide a general summary of the findings in relation to the sizes or magnitudes of these compounds.

In summary, this review confirmed the antifungal, antimicrobial, anticancer, and antioxidant effects of *E. platyloba* DC. Furthermore, the compounds found in *E. platyloba* DC extracts were beneficial for pain relief, skin burn repair with anti-inflammatory properties, and reduction of side effects. while significant, are indeed driven by mechanisms that are complex and multifaceted. It is important to acknowledge the intricacy of these mechanisms and the need for further research to fully understand and appreciate their effects within the framework of these beneficial properties.

Abbreviations: PRISMA: Preferred Reporting Items for Systematic Reviews, MIC: minimum inhibitory concentration, MBC: minimum bactericidal concentration, LDL: low-density lipoprotein, HDL: high-density lipoprotein, TG: Triglycerides, TSH: Thyroid-stimulating hormone, T4: type of thyroid hormone.

Author's contributions: Zahra Pilevar: Writing - Original Draft and Conceptualization; Roohallah Ferdousi: Investigation; Mansoureh Taghizadeh: Search strategy and Investigation; Vahid Ranaei: Methodology; Nasim Maghboli Balasjin and Danik Martirosyan: writing—

review and editing; Hedayat Hosseini: Project administration and Supervision.

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