ALGAE IN PHARMACOLOGY AND MEDICINE APPLICATIONS: A REVIEW

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ABSTRACT

Algae occupy a distinguished place among living organisms due to their properties which make them classified as a powerful and promising tool as a natural resources. The last century has been accelerated their using for many purposes with low cost.Algae displayed a broad spectrum of biological activities due to their secondary metabolites compounds content. Thereby, algae crude extracts and their derived products benefit for multiuse purposes in the field of pharmacology and medicine research.Their richness in bioactive compounds makes them a good and useful candidate for pharmacological and medicinal applications. Their importance in vast applications as antimicrobial, antiviralantioxidant, anticancer, antidiabeticand anti-inflammatorywill discuss in the current review.

Key words: Algae, Antimicrobial, Antiviral,Antioxidant, Anticancer, Anti-inflammatory

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INTRODUCTION

Chemical drugs used for long time to combat differentdiseases induced by pathogens infection. Despite the benefit effects of some microrganisms such bacterial and fungallike *Aspergillus* spp. and *Candida* spp. strains. However, different diseases and lost in other living organisms infrequently reported causing by the mentioned and other pathogens. Even some pathogen strains became resistant to antibiotic like *Staphylococcus aureus* and *Acinetobacter baumannii* bacterial(Saleh *et al*., 2015)and *Candida* spp. fungal (Howard *et al*., 2009) pathogens. These drugs proved their efficacy in therapy treatment. However, their toxicity effect combined with expensive price limited their application particularly in undeveloped countries (Wang *et al*., 2012). Thereby, looking for alternative tool to overcome antibiotics treatment failure is requested. Combating of new appeared diseases combined with multidrug resistant pathogens appearance considered as a great challenges requested novel therapeutic tool developing (Bouhlal *et al*., 2010). So, scientists focused on natural resources that could be integrated in cure systems including higher plants, algae, lichens crude extracts and their derivations to be used as a potential choice.

Among living organisms, algae displayed a broad spectrum of biological activities. These natural resources,rich in different bioactive compounds named secondary metabolites (flavonoids, carbohydrates, phenols, terpenoids and tannins compounds,..etc.). Indeed, their abundance worldwide as renewable resources with low cost make them a potent agent not only against bacterial and fungal pathogens but also against other pathogens and thereby a benefit agent as antioxidants, antiviral, anticancer, anti-inflammatory, and antidiabetic activities.

Among marine algae, macroalgae are important ecologically and commercially through the world, particularly in Asian countries such as China, Japan and Korea. Earlier, since 3000 BC, they were used in traditional remedies (de Almeida *et al*., 2011). In this regards, brown algae used in the treatment of hyperthyroidism and other glandular disorders in Japan and China(Francisco and Erickson 2001; de Almeida *et al*., 2011). The latest workers reported their importance against cardiovascular pathogens due to their unsaturated lipids content.

It has been demonstrated that, amongst marine natural products, approximately 9% of biomedical compounds have been isolated from algae (Jha and Zi-rong 2004). Shannon and Abu-Ghannam (2016) reported the efficacy of algae as natural source for medicine application. Even, they reported that during the year 2013, more than 1000 bioactive compounds (anticancer, antiviruses, antimicrobial, and anti-hypertension) from algae were isolated and characterized worldwide.

Their application in pharmacology and medicine to cure some diseases as a

complement or/and medicine treatment, frequently increased worldwide. It has been demonstrated that algal cell walls (green, red and brown) composed mainly polysaccharides and their derived including alginic acid and alginates (Vera*et al*., 2011; Usov 2013), carrageenans (Vera*et al*., 2011), galactansand agar, laminarans (*e.g*., *Laminaria* or *Saccharina* spp.) (Rioux *et al*., 2007),fucoidans/fucans (Tutor and Meyer 2013; Cardoso *et al*., 2014), ulvans (mainly *Ulva* spp.) (Alves *et al*., 2013), lipids, fatty acids and sterols, (Kumari *et al*., 2013), phenols *(*Gupta and Abu-Ghannam 2011) gave algae their biological function (Balboa *et al*., 2013; Usov 2013; Pérez *et al*., 2016). Whereas, other compounds like pigments, lectins, alkaloids, terpenes and halogenated compounds play a minor role in algal biological activity (Pérez *et al*., 2016).

Overall, the current contribution focuses on therapeutic agents derived from algae which are considered as a potential and natural source functional ingredients in pharmacological and medicinal therapy.

- **Antibacterial effect**

Biomedical interest in algae species as antimicrobial agent has been reported in many investigations. This effect could be related to bioactive compounds known assecondary metabolites (indole alkaloids, peptides, ketones, and halogenated furanones, phlorotannins, sterols, alkenes, aldehydes, shikimic acid polysaccharides, fatty acids, alcohols, aromatic organic acids, terpenes, polyacetylenes, polyketides and hydroquinones) (Mayer *et al*., 2013; Blunt *et al*., 2015; Shannon and Abu-Ghannam 2016;Saleh *et al*., 2017). In this regards, *e.g. Turbinaria ornata* and *Sargassum polycystum* (Saowapa *et al*., 2015), *Enteromorpha intestinalis* (Ibrahim and Lim 2015), *Padina tetrastromatica* (Maheswari *et al*., 2017), *Ulva lactuca* (Chlorophyta), *Dilophus spiralis* (Phaeophyta) and *Jania rubens* (Rhodophyta) (Saleh and Al-Mariri 2017), *Codium tomentosum* (Chlorophyceae); *Corallina mediterranea* and *Hypnea musciformis* (Rhodophyceae), and *Sargassum vulgare* (Phaeophyceae) (Saleh *et al*., 2017) were used as antimicrobial agent. Moreover, Akremi*et al*. (2017) reported antimicrobial inhibitory effect of *Dictyopteris membranacea* brown algae.

To earlier, algal bactericidal compounds were first extracted from *Chlorella vulgaris* using chloroform and benzene fatty acid extracts of chlorellin; and proved its efficacy in *Bacillus subtilis, Staphylococcus aureus, Streptococcus pyogenes* and*Pseudomonas aeruginosa* inhibition (Pratt *et al*., 1944).

Shannon and Abu-Ghannam (2016) reported that pharmacological properties of the mentioned bioactive compounds regarding some of them still uncertain. However, inhibition bacterial ways induced by them have been proposed.

For example, polysaccharides and their derivatives display an important role as antibacterial agent. Where, glycoprotein-receptors found on polysaccharides cell-surface bind with cellular wall compounds, cytoplasmic membrane, and bacterial

DNA; leading to increasing permeability of the cytoplasmic membrane, protein leakage, and binding of bacterial DNA (He *et al*., 2010; Pierre *et al*., 2011; Amorim *et al*., 2012). As for other bioactive compounds liketerpenes, Lane *et al*. (2009) isolated bromophycolides (diterpene-benzoate macrolides) from the *Callophycus serratus* red alga using water, methanol and dichloromethane. The previous research reported that extracts significantly inhibited multidrug -resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium*. Based on this observation, we suggest that the antibacterial mechanism could be related to the hydrophobicity and conformational rigidity of the tetrahydropyran structure. As for chrysophaentins, Plaza *et al*. (2010) extracted eight compounds from the *Chrysophaeum taylori* algawith hexane, chloroform and methanol. The previous scientists reported the potential extracts for inhibition of MRSAin vitro, vancomycin-resistant *Enterococcus faecium* and MRSA. They proposed thatthechrysophaentinunlike any existing antibacterial agent. Where, functional groups included in chrysophaentin play as enzyme inhibitors through binding with guanosine triphosphatase of bacterial cells. Consequently, preventingof protein called FtsZ (filamenting temperature-sensitive mutant Z)synthesized, requested for bacterial cell (Kefferet *al*., 2013;Li and Ma 2015). Algal antibacterial agent has been summarized in Table 1.

- **Antifungal effect**

It is known that fungal infection caused high morbidity and mortality rates. In this regards, due to low fungal infection rates compared to bacterial one, discovery of new antifungal drug has seen a slow and little progress. However, augmentation fungal infection currently occurred encouraged scientists worldwide to look for a new antifungal drugs reflecting in increasing publications number in this approach since 1960 (Ngo *et al*., 2016; Scorzoni *et al*., 2017). Different strategies have been employed to fungi treatment involving fungal RNA synthesis and cell wall and membrane components. Even, fungal pathogens developed different mechanisms resistance to drugs. From this point of view, discovery of new antifungal drugs is requested. One of these mechanisms is to combined more than one drug together leading to increasing action potent of drug through synergetic effect improvement and antagonist effect decrease (Johnson *et al*., 2004; Scorzoni *et al*., 2017).

However, discovery of new antifungal drugs seem to be a great challenge because many factors such as current limited antifungal drugs which leading to increase mortality rates; the highly toxic effect of some compounds; similarity exist between some of these fungal and human cells(Scorzoni *et al*., 2017)and appearance of new multidrugs resistant fungal pathogens like *Candida* spp. fungal (Howard *et al*., 2009).

Natural drugs proved their efficient and benefit application as a safety antifungal agent with low cost. Algae among natural

resources showed their potent as antimicrobial agent due their bioactive constituents richness

Previously, Padmakumar and Ayyakkannu (1997) reviewed antimicrobial activity (bacterial and fungal pathogens) of 80 marine algae species. They reported that 70% out of algae showed antibacterial effect, whereas, only 27.5% of them showed antifungal effect. Importance of algae as antifungal agent has been summarized in Table 2.

- **Antiviral effect**

Algae and their derived compounds in particularly polysaccharides displayed an antiviral properties also by inhibiting virus binding into the host cells or by repression DNA replication and protein synthesis (Ahmadi*et al*., 2015) or due to carbohydrates content (Neushul 1990). In this regards, different algae species were used as a natural antiviral source *e.g.* red marine alga *Ceramium rubrum* (Serkedjieva 2004), polysaccharidesform*Fucus vesiculosus* and *Spatoglossum schröederi* brown seaweed (Queiroz *et al*., 2008), Rhodophyceae (Bouhlal *et al*., 2010), marine algae (Kim *et al*., 2011), marine polysaccharides (Wang *et al*., 2012), freshwater algae *Anabaena sphaerica*, *Chroococcus turgidus*, *Oscillatoria limnetica* and *Spirulina platensis* (blue – green algae, cyanobacteria) and *Cosmarium leave* (green algae) (Abdo *et al*., 2012)and marine algal polysaccharides (Ahmadi *et al*., 2015). Antiviral algal effect has been summarized in Table 3.

- **Antioxidant effect**

It has been reported the importance of algae extracts and their derivatives also as antioxidant agent like, edible seaweed *Palmaria palmata* (Yuan *et al*., 2005), *Laminaria japonica* (Wang *et al*., 2010a), different algal extracts (Lee *et al*., 2013), four *Chaetomorpha* spp. (Chlorophyta) (*C. aerea, C. crassa, C. linum* and *C. brachygona*) (Farasat *et al*., 2013), *Turbinaria ornata* and *Sargassum polycystum* (Saowapa *et al*., 2015), tropical seaweeds (Yin *et al*., 2015), polyphenolic compounds from marine algae (Fernando *et al*., 2016) and *Padina tetrastromatica* (Maheswari *et al*., 2017). Algae role as antioxidant agent with different mechanisms involved in this function has been summarized in Table 4.

- **Anticancer effect**

It has been demonstrated that marine algae formed the major anti-tumour agents (polysaccharides, fucoidans, phycocyanin (PC), chlorophyll, pheophytin, carotenoids, fucoxanthin, siphonaxanthin, pheophytin, stypodiol diacetate, glycoprotein, meroditerpenoids, cannabinoids, sargachromanol and monoterpenes) (Zanchett and Oliveira-Filho 2013; Sharif *et al*., 2014). In this regards, various algae species were used for fight cancer (Xie *et al*., 2016; Alves *et al*., 2016b), *e.g. Chlorella vulgaris* (Hasegawa *et al*., 2000), edible seaweed *Palmaria palmata* (Yuan *et al*., 2005) , brown algae *Cladosiphon novae-caledoniae* (Ye *et al*., 2005), brown algae *Padina pavonica* and *Cystoseira mediterranea* (Taskin *et al*., 2010), different algal extracts (green, red and brown) (Lee

et al., 2013) and brown algae (Moghadamtousi *et al*., 2014). Among anti-tumour agents, oxygenated fucosterols isolated from the *Turbinaria conoides* brown alga exhibited anticancer effect (Sheu *et al*., 1999). Indeed, fucoidan isolated from *Cladosiphon novae-caledoniae* (brown) revealed anticancer effect against human fibrosarcoma HT1080 cells(Ye *et al*., 2005). Recently, Palanisamy *et al*. (2017b) reported also fucoidan isolated from *Sargassum polycystum* (brown) against MCF-7 cell line. Whereas, Athukorala *et al*. (2006) reported polyphenolic and polysaccharide isolated from *Ecklonia cava* (brown algae) for human leukemia (U-937) cells, mouse melanoma (B-16), murine colon cancer cell line (CT-26) and human leukemia (THP1) therapy. Overall, anticancer algal effect has been summarized in Table 5.

- **Antidiabetic effect**

Diabetes is a chronic disease characterized by high blood glucose level and acute complications such as hypoglycaemia. So many anti-diabetic drugs were employed to overcome diabetes. However, type 2 diabetes mellitus (T2DM) frequently increased though recent decades, indeed, huge T2DM patients number suffered hyperglycemia (Lin and Liu 2012). Thereby, scientists focused on searching of new anti-diabetic agents to cure this disease. One approach is to increase glucose and maltose levels through reducing starch digestion by some enzymes inhibition like alpha-amylase and alpha-glucosidase (Eichler *et al*., 1984; Sudha *et al*., 2011; Unnikrishnan *et al*., 2015b). Overall, algal extracts control the blood glucose levels through the inhibition of carbohydrate hydroloyzing enzymes and protein tyrosine phosphatase 1B enzymes, insulin sensitization, glucose uptake effect and other protective effects against diabetic complications(Unnikrishnan *et al*., 2015a; Unnikrishnan and Jayasri 2016).

It has been demonstrated that marine living organisms formed a good resources for diabetes management *e.g.* sponges (31%), red algae (4%), brown algae (5%), green algae (1%), microorganisms (15%), coral (24%), ascidians (6%), molluska (6%), others (8%) (Bhattacharjee *et al*., 2014).

Marine algae due to their secondary metabolites content, significantly play an important role in the glucose-induced oxidative stress modulation and starch digestive enzymes inhibition, make them a good candidate for diabetes management (Newman *et al*., 2003; Lee *et al*., 2008). Among these bioactive compounds, antioxidants exhibited a major role in scavenging free radicals and modulate of oxidative stress related to diseases like diabetes (Unnikrishnan *et al*., 2015b). Moreover, bromophenols (BPs) isolated from marine algae can play anti-diabetic agent though inhibition of protein tyrosine phosphatase 1B and a-glucosidase activity (Lin and Liu 2012). Indeed, Lee *et al*. (2004) reported antidiabetic fucosterol isolated from *S. wightii* through free radicals scavenging.

Whereas, Lee and Jeon (2013) reported different anti-diabetic mechanisms in relation to phlorotannins (a-glucosidase, a-

amylase and protein tyrosine phosphatase 1B (PTP 1B) enzyme inhibition, glucose uptake and improvement of insulin sensitivity type 2 diabetic db/db) from brown algae .

Maeda (2013) reported brown algae importance as antidiabetic agent due to their content of water soluble components and lipid components (fatty acids, polyphenols and fucosterol fucoxanthin). Where, Fucoxanthin play a critical role in uncoupling protein 1 (UCP1) expression induction in white adipose tissue (WAT), leading to energy dissipation through fatty acids oxidation and heat production. Moreover, fucoxanthin exhibited a role in insulin resistance improvement and blood glucose levels ameliorating .Antidiabetic algal effecthas been summarized in Table 6.

- **Anti-inflammatory effect**

Inflammation is characterized as a complex physiological processes including immune system activation. It frequently occurs after physical injury or pathogenic infection by bacterial, viruses or tumor cells in the host (Calder 2006; Robertson *et al*., 2016).Whereas, Esser *et al*. (2015) reported that the synthetic pharmacological agents used for inflammation inhibition seem to be promise in metabolic diseases such as type 2 diabetes and CVD. Chronic use of such drugs however, is often correlated with different gastrointestinal side effects (Sostres *et al*., 2010; Robertson *et al*., 2015). Crude algae-extracts and their derived compounds displayed anti-inflammatory activity (D'Orazio*et al*., 2012) by pro-inflammatory cytokine inhibition and eicosanoid production, and inhibition of pro-inflammatory genes expression (Vo *et al*., 2011; Lee *et al*., 2013; Robertson *et al*., 2015). In this regards, many reports indicated their importance as anti-inflammatory agent, *e.g.Chlorella vulgaris* (Hasegawa *et al*., 2000),brown algae *Ishige okamurae* (Vo *et al*., 2011), different algal extracts(Lee *et al*., 2013), *Chondrus crispus*, *Palmaria palmata* and *Porphyra dioica* red algae (Robertson *et al*., 2015).Anti-inflammatory algal effecthas been summarized in Table 7.

Table 1. Antibacterial effect of different algal species.

Algae species	Pathogen(s)	Reference
Falkenbergia hillebrandii (red)	*Enterococcus faecalis*, *Salmonella typhi* and *Shigella* spp.	Manilal *et al*., 2009
Gelidium sequipedale (red)and *Laminaria ochroleuca* (brown)	*E. coli*, *Pseudomonas sp*, *S. aureus*, *Bacillus sp.* & *Streptococcus faecali*	Boujaber *et al*., 2016
Ulva lactuca (green), *Dilophus spiralis* (brown) and *Jania rubens* (red)	*Streptococcus pyogenes*,*Micrococcus luteus*, *Shigella flexneri* and Vibrio cholerae	Saleh and Almariri 2017
Caulerpa racemosa, *U. lactuca* (green) *J. adhaerens* (red), *P. gymnospora* and *S. polyceratium* (brown)	*Bacillus subtilis*, *Micrococcus luteus and S. aureus*, *E. coli* and *K. pneumoniae*	Alves *et al*., 2016a
Codium tomentosum (green); *Corallina mediterranea* and *Hypnea musciformis* (red), and *Sargassum vulgare* (brown)	10 bacterial isolates	Saleh *et al*., 2018
J. ruben (red)	9 bacterial isolates	Karabay-Yavasoglu *et al*., 2007
Padina tetrastromatica (brown)	*Salmonella typhi*, *Vibrio cholera*, *Shigella flexneri* and *Pseudomonas aeruginosa*	Maheswari *et al*., 2017
Padina tetrastromatica (brown)	*S. aureus*, *B. subtilis*, *Lactobacillus acidophilus*, *P. aeruginosa*, *E. coli* & *Proteus mirabilis*	Pushpara *et al*., 2014
Sargassum polycystum and *S. tenerrimum* (brown)	12 bacterial isolates	Kausalya and Rao 2015
19 marine algae species (6 green, 8 brown and 5 red)	8 bacterial isolates	Alghazeer *et al*., 2013
Sargassum wightii (brown)	11 bacterial isolates	Chandrasekaran *et al*., 2014b
Seven cyanobacteria species	8 bacterial isolates	Abo-State *et al*., 2015
Scytosiphon lomentaria, *Padina pavonica*, *Cystoseira mediterranea (brown)*, *Hypnea musciformis and Spyridia filamentosa (red)*	*S. aureus*, *S. typhimurium*, *E. coli*, *Enteroccus faecalis*	Taskin *et al*., 2010
U. lactuca and *Enteromorpha compressa* (green), *Padina pavonica* (brown) and *J. rubens* (red)	6 bacterial isolates	Elnabris *et al*., 2013
Acanthophora spicifera (red)	Methicillin -resistant *S. aureus* (MRSA) &*P. aeruginosa*	Zakaria *et al*., 2011
H. musciformis (red)	*E. coli*,*S. typhi*, *P. aeruginosa*, *S. aureus* and *P. mirabilis*	Shareef Khan *et al*., 2012
U. lactuca,*U. reticulata* (green), *S. wightii*, *S. marginatum* (brown), *Gracilaria verrucosa* & *G. edulis* (red)	*E. faecalis*	Chandrasekaran *et al*., 2014a
Ulva intestinalis (green) and *Gracilaria fisheri* (red)	13 bacterial isolates	Srikong *et al*., 2015
H. muciformis (red)and *S. myricocystum* (brown)	*K. pneumoniae*, *Enterobacter aerogenes*, *E. coli* and *P. aeruginosa*	Kandhasamy and Arunachalam 2008
32 seaweeds (13 green and 12 brown)	*E. coli*, *Staphylococcus aureus* , *Enterococcus faecalis*, *K. pneumoniae* and *E. faecalis*	Chiheb *et al*., 2009
Avrainvillea nigricans, *Codium decorticatum* (green), *Halymenia floresia* (red), *Laurencia obtuse*, *S. filipendula* and *S. hystrix* (brown).	*S. aureus*, *B. subtilis*, *S. agalactiae*, *E. coli*, *P. aeruginosa*, *K. pneumonia*, *Shigella flexneri*.	Morales *et al*., 2006
26 red seaweeds	*E. coli*, *K. pneumoniae*, *S. aureus* & *E. faecalis*	Rhimou *et al*., 2010
Cladophora prolifera (green)	*E. coli*, *Staphylococcus aureus*, *Enterococcus faecalis* & *Klebsiella pneumoniae*	Zbakh *et al*., 2014
Ulva lactuca (green), *Petalonia fascia* (brown)and *Gelidium spinosum* (red)	*Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis*	El-Shouny *et al*., 2017
Ulva intestinalis (green)	*Bacillus cereus* , *Staphylococcus aureus* , and methicillin-resistant *S. aureus*	Srikong *et al*., 2017
Spatoglossum asperum (brown)	*Aeromonos hydrophila*	Palanisamy *et al*., 2017a

Acanthaphora spicifera (red)	*E. coli, B. subtilis, B. palmitus,* and *P. aeruginosa*	Pandian *et al*., 2011
Halimeda discoidea (green)	*B. cereus, B. licheniformis, B. spizizenii, S. aureus, S. epidermidis, S. aureus* (MRSA), *S. bodyii, P. aerugenosa, A. anitratus, B. subtilis, Citrobacter freundii, K. pneumonia* and *Yersinia* spp.	Afifah *et al*., 2010

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Table 2. Antifungal effect of different algal species.

Algae species	Pathogen(s)	Reference
Ulva lactuca (green), *Dilophus spiralis* (brown) and *Jania rubens* (red)	*Aspergillus niger* and *Candida albicans*	Saleh and Almariri 2017
Gelidium sequipedale (red)and *Laminaria ochroleuca* (brown)	*Candida albicans, Candida tropicalis* and *Cryptococcus neoformans*	Boujaber *et al*., 2016
Asparagopsis taxiformis (red)	*Aspergillus* spp	Genovese *et al*., 2013
Dilsea carnosa, Laurencia pinnatifida, Odonthalia dentata and *Polysiphonia lanosa* (red)	*Aspergillus flavus, A. fumigatus* and *Candida albicans*	Tariq 1991
J. ruben (red)	*Candida albicans*	Karabay-Yavasoglu *et al*., 2007
Acanthaphora spicifera (red)	*Aspergillus niger, Candida albicans* and *Microsporum gypseum,*	Pandian *et al*., 2011
Sargassum polycystum and *S. tenerrimum* (brown)	6 fungal isolates	Kausalya and Rao 2015
Rhodomella confervoides (red), *Ulva lactuca*(green) and *Cystoseira tamaricifolia* and *Padina pavonica* (brown)	*Aspergillus niger, Candida albicans* and *Mucor ramaniannus*	Saidani *et al*., 2012
Scytosiphon lomentaria, Padina pavonica, Cystoseira mediterranea (B), Hypnea musciformis and Spyridia filamentosa ®	*Candida albicans*	Taskin *et al*., 2010
Sargassum vulgare, Cystoseira barbata, Dictyopteris membranacea, Dictyota dichotoma, and *Colpomenia sinuosa*(B*)*	*Alternaria alternata, Cladosporium cladosporioides, Fusarium oxysporum, Epicoccum nigrum, Aspergillus niger, Aspergillus ochraceus, Aspergillus flavus, and Penicillium citrinum*	Khallil *et al.* 2015
Eisenia bicyclis (brown)	*Candida* species	Kim *et al*., 2014
Padina Pavonica and *Sargassum Vulgare* (brown)	*Candida albicans,Candida glabrata, Candida krusei* and *Candida tropicalis*	Khaled *et al*., 2012
Padina Pavonica (brown)	*Fusarium graminearum, Penicillium expansum* and *Alternaria alternata*	Omezzine *et al*., 2009
Sargassum myricocystum (brown), *Gracilaria edulis(* red)	*Colletotrichum falcatum*	Ambika and Sujatha 2015
Turbinaria conoides (brown)	*Pythium aphanidermatum*	Begum *et al*., 2015
Halimeda discoidea (green)	*A. niger, Microsporum gypseum, Penicillium* spp., *rhizopus* spp., *Trichoderma viridae* and *Trichophyton rubrum*	Afifah *et al*., 2010
Stypopodium zonale, L. dendroidea, Ascophyllum nodosum,	*Colletotrichum lagenarium*	Peres *et al*., 2012
S. muticum, Pelvetia canaliculata, Fucus spiralis,		
S. filipendula, S. stenophyllum, L. hyperborea and *G. edulis* (brown)		
Avrainvillea nigricans, Codium decorticatum (green), *Halymenia floresia* (red), *Laurencia obtuse, S. filipendula* and *S. hystrix* (brown).		
	C. albicans, Saccharomyces cerevisae, A. niger and *Trichophyton mentagrophytes*.	Morales *et al*., 2006

Table 3. Antiviral effect of different algal species.

Algae species	Pathogen(s)	Reference
Red algae	Herpes simplex virus (HSV-1 & HSV-2)	Ehresmann *et al*., 1977
Red algae	Herpes simplex virus (HSV)	Neushul 1990
Porphyridium spp. (red)	Murine leukemia virus- MuLV	Talyshinsky *et al*., 2002
Ceramium rubrum (red)	Herpes simplex virus (HSV) type 1 and type 2	Serkedjieva 2004
Red algae	Herpes simplex virus type 2 (HSV-2)	Buck *et al*., 2006
Ulva lactuca (green)	IAV virus	Ivanova *et al*., 1994
Cosmarium leave (green)	Hep-2 cell line	Abdo *et al*., 2012
Fucus vesiculosus and *Spatoglossum schröederi* (brown)	HIV virus	Queiroz *et al*., 2008
Sargassum mcclurei, *Sargassum polycystum and Turbinara ornata* (brown)	HIV virus	Thuy *et al*., 2015
Sargassum swartzii (brown)	HIV-1 virus	Dinesha *et al*., 2016
Constantinea simplex and *Farlowia mollis* (brown)	Herpes simplex virus type 1 and type 2	Richards *et al*., 1978
cyanobacteria	Human immunodeficiency virus (HIV)	Schaeffer and Krylov 2000
Red and blue-green	Hepatitis C virus (HCV)	Takebe *et al*., 2013
Red algae *Nothogenia fastigiata*	Herpes simplex virus type 1 (HSV-1)	Damonte *et al*., 1996
Bue-green	Herpes simplex virus (HSV-1 & HSV-2)	Patterson *et al*., 1993
Marine algae	HIV virus	Kim *et al*., 2015
Turbinaria conoides	herpes simplex virus-1 (strain KOS), herpes simplex virus-2 (strain G), vaccinia virus, vesicular stomatitis virus, herpes simplex virus-1 TK- KOS ACVr , coxsackie virus B-4, sindbis virus, punta toro virus, reovirus-1 (ATCC VR-230) and parainfluenza virus-3 (ATCC VR-93)	Kumar *et al*., 2009

Table 4. Antioxidant effect of different algal species.

Algae species	Mechanism	Reference
Chaetomorpha spp. (green)	Total phenolic and flavonoid	Farasat *et al*., 2013
Cladophora prolifera (green)	Phenol	Zbakh *et al*., 2014
Ulva intestinalis (green)	Total phenolic compounds (TPC)	Srikong *et al*., 2017
Ulva clathrata, U. linza Linnaeus, *U. flexuosa* & *U. intestinalis*	Total phenolic and flavonoid	Farsat *et al*., 2014
Enteromorpha prolifera (green)	Phenolic compounds	Cho *et al*., 2011
Palmaria palmata (brown)	Polyphenol	Yuan *et al*., 2005
Padina Pavonica and *Sargassum Vulgare* (brown)	Phenolic compounds	Khallil *et al*. 2012
Padina tetrastromatica (brown)	Fatty acids and a flavone compound (2-Phenyl-4H-1-benzopyran-4-one)	Maheswari *et al*., 2017
Laminaria japonica (brown)	Fucose, galactose and sulfate group	Wang *et al*., 2010a
Turbinaria ornata and *Sargassum polycystum* (brown)	Phenol	Saowapa *et al*., 2015
Turbinaria ornata (brown)	Polyphenol	Vijayabaskar and Shiyamala 2012
Sargassum glaucescens (brown)	Fucoidan	Huang *et al*., 2016
Sargassum cristaefolium (brown)	Fucose-containing sulfated polysaccharides, also termed “fucoidans"	Wang *et al*., 2015
Spatoglossum asperum (brown)	Sulfated polysaccharides	Palanisamy *et al*., 2017a
Sargassum polycystum (brown)	Fucoidan	Palanisamy *et al*., 2017b
8 marine cyanobacteria species	Lipophilic and hydrophilic	Rai and Rajashekhar 2015
Spirulina platensis (blue-green microalga)	Elevated levels of testicular SOD, CAT, zinc, and GSH and a decrease of MDA	Bashandy *et al*., 2016

Table 5. Anticancer effect of different algal species.

Algae species	Pathogen(s)	Reference
Cladosiphon novae-caledoniae (brown)	Human fibrosarcoma HT1080 cells	Ye *et al.*, 2005
Scytosiphon lomentaria, P. pavonica, Cystoseira mediterranea (brown), *Hypnea musciformis and Spyridia filamentosa (red)*	Tumor cell lines (MCF-7, DU 145, LNCaP & PC3)	Taskin *et al.*, 2010
Ecklonia cava (brown)	Human leukemia (U-937) cells, mouse melanoma (B-16), murine colon cancer cell line (CT-26) and human leukemia (THP1)	Athukorala *et al.*, 2006
Sargassum polycystum (brown)	MCF-7 cell line	Palanisamy *et al.*, 2017b
Spirulina platensis (blue-green microalga)	Human colon cancer cell line Caco-2	Śmieszek *et al.*, 2017
Gracilaria tenuistipitata (red)	Ca9-22 oral cancer cells	Yeh *et al.*, 2012a
Gracilaria tenuistipitata (red)	Ca9-22 oral cancer cells	Yeh *et al.*, 2012b
microalgae *Navicula incerta*	Human hepatoma HepG2 cells	Kim *et al.*, 2014

Table 6. Antidiabetic effect of different algal species.

Algae species	Mechanism	Reference
Sargassum polycystum and *Sargassum wightii* (brown)	α-amylase, α-glucosidase and Dipeptidyl peptidase-IV (DPP-IV) inhibitors	Unnikrishnan *et al*., 2015a
Chaetomorpha aerea, *Enteromorpha intestinalis*, *Chlorodesmis*, and *Cladophora rupestris* (green)	Alpha-amylase, alpha-glucosidase inhibitors, and antioxidant compounds	Unnikrishnan *et al*., 2015b
Irish seaweeds *(A. nodosum, F. serratus, F. vesiculosus and P. canaliculata) (brown)*	α-amylase and α-glucosidase inhibitors	Lordan *et al*., 2013
Pelvetia siliquosa (brown)	decrease in serum glucose concentrations, and exhibited an inhibition of sorbitol accumulations in the lenses.	Lee *et a*l., 2004
Rhodomela confervoides (red)	Protein tyrosine phosphatase 1B (PTP1B) inhibition	Shi *et al*., 2008

Table 7. Anti-inflammatoryeffect of different algal species.

Algae species	Bioactive compounds	References
Green, red and brown algae	-	Lee *et al*., 2013
Chondrus crispus, *Palmaria palmata* and *Porphyra dioica* (red)	-	Robertson *et al*., 2015
Marine alge (red, green, brown, and blue-green algae)	-	Lee *et al*., 2013
Gracilaria spp. (red)	-	de Almeida *et al*., 2011
Gracilaria tenuistipitata (red)	-	Chen *et al*., 2013
Porphyridium spp. (red)	-	Talyshinsky *et al*., 2002
Polyopes affinis (red)	-	Lee *et al*., 2011
Neorhodomela aculeata (red)	-	Lim *et al*., 2006
Laurencia glandulifera (red)	-	Chatter *et al*., 2011
Porphyra yezoensis (red)	Glycoprotein	Shin *et al*., 2011
Gracilaria verrucosa (red)	(E)-10-Oxooctadec-8-enoic acid and (E)-9-Oxooctadec-10-enoic acid	Lee *et al*., 2009
Lithothamnion corallioides (red)	Multi-mineral aquamin	Ryan *et al*., 2011
Delesseria sanguinea (red)	Sulfated polysaccharides	Grunewald *et al*., 2009
Bryothamnion triquetrum (red)	-	Cavalcante-Silva *et al*., 2012
Gracilaria caudate (red)	Sulfated polysaccharide	Chaves *et al*., 2013
Gelidium crinale (red)	Galactan	de Sousa *et al*., 2013
Hypnea cervicornis (red)	Mucin-binding agglutinin	Bitencourt *et al*., 2008
Pterocladiella capillacea (red)	Lectin	Silva *et al*., 2010
Dunaliella bardawil (green)	Antioxidant beta-carotene	Lavy *et al*., 2003
Ulva conglobata (green)	-	Jin *et al*., 2006
U. lactuca (green)	-	Margret *et al*., 2009
Chlorella marina (green)	Lycopene	Renju *et al*., 2013
Dunaliella tertiolecta (green)	Mixture of phytosterols	Caroprese *et al*., 2012
Caulerpa mexicana (green)	Nociception	Bitencourt *et al*., 2011
Caulerpa cupressoides (green)	Lectin	Vanderlei *et al*., 2010
Caulerpa cupressoides (green)	Sulfated polysaccharide	Rodrigues *et al*., 2012
Chlorella vulgaris (green)	-	Hasegawa *et al*., 2000
Ishige okamurae (brown)	-	Vo *et al*., 2011

Ecklonia cava (brown)	-	Kim and Bae 2010
Ishige okamurae (brown)	-	Kim *et al*., 2009
Lobophora variegata (brown)	Sulfated polysaccharides	Medeiros *et al.*, 2008
Lobophora variegata (brown)	Sulfated polysaccharides	Paiva *et al*., 2011
Sargassum wightii (brown)	Alginic acid, an anionic polysaccharide	Sarithakumari *et al*., 2012
Lobophora variegata (brown)	Fucans	Siqueira *et al*., 2011
Sargassum vulgare (brown)	Fucans	Dore *et al*., 2013
Spatoglossum schroederi (brown)	Fucans	Farias *et al*., 2011
Myagropsis myagroides (brown)	Carotenoid fucoxanthin	Heo *et al*., 2010
Eisenia bicyclis, *Ecklonia cava*- and *Ecklonia kurome* (brown)	Polyphenol phlorotannins	Kim *et al*., 2011
Sargassum siliquastrum (brown)	Sargachromanol G	Yoon *et al*., 2012
Sargassum wighti (brown)	-	Pramitha and Kumari 2016

- : Not identified

CONCLUSION

In spite of manyscientific advances within the field of algae in wide range of pharmacology and medicine research and application, only a few of algae species were used. On the other hand, the majority of research covering algal employment in pharmacology and medicine focuses on the effectiveness of their crude extracts, and only some studies went further towards obtaining extract fractions and testing their biological potency. Research on application of algae in pharmacology and medicine focused on their antimicrobial (antibacterial, antifungal and antiviral) activity. However, little attention has been given to their antidiabetic applications.Based upon these observations and in order to maximize the benefit of algae within this field many factors need further attention: I) Discovery a new and valuable algae species and testing their biological activity as a new agent. II) Focusing on the most potent algae species in each field of study combined with an in-depth study regarding their fractions potency separately. III) Some research exclusively focused on certain species for therapy of certaindiseases,and they need further attention against other diseases. Moreover, some algae species displayed multiuse functions suchas *Sargassum* spp.,need further attention regarding the discovery of other new functions.

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