REVIEW ARTICLE

Prospective Phycocompounds for Developing Therapeutics for Urinary Tract Infection

Ajit Kumar Bishoyi[1] · Anjali Lakra[1] · Chinmayee Priyadarsani Mandhata[1] · Chita Ranjan Sahoo[1] ·
Rabindra Nath Padhy[1] 📵

Abstract

Antibiotic resistance of bacteria is causing clinical and public health concerns that are challenging to treat. Infections are becoming more common in the present era, and patients admitted to hospitals often have drug-resistant bacteria that can spread nosocomial infections. Urinary tract infections (UTIs) are among the most common infectious diseases affecting all age groups. There has been an increase in the proportion of bacteria that are resistant to multiple drugs. Herein is a comprehensive update on UTI-associated diseases: cystitis, urethritis, acute urethral syndrome, pyelonephritis, and recurrent UTIs. Further emphasis on the global statistical incidence and recent advancement of the role of natural products in treating notorious infections are described. This updated compendium will inspire the development of novel phycocompounds as the prospective antibacterial candidate.

Introduction

Infections from multidrug-resistant (MDR) bacteria, mycobacteria, and fungi are wearisome health problems, causing several comorbidities, even physical disabilities from Hansen's disease and ultimate mortalities [1]. Urinary tract infections (UTIs) are among the most commonplace infectious diseases [2], affecting all age groups, and even children were seen infected in hospitals and communities [3]. It would not be out of place to state that every female gets a UTI at least once in her lifetime. It is often infected in adult females with a challenged immune system. The short physical distance between vaginal and rectal openings is the contrivance to super-infections from rectal microbiota [2]. About 150 million people are diagnosed with UTIs yearly [4].

The occurrence of any infection depends on several factors, such as improper functioning of the immune system and the bacterial/fungal virulent status, i.e., MDR strains of infectious bacteria that survive in the body. The most common causative agents of UTI-MDR bacteria are *Escherichia coli*, *Staphylococcus aureus,* and *Acinetobacter baumannii* [5]. Thus, it became resistant to the most common antibacterial, which no longer remains in mainstream medicine today; therefore, chemical modifications were done [1, 6].

Moreover, the bloodstream infection leads to the spread of the infecting bacteria to all innards through blood, wherein those colonize; sometimes, the bacterial growth leads to toxic shock syndrome (TSS) and bacteremia (Fig. 1) [7, 8]. As it is known, both TSS and bacteremia lead to fatality without a timely use of some suitable antibacterial(s), assessed from the MDR nature of bacterial strains [9]. *Staphylococcus* sp., such as *S. aureus* or *S. saprophyticus,* is the second most common genus of the causative bacteria of acute UTI, after *E. coli*, and it accounts for 5–15% of the reported UTIs and usually affects younger women [10]. Indeed, *Staphylococcus* sp. is mostly a cutaneous infection that can spread to the urethra through sexual intercourse. Moreover, the complicated UTIs were attributed to *Klebsiella* sp.; pregnant women are more prone to this infection because the enlarged uterus blocks the required free urinary passage to wash out the infecting bacterial microbiota [11] (Fig. 2).

Ajit Kumar Bishoyi and Anjali Lakra have equally contributing to this work.

✉ Chita Ranjan Sahoo
chitaranjan.biotech@gmail.com

✉ Rabindra Nath Padhy
rnpadhy54@gmail.com

1 Central Research Laboratory, Institute of Medical Sciences & Sum Hospital, Siksha 'O' Anusandhan Deemed to Be University, Bhubaneswar, Odisha 751003, India
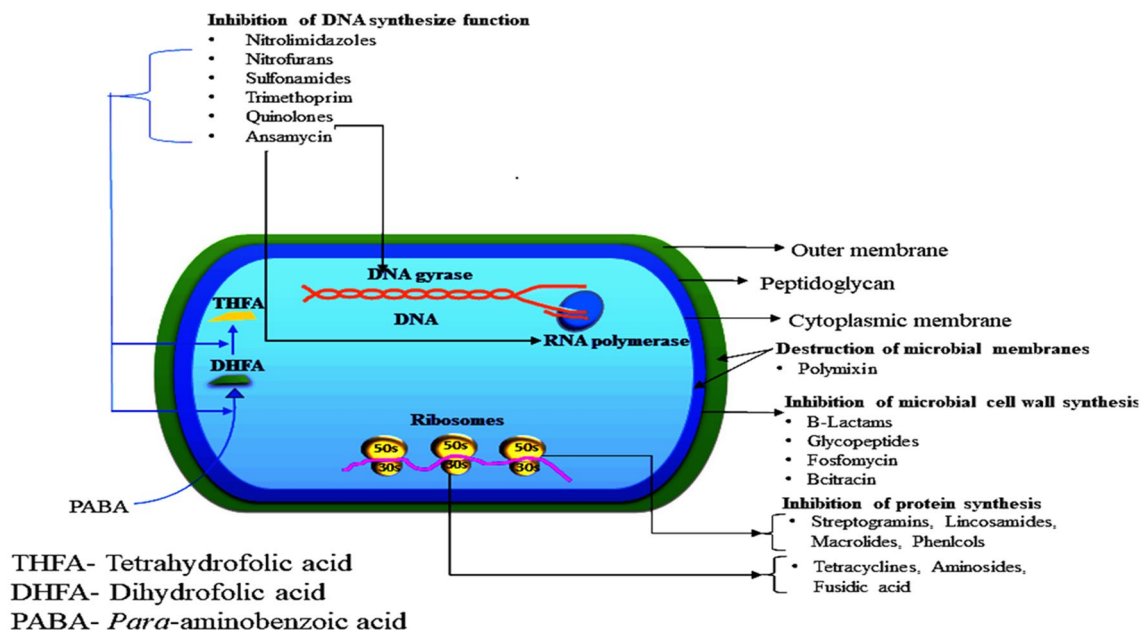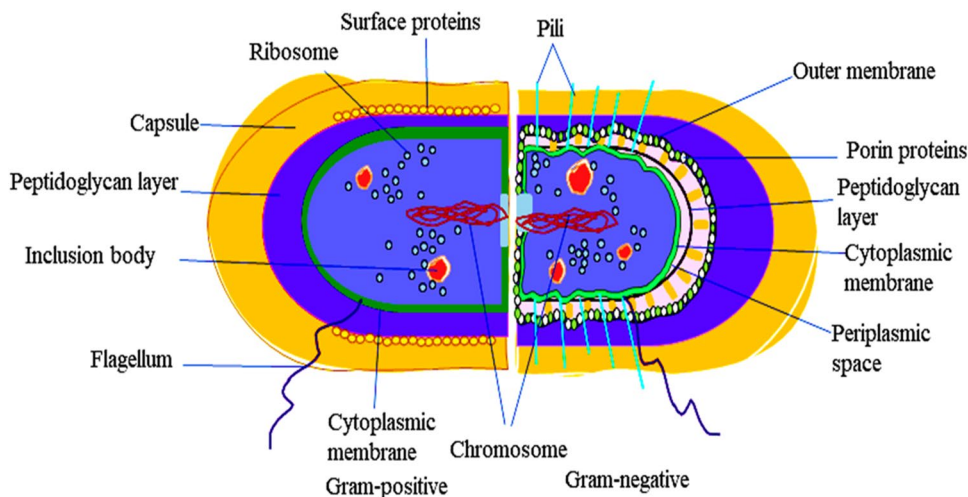
Inhibition of DNA synthesize function
- Nitrolimidazoles
- Nitrofurans
- Sulfonamides
- Trimethoprim
- Quinolones
- Ansamycin

DNA gyrase

THFA

DNA

RNA polymerase

DHFA

Ribosomes

50s 50s 50s

30s 30s 30s

PABA

→ Outer membrane
→ Peptidoglycan
→ Cytoplasmic membrane

Destruction of microbial membranes
- Polymixin

Inhibition of microbial cell wall synthesis
- B-Lactams
- Glycopeptides
- Fosfomycin
- Bcitracin

Inhibition of protein synthesis
- Streptogramins, Lincosamides, Macrolides, Phenlcols
- Tetracyclines, Aminosides, Fusidic acid

THFA- Tetrahydrofolic acid
DHFA- Dihydrofolic acid
PABA- *Para*-aminobenzoic acid

Fig. 1 Inhibition mechanism of UTIs

Fig. 2 Schematic representation of cellular structure of bacteria

Surface proteins   Pili

Ribosome

Capsule

Outer membrane

Peptidoglycan layer

Porin proteins

Peptidoglycan layer

Inclusion body

Cytoplasmic membrane

Flagellum

Periplasmic space

Cytoplasmic membrane

Chromosome

Gram-positive

Gram-negative

Recent trends in the study of plant products and the development of new drugs have established natural products as a significant source of druggable compounds against multiple diseases [12]. It is a common belief that natural medicines are usually potentially less toxic than their synthetic-prepared drugs [1]. A broad range of naturally occurring antimicrobial chemicals has been found in marine environments. These have shown remarkable increases in bioactive compounds, and concomitant algal-based products are significant therapeutic activities. However, conventional antimicrobials prefer those derived from natural sources because these are more effective, safer for the environment, and have fewer adverse effects [13].

Modern medicine's most challenging issue is preventing the spread of more dangerous MDR bacterial pathogens. MDR bacterial infections account for over 700,000 annual fatalities worldwide, but estimates suggest that number might increase to 10 million by 2050 [9]. An extensive search for novel antimicrobial compounds that could reduce the existing dependence of modern medicine on standard antibiotics is essential to halt the trend of adding newer antibiotic classes that are gradually resistant to the newly generated bacterial strains [10].

This review considers a comprehensive update on UTI-associated diseases, namely cystitis, urethritis, acute urethral syndrome, pyelonephritis, and uncomplicated, complicated,

and recurrent UTIs. Further emphasis on the global statistical incidence and recent advancement of the role of natural products in treating notorious infections are described. This updated compendium would inspire the development of novel phycocompounds as the prospective antibacterial candidate(s).

Urinary Tract Infection: A Global Threat

Post-COVID infection cases have increased, and patients admitted to hospitals carry drug-resistant bacteria that spread nosocomial. The antibiotic resistance of MDR bacteria produces clinical and public health concerns that are difficult to treat. This is because of the rise in the prevalence of multidrug-resistant bacteria (Fig. 3) [5]. There have been several reports of the emergence of MDR bacterial strains in various geographical places; this phenomenon is related to the local use of antibiotics. MDR microorganisms travel across regions, leading to global infection scenarios of individual harmful bacteria. These strains are more dangerous than drug-sensitive variants, and MDR bacteria are more antibiotic-resistant [8]. The administration of antibiotics for the treatment of a broad range of infections leads to the gradual development of antibiotic resistance in bacterial strains (Fig. 4). Even among bacteria that are not linked to one another phylogenetically, the bacterial consortia facilitate the interchange of genetic characteristics, which is necessary for the establishment of MDR bacterial microbiota [12]. Recently, the resistance mechanisms have resulted in the concurrent development of resistance to several antibiotic classes, resulting in hazardous MDR bacterial strains, some of which are also known as superbugs, the MDR-MRSA (multidrug-resistant-methicillin-resistant *S. aureus*) (Fig. 2). Because of the recent emergence of newer initially harmless microbes, the emergence of multidrug resistance in pathogenic strains occurred; eventually, the potential use of MDR *bacilli* became a possibility [7].

The clinical manifestations of UTI include harmless conditions as well as those that are potentially fatal. Any component of the urinary tract, including the urethra (which can develop urethritis), the bladder (which can develop cystitis), the ureters, and the kidneys, is susceptible to infection (pyelonephritis). In certain patients with lower UTIs, the disease could even ascend or cause pyelonephritis as well as male genital infections, including such prostatitis and epididymis-orchitis, or it can progress to severe and life-threatening urosepsis if it is not treated or if the case cannot be resolved with antibiotics (Fig. 1). This can happen in the absence of treatment or in issues where the infection cannot be resolved with antibiotics [11].

UTIs can be divided into three categories: lower, which affects only the bladder; upper, which affects the pyelonephritis; and either uncomplicated as well as complicated. An uncomplicated urinary tract infection (UTI) develops in a usual host that is not pregnant, does not have any structural or physiological abnormalities, and has not been outfitted (for example, with a catheter) [12, 13]. The urethra serves as the exit point for urine and allows the entry of microbiota into the urinary tract. However, these microbes are regularly flushed out through frequent urination in both
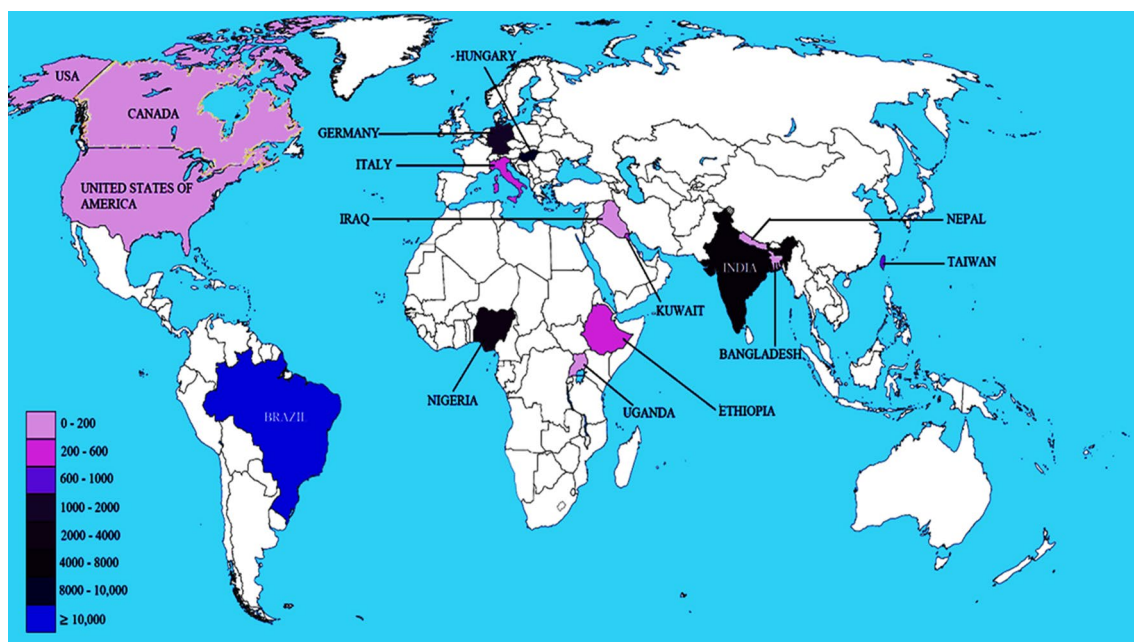

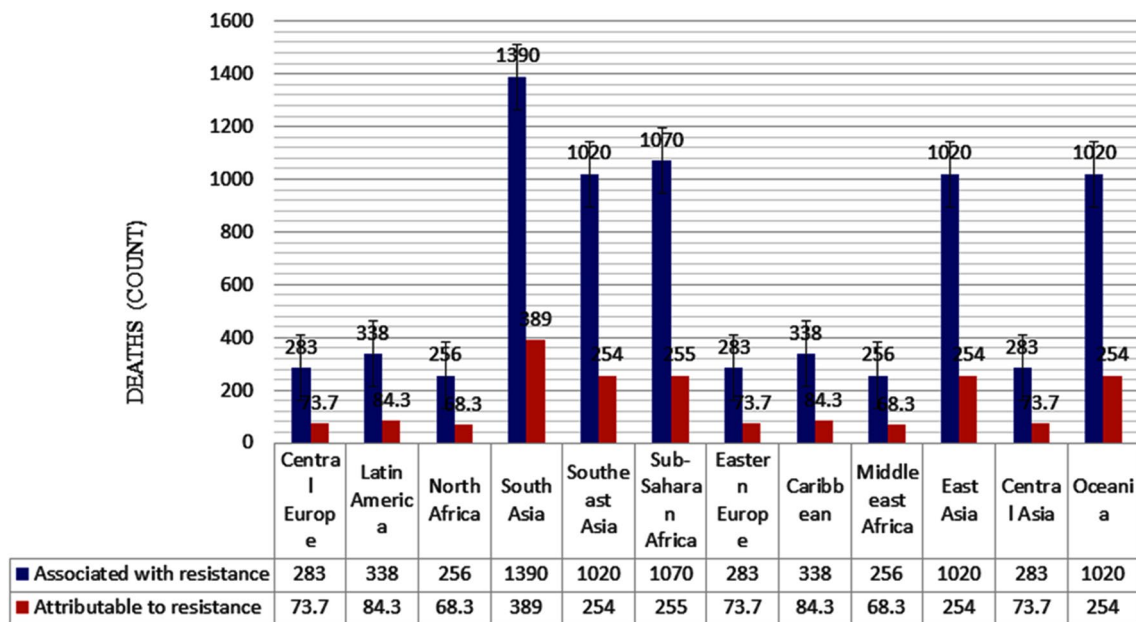**Fig. 3** Patients are affected by urinary tract infections worldwide

Fig. 4 Global incidence of antibiotic resistance and mortality rate

men and women (Fig. 1). Urine acts as a portal for releasing microbes from the urethra into the urinary tract. In addition, the opening of the urethra in women is close to vaginal cavities and even the rectum, contributing to the development of UTIs. Although *E. coli* is responsible for eighty percent of all cases of infection, in addition to the illness caused by *E. coli*, gram-positive cocci and other organisms can also cause urinary tract infections (UTIs) (Fig. 2) [4, 11]. When a bladder infection takes place, it is frequently followed by a condition of the kidneys. This, in turn, leads to a blood-borne disease, which, in extreme cases, can result in fatal consequences, including death. Because of this, severe cases of urinary tract infection (UTI) have the potential to take lives, but with the proper treatment, patients can make a speedy recovery and avoid spreading the infection. Cystitis is an infection of the lower urinary system caused by bacteria usually found in the bladder. This illness is often followed by pyelonephritis, which is an infection of the upper urinary tract. This may result from BSI, and the antibiotics are resistant to UTIs (Fig. 4) [13].

Associated Diseases

Cystitis

Inflammation of the urinary bladder causes pain and discomfort from the infection by bacteria found in the fecal microbiota. These bacteria colonize the vaginal and periurethral openings and then enter the bladder. Urine is slightly acidic, with urea and uric acid contributing to the demise of infectious bacteria and fungi. Infection from *E. coli* can be confirmed by the complex with a sugar called d-mannose, which is a kind of monosaccharide that is found in the bladder. Furthermore, enterococci and non-UTIs are caused by infection from 5 to 10% coliform aerobic Gram-negative rods. Moreover, the clinical manifestations are distinguished by symptoms such as dysuria, urine frequency, and urgency and may also be accompanied by discomfort in the suprapubic region. These are the signs of a lower UTI, which has still not moved beyond the bladder; infection is the most prevalent cause of inflammation [7].

Urethritis

Infections with microorganisms are typically the root cause of urethral annoyance. The related symptoms may be comparable to cystitis. Infectious causes, such as the fungus *Chlamydia trachomatis* or the bacterium *Neisseria gonorrhoeae*, are typically acquired via sexual intercourse and do not climb to the bladder. The urethra is the principal entry point for organisms into the bladder and BSI; the particular infections of the urethra are the typical course of UTI [8, 13].

Acute Urethral Syndrome

A 'urethral syndrome' is diagnosed when the clinical signs and symptoms of a UTI are present. Still, the urine culture does not show any positive results for the infection from any bacterium. Patients visit the hospital complaining of a bacterial infection in their lower urinary tract, which may be

caused by microorganisms or chronic diseases like diabetes. Patients may also be admitted to the facility complaining of pain in their lower urinary tract with fungi [5].

Pyelonephritis

Pyelonephritis is the infection of the kidneys from the beginning of the UTI; clinical manifestations of pyelonephritis are often more complex than those of lower urinary tract infections. Pyelonephritis occurs when bacteria from the infected bladder migrate to the kidneys. Symptoms of a lower urinary tract infection often precede an upper urinary tract infection [5, 11]; by empiric therapy or administration of some antibiotic of the higher generation or the ongoing drug of the regions, the lower UTIs are usually controlled being prompted by the unbearable pain in the lower abdomen.

Recurrent Urinary Tract Infection

A recurrence of the symptoms of a UTI after the infection may occur from the continued presence of MDR bacterial strains for the recurrence of symptoms. In adults, the recurrent UTI could be the occurrence of three or even more UTI episodes in one year [4, 6].

Statistics of Urinary Tract Infections

There were 274 million new UTIs worldwide in 2017 in people of all ages and sexes. Every year, symptomatic UTIs affect one or more episodes for about 10% of women in the USA. Women between the ages of 18 and 24 years who are sexually active have the highest prevalence of the infection. The symptoms disappear in approximately one-quarter of these women, and an equal ratio becomes infected with the causative microorganisms. The incidence of UTIs in males is lower than in women, particularly in men with urologic structural abnormalities [7, 11].

Biomass Production

Algal biomass production involves numerous phases, including culture, harvesting, and dehydration of the biomass. The open pond and closed photobioreactor (PBR) technologies are the two methods for generating or cultivating algal biomass. Then, two systems—natural waterways (ponds, lakes, and lagoons) and artificial ponds (circular and raceway)—are used to categorize the production of open ponds. The open pond is a less expensive way to produce vast amounts of algal biomass than the PBR. However, the PBR offers a tremendous and well-managed closed culture environment for growing, avoiding risk or contamination from molds, bacteria, protozoa, and competition by other algae. It is typically positioned outside to use the accessible energy sources

from sunshine. PBR is divided into three categories: flat plate, vertical column, and tubular. However, the PBR offers a tremendous and well-managed closed culture environment for growing, avoiding risk or contamination from molds, bacteria, protozoa, and competition by other algae. To make use of the accessible energy sources from sunshine, it is typically positioned outside.

The algal biomass can be separated from the culture medium or harvested by four processes: biomass aggregation (flocculation and ultrasound), flotation, centrifugation, and filtration. Combining two or more procedures is sometimes done to boost efficiency. The selection of the harvesting technique is influenced by several algae-related factors, including the density, size, and intended end products. In the biomass dehydration process, as soon as algal biomass is removed from the growing medium, it is processed to the next stage to avoid rotting or to increase its shelf life. The three most common drying or dehydrating methods are sun drying, spray drying, and freeze-drying. The desired outcomes are determined by the technique picked [14, 15].

Extraction of Phycochemicals

Algae have minerals, lipids, proteins, and carbohydrates as components. The algal biomass is pre-treated to release the stored bioactive component in the cells to use the compounds for various applications, such as biofuels/energy and agricultural use. A variety of techniques, including physical, mechanical (bead milling, homogenization, microwave, ultrasonic, and pulsed electric field), chemical (solvent, acid, and alkali), and biological (enzymes) procedures, can be used to lyse the cell walls to extract all the necessary components. A pre-treatment process method is selected based on the required end products [14].

Synergistic Effect of Phycochemicals for UTI Prevention

There has been a concerning rise in MDR bacterial strains in recent years; it has become increasingly important to locate alternative sources of antibacterial for timely control, lest increasingly higher generations of antibiotics be used. Unfortunately, the use of any newer antibiotics would induce the emergence of deadlier MDR bacterial strains, as the phenomenon of the emergence of drug-resistance bacteria is an inducible event in nature, wherein the Darwinian principle of the 'struggle for existence and survival of the fittest' is operative in microbes was nor proved by Darwin or his followers. Massively exchanging genetic characters in bacterial consortia in the body or the environment is a natural process [12]. Furthermore, research in biomedical and natural products and the utilization of bioactive chemicals derived from medicinal plants as therapeutic agents has been

a significant area of research. Likewise, algae also create an extensive range of primary and secondary metabolites with a wide range of biological activities, with inherent amino acid residues, terpenoids, phlorotannin, steroids, phenols, ketones, alkenes cyclic polysulfides, and a few more (Fig. 5) [8]. Natural compounds with pharmacological effects can be sourced from marine algal species due to their unique structural composition in blue-green algae. Incidentally, seaweed or macroalgae are highly valued because of their medicinal substances of curiosity [6].

Algae have emerged as a rich source of novel therapies since the 1940s. The three significant algae families, namely, Rhodophyceae, Phaeophyceae, and Chlorophyceae, account for most of the approximately 2400 natural products identified. Indeed, antibacterial activity was thought of as a way to identify algae as the notable medicinal potential for the production of pharmacologically active algal compounds (Table 1) [59] because of their naturally inherent secondary metabolites that have antibacterial activity against infectious bacteria invitro often envisaged. Apart from the antibacterial activity, anticoagulant and antifouling activity are identified with algal chemicals. Antimicrobial substances such as chlorellin derivatives, acrylic acid, halogenated aliphatic compounds, phenol inhibitors, and the more recently known

guanine sesquiterpenes and labdane diterpenoids were also documented in macroalgae (Table 2) [60, 61]. These antimicrobial agents were found to inhibit the growth of microorganisms in vitro (Fig. 2).

Blithely, it was found that marine algae produce a wide variety of bioactive secondary metabolites that act as antimicrobial, antifeedant, antihelmintic, and cytotoxic agents. The bioactive substances produced by marine algae are alkaloids, polyketides, cyclic peptides, polysaccharides, phlorotannins, diterpenoids, sterols, diterpenoids, quinones, lipids, and glycerols [13]. Because of the prokaryotic photosynthesizing metabolic activity, these organisms have biotechnological advantages over other organisms like plants and fungi. These advantages include the production of several compounds of curiosity that have potential applications in food, bioenergy production, and health biomaterials [13, 60].

Pigments, carotenoids, C-phycobilin, peptides, fatty acids, and polysaccharides are biologically active compounds formed by cyanobacteria. These biologically active molecules present considerable promise for pharmaceutical and cosmeceutical applications due to their antioxidant, anticancer, antimicrobial activity, antiviral, skin-regenerative, immunomodulatory, and immune-stimulatory activities. Cyanobacterial pigments have inhibited
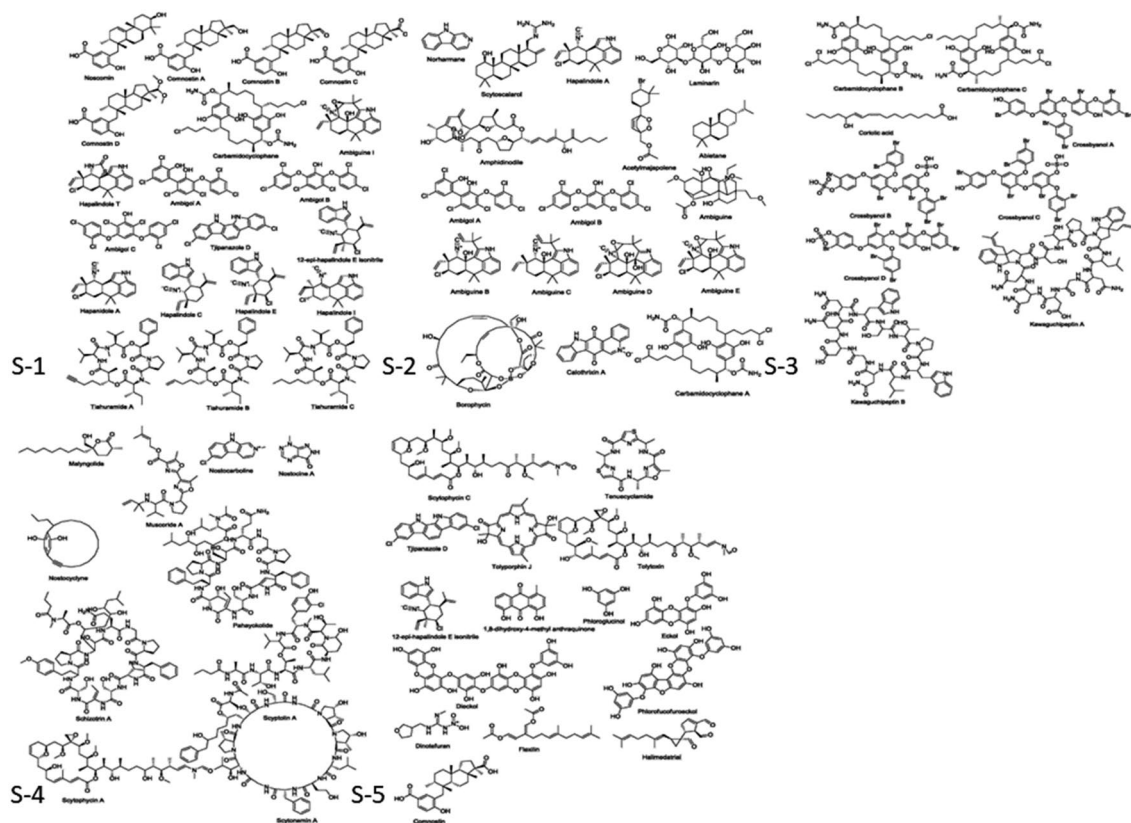

Fig. 5 Bioactive compounds of algae

Table 1 Algae-mediated inhibitory actions of UTIs

Algal Strains	UTI pathogens	Antimicrobial activity (ZOI in mm)	Reference
Blue-green algae (Cyanobacteria)			
Family: *Spirulinaceae*			
S. platensis	*E. coli, Pseudomonas* sp., *Aeromonas* sp., *Vibrio* sp.	ND	[16]
	E. coli	ND	[17]
Spirulina major	*S. enteritidis*	8 (B); 8 (tH)	[18]
	E. coli	8 (M); 9 (Eo); 9 (B); 8 (A); 8 (H); 11 (tH)	
Family: *Microcystaceae*			
M. aeruginosa	*E. coli, Pseudomonas* sp., *Aeromonas* sp., *Vibrio* sp., *K. pneumoniae*		[16]
A. platensis	*E. coli*	10 (E)	[19]
Family: *Nostocaceae*			
Nostoc sp.	*P. aeruginosa, E. coli*		[16]
	E. coli	13.3 (M); 14.3 (Eo); 12 (C)	[20]
	P. aeruginosa	13.9 (M); 11.8 (Eo); 10 (C)	
	K. pneumoniae	19 (M);20.3 (Eo); 12.3 (C)	
	B. subtilis	17 (M); 12.4 (Eo); 11.1 (C)	
	S. aureus	18.3 (M); 14.2 (Eo); 12.2 (C)	
	S. typhi	14.1 (M); 13.5 (Eo); 10 (C)	
	P. vulgaris	11 – 16 (M/10 µg): < 10 (M/20 µg): < 10 (M/30 µg): 11–16 (M/40 µg)	[21]
	K. pneumoniae	< 10 (M/10 µg); < 10 (M/20 µg); 11 – 16 (M/30 µg); 11–16 (M/40 µg)	
	P. aeruginosa	11 – 16 (M/10 µg); 11–16 (M/20 µg); < 10 (M/30 µg); < 10 (M/40 µg)	
	E. coli	< 10 (E/40 µg)	
A. sphaerica	*E. coli*	ND	[16]
A. oryzae	*B. cereus*	12.5 ± 0.35 (A); 9.33 ± 0.54 (C); 9.5 ± 0.35 (M); 12.6 ± 0.12 (P)	[22]
	M. luteus	11.33 ± 0.2 (A); 9.66 ± 0.2 (C); 7.33 ± 0.2 (M); 8.33 ± 0.2 (P)	
	K. aerogenes	7.6 ± 0.2 (A); 9.33 ± 0.2 (C); 10.33 ± 0.2 (M); 11.83 ± 0.2 (P)	
Anabaena sp.	*E. faecalis*	< 10 (E/40 µg); 11 – 16 (M/40 µg)	[21]
Family: *Oscillatoriaceae*			
O. limnetica	*E. coli, K. pneumoniae, P. aeruginosa*	ND	[16]
	S. enteriditis	9 (tH)	[18]
O. limosa	*S. enteritidis*	10 (Eo); 9 (B); 8 (A); 8 (H); 8 (tH)	[18]
	E. coli	8 (Eo); 8 (B); 8 (A); 8 (H); 9 (tH); 8 (M)	
Oscillatoria sp.	*E. coli*	10	[23]
	K. pneumoniae	9; 8	
	C. albicans	12	
O. sancta	*E. coli*	12.4 (M); 16.1 (Eo); 10 (C)	[20]
	P. aeruginosa	8.2 (M); 10 (Eo); 7.4 (C)	
	K. pneumoniae	16 (M); 13.3 (Eo); 10 (C)	
	C.albicans	12 (M); 16 (Eo); 12 (C)	
	S. aureus	13.3 (M); 14.2 (Eo)	
	S. typhi	10.2 (M); 10.4 (Eo); 8 (C)	
	B. subtilis	12.2 (M); 14.3 (Eo); 9.8 (C)	
	P. vulgaris	8 (M)	[24]
	P. mirabilis	10 (M)	
	S. aureus	8 (M); 7 (Eo); 9 (H)	
L. birgei	*P. mirabilis*	8 (M)	[24]
	P. vulgaris	8 (M)	
Lyngbya sp.	*P. aeruginosa*	11 – 16 (E); 11 – 16 (M)	[21]
	V. cholerae	< 10 (M)	
Phormidium sp.	*C. albicans*	9 (E)	[23]
	E. coli	11 – 16 (E)	[21]
P. tenue	*S. enteritidis*	7 (B)	[18]
	E. coli	8 (Eo);8 (B);8 (A);8 (M); 10 (tH)	

Table 1 (continued)

Algal Strains	UTI pathogens	Antimicrobial activity (ZOI in mm)	Reference
Family: *Chroococcaceae*			
C. turgidus	*E. coli*	ND	[16]
Chroococcus sp.	*P. aeruginosa*	11 – 16 (E); 11 – 16 (M)	[21]
	K. pneumoniae	> 17 (M)	
Family: *Synechococcaceae*			
Synechococcus sp.	*P. aeruginosa*	12.5 ± 0.71	[17]
	P. aeruginosa	14 ± 1.41	
	K. pneumoniae	< 10 (E)	[21]
	E. faecalis	– 16 (E)	
	P. aeruginosa	11 – 16 (E)	
Family: *Aphanizomenonaceae*			
N. spumigena	*B. cereus*	12.66 ± 0.2 (A); 7.83 ± 0.2 (C); 7.33 ± 0.2 (P)	[22]
	M. luteus	12.33 ± 0.4 (A); 11.66 ± 0.2 (C); 7.13 ± 0.16 (P)	
	K. aerogenes	13.83 ± 0.2 (A)	
Family: *Merismopediaceae*			
S. pevalekii	*K. pneumoniae*	5.5	[25]
	E. coli	12	
	S. aureus	14	
Family: *Rivulariaceae*			
R. mesenterica	*E. coli*	25.7 ± 0.9 (Eo); 16.2 ± 1.1 (M)	[26]
	B. cereus	18.4 ± 1.1 (Eo); 12.7 ± 0.5 (M)	
	M. luteus	25.3 ± 1.4 (Eo); 12.2 ± 1.7 (M)	
	P. aeruginosa	17.9 ± 1.2 (Eo); 14.6 ± 0.9 (M)	
	S. aureus	17.9 ± 0.3 (Eo); 14.7 ± 0.9 (M)	
	K. pneumoniae	12.5 ± 0.5 (Eo); 10.3 ± 0.5 (M)	
	C. albicans	14.4 ± 1.5 (Eo); 14.6 ± 0.5 (M)	
Calothrix sp.	*P. aeruginosa*	< 10 (E)	[21]
	E. coli	> 17 (E)	
Family: *Hapalosiphonaceae*			
W. prolifica	*E. coli*	ND	[27]
Family: *Romeriaceae*			
R. gracilis	*P. aeruginosa*	10.5 ± 0.71 (M); 11 ± 1.41 (Eo)	[17]
Diatom			
Family: *Phaeodactylaceae*			
P. tricornutum	*Vibrio* sp.	ND	[16]
Family: *Bacillariaceae*			
Nitzschia sp.	*S. aureus*	14.6 (Eo)	[28]
	E. coli	18.3 (Eo); 13.6 (M)	
Green algae			
Family: *Chlorellaceae*			
C. vulgaris	*E. coli, Pseudomonas* sp., *Aeromonas* sp., *Vibrio* sp., *K. pneumoniae*	ND	[16]
	S. enteritidis	9 (B)	[18]
	E. coli	9 (Eo); 9 (B); 9 (A); 9 (H); 11 (tH)	
	S. aureus	9	[29]
	E. aerogenes	10	
Chlorella sp.	*P. aeruginosa*	8—10.9	[30]
	E. coli	9	
	K. pneumoniae	8.6	
	E. coli	14 (M); 12.6 (Eo); 12.2 (C)	[20]
	P. aeruginosa	15.2 (M); 13.7 (Eo); 13.1 (C)	
	K. pneumoniae	14.8 (M); 13.8 (Eo); 13.5 (C)	
	C. albicans	19.8 (M); 19.1 (Eo); 19.1 (C)	
	B. subtilis	17.9 (M); 18.6 (Eo); 17.9 (C)	
	S. aureus	15.2 (M); 17.6 (Eo); 17 (C)	

Table 1 (continued)

Algal Strains	UTI pathogens	Antimicrobial activity (ZOI in mm)	Reference
	S. typhi	14.2 (M); 13.1 (Eo); 13.1 (C)	
Family: *Haematococcaceae*			
H. pluvialis	*E. coli*	ND	[16]
Family: *Oedogoniaceae*			
O. echinospermum	*E. coli*	1 (M); 12.2 (Eo); 12.1 (C)	[20]
	P. aeruginosa	12.4 (M); 13 (Eo); 12 (C)	
	K. pneumoniae	14 (M); 12.4 (Eo); 12 (C)	
	S. typhi	12 (M); 11.8 (Eo); 12.4 (C)	
	S. aureus	12 (M); 12 (Eo); 11 (C)	
	B. subtilis	12 (M); 13 (Eo); 13.5 (C)	
	S. typhi	7 (M); 7 (Eo); 7 (H)	[24]
	P. mirabilis	7 (Eo)	
Family: *Zygnemataceae*			
S. crassa	*C. albicans*	12 (M); 13 (Eo); 13 (C)	[20]
	S. aureus	8.3 (Eo)	
	S. typhi	11.7 (Eo)	
	P. mirabilis	9 (M)	[24]
	S. aureus	8 (Eo)	
S. decimina	*P. mirabilis*	9 (M)	
	S. aureus	12 (M); 9 (H)	
S. gratiana	*E. coli*	9 (Eo)	
	S. typhi	7 (M)	
	P. vulgaris	10 (Eo)	
	P. mirabilis	9 (Eo)	
S. biformis	*P. vulgaris*	8 (M)	
	S. aureus	8 (H)	
S. condensata	*P. mirabilis*	8 (M)	
Family: *Ulvaceae*			
U. lactuca	*E. coli*	18 (M); 22 (Eo); 26 (C)	[20]
	P. aeruginosa	13 (M); 13 (Eo); 23 (C)	
	K. pneumoniae	14.8 (M); 15.2 (Eo); 19.9 (C)	
	C. albicans	13.6 (M); 13 (Eo); 17.7 (C)	
	B. subtilis	11.6 (M); 12.7 (Eo); 17.4 (C)	
	S. aureus	10.1 (M); 12 (Eo); 17.2 (C)	
	S. typhi	12.3 (M); 13 (Eo); 16 (C)	
	E. coli	18 ± 0.1 (A); 36 ± 0.03 (Eo); 13 ± 0.06 (M); 11 ± 0.02 (W)	[2]
	K. pneumoniae	20 ± 0.7 (A); 34 ± 0.3 (Eo); 26 ± 0.1 (M); 21 ± 0.5 (W)	
	P. mirabilis	7 ± 0.06 (A); 39 ± 0.01 (Eo); 23 ± 0.01 (M); 13 ± 0.03 (W)	
	S. aureus	11 (C)	[31]
	E. coli	10 (C)	
	C. tropicalis	0.29 ± 0.06 (Eo)	[32]
	Streptococcus sp.	10 (Aq)	[33]
	E. coli	9 (Aq)	
	P. aeruginosa	11 (Aq)	
	P. mirabilis	9 (Aq)	
	K. pneumoniae	10 (Aq)	
	M. luteus	7 (Aq)	
	B. subtilis	9 (Aq)	
	S. aureus	10 (Aq)	

Table 1 (continued)

Algal Strains	UTI pathogens	Antimicrobial activity (ZOI in mm)	Reference
E. prolifera	*E. coli*	11.3 (M); 12.5 (Eo); 12 (C)	[20]
	P. aeruginosa	12.2 (M); 13.1 (Eo); 13.1 (C)	
	K. pneumoniae	10 (M); 12 (Eo); 12.7 (C)	
	C. albicans	13 (M); 15 (Eo); 16.1 (C)	
	B. subtilis	10.8 (M); 12.8 (Eo); 11.6 (C)	
	S. aureus	10 (M); 11 (Eo); 12.3 (C)	
	S. typhi	11 (M); 13 (Eo); 11 (C)	
E. linza	*C. tropicalis*	0.43 ± 0.05 (Eo); 2.75 ± 0.17 (M)	[32]
Family: *Cladophoraceae*			
C. antennina	*K. pneumoniae*	1–5	[34]
	P. aeruginosa	1–5	
	S. aureus	6–10	
C. socialis	*E. coli*	7 (M)	[35]
	S. xylosus	> 7 (M)	
Family: *Valoniaceae*			
V. pachynema	*P. aeruginosa*	1–5	[34]
	M. luteus	9.33 ± 0.33 (M)	[36]
	S. marcescens	8 ± 0.58 (M)	
Family: *Caulerpaceae*			
C. taxifolia	*E. coli*	24	[37]
	P. mirabilis	27	
	P. aeruginosa	20	
	K. pneumoniae	19	
	Enterobacter sp.	16	
C. racemosa	*E. coli*	9.5 ± 0.2 (E); 9.5 ± 0.3 (M)	[38]
	E. faecalis	8 ± 1.7 (E); 8 ± 0.8 (M)	
	P. aeruginosa	14.3 ± 0.3 (E)	
	Salmonella sp.	10.5 ± 1 (E)	
	S. aureus	19.2 ± 1.2 (E); 19.8 ± 0.4 (M)	
Family: *Halimedaceae*			
H. opuntia	*E. coli*	14 ± 0.05 (M); 13 ± 0.05 (Eo); 12 ± 0.07 (D)	[39]
	K. pneumoniae	16 ± 0.02 (M); 19 ± 0.08 (Eo); 13 ± 0.02 (P); 15 ± 0.07 (D)	
	E. aerogenes	15 ± 0.07 (M); 12 ± 0.05 (Eo); 12 ± 0.05 (D)	
Family: *Scenedesmaceae*			
Scenedesmus sp.	*P. aeruginosa*	7–8	[30]
	E. coli	7.7	
	K. pneumoniae	9	
Family: *Coccomyxaceae*			
C. onubensis	*P. aeruginosa*	7.4 ± 0.1 (Dich); 7.1 ± 0.1 (E); 7.3 ± 0.3 (A); 7.6 ± 0.6 (M)	[40]
	E. coli	13.8 ± 0.4 (DEth); 17.2 ± 1.4 (C); 7.4 ± 0.1 (Dich); 7.1 ± 0.1 (E); 7.3 ± 0.3 (A); 7.6 ± 0.6 (M)	
	P. mirabilis	7.4 ± 0.7 (DEth); 15.9 ± 0.4 (C); 7.7 ± 0.5 (Dich); 7.8 ± 0.3 (E); 8.8 ± 0.4 (A); 7.5 ± 0.3 (M)	
	C. albicans	7.1 ± 0.1 (DEth); 7.2 ± 0.2 (Dich); 8 ± 0.1 (E); 13.7 ± 0.1 (A); 10.5 ± 0.5 (M)	
Family: *Desmidiaceae*			
Cosmarium sp.	*M. luteus*	19.5 ± 3.5 (M); 13.5 ± 2.21 (A); 19.5 ± 2.21 (W)	[41]
	E. coli	8.5 ± 0.7 (A:M); 8 (A); 8.5 ± 0.7 (H)	
	S. aureus	14.5 ± 0.7 (A:M); 23.5 ± 0.7 (W)	
Family: *Dunaliellaceae*			
Dunaliella sp.	*E. coli*	12 – 14	[42]
Family: *Prasiolaceae*			
D. olivaceus	*E. faecalis*	9.7	[29]
	S. aureus	15	
Family: *Chlorococcaceae*			

Table 1 (continued)

Algal Strains	UTI pathogens	Antimicrobial activity (ZOI in mm)	Reference
C. humicola	*S. aureus*	11	[29]
	E. aerogenes	8.5	
	E. faecalis	9.5	
Family: *Ulotrichaceae*			
Ulothrix sp.	*S. aureus*	18.6 (Eo)	[28]
	E. coli	14.3 (Eo); 15.6 (M)	
Family: *Chaetophoraceae*			
Stigeoclonium sp.	*E. coli*	17.3 (Eo); 14.6 (M)	[28]
Red algae			
Family: *Rhodomelaceae*			
A. spicifera	*E. coli*	14.9 (M); 15.7 (Eo)	[20]
	P. aeruginosa	14.5 (M); 14 (Eo)	
	K. pneumoniae	12 (M); 11 (Eo); 6.23 (C)	
	C. albicans	11.9 (M); 10.7 (Eo)	
	B. subtilis	17 (M); 14.3 (Eo); 6 (C)	
	S. aureus	12.9 (M); 13.2 (Eo)	
	S. typhi	13.2 (M); 14.2 (Eo)	
	E. coli	1–5	[34]
	P. aeruginosa	1–5	
L. papillosa	*E. coli*	12.33±0.5	[43]
	P. aeruginosa	11.66±0.5	
L. majuscula	*S. aureus*	7 – 12 (Ela)	[44]
	Pseudomonas sp.	12 – 18 mm (Ela)	
	E. coli	12 – 18 (Iso)	
	Salmonella sp.	25- 30 (Ela); 19–24 (Iso)	
	K. pneumoniae	19 – 24 (Ela); 19 – 24 (Iso)	
L. brandenii	*E. coli, Salmonella* sp., *M. luteus, S. aureus, V. cholera, B. subtilis*	ND	[34]
Polysiphonia sp.	*E. coli*	8.33±0.5	[43]
	P. aeruginosa	9.33±0.5	
Family: *Halymeniaceae*			
G. lithophila	*E. coli*	10–15	[34]
	K. pneumoniae	6–10	
	P. aeruginosa	6–10	
	S. aureus	10–15	
G. filicina	*E. coli*	11.33±0.5	[43]
	P. aeruginosa	9.7±0.5	
Family: *Gracilariaceae*			
G. corticata	*Streptococcus* sp.	9 (Aq)	[33]
	M. luteus	10 (Aq)	
	P. mirabilis	17 (Aq)	
	P. aeruginosa	12 (Aq)	
	K. pneumoniae	12 (Aq)	
	E. coli	10 (Aq)	
G. ornata	*E. coli*	ND	[45]
G. changii	*P. aeruginosa*	MIC – 6.25 mg/mL	[46]
G. verrucosa	*E. coli*	11.41	[47]
Family: *Gelidiaceae*			
G. spinosum	*E. coli*	7±0.15 (A); 20±0.5 (Eo); 20±0.05 (M); 6±0.03 (W)	[2]
	K. pneumoniae	10±2.6 (A); 16±0.4 (Eo); 12±0.7 (M); 12±0. (W)	
	P. mirabilis	10±3.2 (A); 22±0.3 (Eo); 19±0.5 (M); 7±0.5 (W)	

Table 1 (continued)

Algal Strains	UTI pathogens	Antimicrobial activity (ZOI in mm)	Reference
Family: Galaxauraceae			
A. fragilis	*E. coli*	10.5 ± 0.5 (E); 12 ± 1 (M)	[38]
	P. aeruginosa	9.7 ± 0.7 (E)	
	Salmonella sp.	10 ± 1 (E)	
	S. aureus	9 ± 1 (E); 7.8 ± 0.6 (M)	
Brown algae			
Family: *Dictyotaceae*			
D. dichotoma	*E. coli*	1–5	[34]
	P. aeruginosa	1–5	
	S. aureus	1–5	
	E. coli	10 ± 1.0	[43]
	P. aeruginosa	8 ± 1.0	
	P. mirabilis	10 (Aq)	[33]
	S. aureus	9 (C)	[31]
	E. coli	10 (C)	
P. tetrastromatica	*K. pneumoniae*	6–10	[34]
	P. aeruginosa	6–10	
	S. aureus	10–15	
	Streptococcus sp.	8 (Aq)	[33]
	E. coli	13 (Aq)	
P. gymnospora	*S. aureus*	MIC – 500 µg/mL	[48]
	E. coli	11.3 ± 0.8 (E); 13.3 ± 0.3 (M)	[38]
	E. faecalis	9 ± 0.5 (E); 7 ± 0.5 (M)	
	P. aeruginosa	10 ± 1.2 (E)	
	Salmonella sp.	9.5 ± 1.2 (E); 15 ± 1 (M)	
	S. aureus	17.8 ± 0.8 (E); 11.5 ± 0.5 (M)	
S. marginatum	*E. coli*	6–10	[34]
	P. aeruginosa	1–5	
	S. aureus	10–15	
Family: *Scytosiphonaceae*			
P. fascia	*E. coli*	11 ± 1.6 (A); 13 ± 0.2 (Eo); 6 ± 0.4 (M)	[2]
	K. pneumoniae	8 ± 2.6 (Eo); 8 ± 0.06 (M)	
	P. mirabilis	13 ± 0.03 (A); 8 ± 3 (Eo); 9 ± 0.6 (M); 5 ± 0.02 (W)	
Family: *Sargassaceae*			
T. ornata	*E. coli*	8.6 ± 0.5	[43]
	P. aeruginosa	9.7 ± 0.5	
T. triquetra	*E. coli*	19 ± 0.05 (M); 11 ± 0.05 (Eo); 12 ± 0.02 (P); 13 ± 0.07 (D)	[39]
	K. pneumoniae	18 ± 0.12 (M); 16 ± 0.05 (Eo); 14 ± 0.05 (P); 17 ± 0.05 (D)	
	E. aerogenes	17 ± 0.07 (M); 11 ± 0.06 (Eo); 13 ± 0.08 (P); 15 ± 0.07 (D)	
C. myrica	*E. coli*	11 ± 1 (E); 8 ± 1 (M)	[38]
	P. aeruginosa	9 ± 0.5 (E); 8 ± 0.7 (M)	
	Salmonella sp.	8.5 ± 0.5 (M)	
	S. aureus	10 ± 0.5 (E); 17 ± 1 (M)	
C. trinodis	*E. coli*	7 ± 0.5 (E); 10 ± 1.2 (M)	
	E. faecalis	13 ± 1 (E); 12 ± 2 (M)	
	P. aeruginosa	9 ± 0.3 (M)	
	Salmonella sp.	10 ± 0.4 (E); 10 ± 0.4 (M)	
	S. aureus	11 ± 0.4 (E); 11.5 ± 0.5 (M)	
	E. coli	8.6 ± 0.5	[43]
	P. aeruginosa	8.33 ± 0.5	
Family: *Lessoniaceae*			
E. kurome	*C. jejuni, S. aureus, E. coli, B. cereus, S. enteriditis*	ND	[49]

Table 1 (continued)

Algal Strains	UTI pathogens	Antimicrobial activity (ZOI in mm)	Reference
E. cava	*S. aureus*	MIC: 500 µg/mL (Eo); 250 µg/mL (E)	[50]
	S. enteritidis	MIC: 2000 µg/mL (Eo); 250 µg/mL (E)	
E. stolonifera	*E. coli*	MBC: 256 µg/mL	[51]
	B. subtilis	MBC: 64 µg/mL	
	K. pneumoniae	MBC: 256 µg/mL	
Brown seaweed			
Family: *Sargassaceae*			
S. latifolium	*Salmonella* sp.	> 10 (A); 7 (M)	[55]
	E. coli	> 7 (A); 7 (M)	
	P. aeruginosa	> 7 (A); 7 (M)	
	E. faecalis	> 7 (A); 7 (M)	
	S. xylosus	> 10 (A); 7 (M)	
S. platycarpum	*Salmonella* sp.	> 7 (A); 7 (M)	
	E. coli	> 7 (A); 7 (M)	
	P. aeruginosa	> 7 (A); 10 (M)	
	E. faecalis	> 10 (A); 7 (M)	
	S. xylosus	7 (A); 10 (M)	
S. vulgare	*P. aeruginosa*	11.1 (M); 12.7 (Eo); 12 (C)	[20]
	K. pneumoniae	13.5 (M); 14 (Eo); 13.9 (C)	
	C. albicans	11 (M); 11.2 (Eo); 10 (C)	
	S. typhi	13.7 (M); 10.3 (Eo); 10.3 (C)	
	S. aureus	12.8 (M); 12.7 (Eo); 11.6 (C)	
	B. subtilis	10.9 (M); 11.2 (Eo); 11.3 (C)	
S. swartzii	*E. coli*	15 ± 0.28	[52]
	P. aeruginosa	11 ± 0.48	
	E. faecalis	10 ± 0.68	
	Proteus vulgaris	7 ± 0.72	
	A. hydrophilla	2 ± 0.32	
	Shigella flexneri	6 ± 0.78	
S. wightii	*E. coli*	8 (Eo); 9 (M); 9 (Aq)	[53]
	Enterobacter sp.	7 (Eo); 10 (M); 11 (Aq)	
	Proteus sp.	12 (Eo); 9 (M); 10 (Aq)	
	Pseudomonas sp.	6 (Eo); 8 (M); 8 (Aq)	
	Klebsiella sp.	6 (Eo); 6 (M); 9 (Aq)	
	M. luteus	10 (Aq)	[33]
	E. coli	13 (Aq)	
	P. aeruginosa	12 (Aq)	
	P. mirabilis	7 mm (Aq)	
	K. pneumoniae	10 (Aq)	
	E. coli	18.6 ± 0.11 (A); 21.5 ± 0.11 (Aq); 25.5 ± 0.86 (M)	[54]
	Enterococcus sp.	22.5 ± 0.52 (A); 18 ± 0.65 (Aq) 22.5 ± 0.52 (M)	
	P. mirabilis	21.1 ± 0.25 (A) 12.1 ± 0.15 (Aq); 25.1 ± 0.33 (M)	
	P. aeruginosa	12.6 ± 0.64 (A); 10.6 ± 0.25 (Aq); 13.0 ± 0.52 (M)	
	K. pneumoniae	11.3 ± 0.51 (A); 8.5 ± 0.56 (Aq); 12.1 ± 0.33 (M)	
S. myriocystum	*E. coli*	10.33 ± 0.5	[43]
	P. aeruginosa	8.57 ± 0.5	
S. crassifolium	*S. aureus*	20.79 ± 0.82 (E); 21.70 ± 1.77 (DEth); 16.62 ± 0.52 (C); 20.28 ± 0.49 (M)	[55]
	P. aeruginosa	8.41 ± 0.09 (E); 18.32 ± 0.40 (DEth); 9.62 ± 0.18 (C); 16.79 ± 0.83 (M)	
S. oligocystum	*P. aeruginosa*	MIC—9.556 ± 0.251 mg/ml	[56]
	S. aureus	MIC—3.175 ± 0.064 mg/ml	

Table 1 (continued)

Algal Strains	UTI pathogens	Antimicrobial activity (ZOI in mm)	Reference
S. hystrix	*E. coli*	8.5 ± 0.5 (E); 11.3 ± 0.3 (M)	[38]
	E. faecalis	7 ± 1.5 (E); 7 ± 1 (M)	
	P. aeruginosa	8 ± 0.8 (E); 15 ± 1 (M)	
	Salmonella sp.	7.5 ± 0.5 (E)	
	S. aureus	11.8 ± 0.8 (E); 13.8 ± 0.8 (M)	
S. dentifolium	*E. coli*	12.3 ± 0.3 (E); 13.3 ± 1.2 (M)	
	P. aeruginosa	9.8 ± 0.4 (E)	
	Salmonella sp.	11 ± 0.6 (E)	
	S. aureus	4.3 ± 0.5 (E); 18 ± 0.5 (M)	
Family: *Cystocloniaceae*			
H. valentiae	*E. coli*	9.0 ± 1.0	[43]
	P. aeruginosa	10 ± 1.0	
H. musciformis	*M. luteus*	12 (Aq)	[33]
	P. mirabilis	13 (Aq)	
	P. aeruginosa	12 (Aq)	
	E. coli	10 (Aq)	
Family: *Corallinaceae*			
C. elongata	*S. aureus*	10 (C)	[31]
	E. coli	11 (C)	
Family: *Codiaceae*			
C. tomentosum	*M. luteus*	9 (Aq)	[33]
	P. mirabilis	8 (Aq)	
	P. aeruginosa	10 (Aq)	
	E. coli	10 (Aq)	
C. decorticatum	*C. tropicalis*	0.54 ± 0.06 (M); 0.34 ± 0.05 (A)	[32]
C. fragile	*E. coli*	11.8 ± 0.3 (E); 14.5 ± 1 (M)	[38]
	E. faecalis	9 ± 0.7 (E); 9 ± 1 (M)	
	P. aeruginosa	9 ± 0.8 (E); 7.5 ± 0.5 (M)	
	Salmonella sp.	10 ± 0.5 (E); 6 ± 0.6 (M)	
	S. aureus	10 ± 0.2 (E); 11.3 ± 1.3 (M)	
Family: *Dictyotaceae*			
D. membranacea	*P. aeruginosa*	12.8 (M); 11.4 (Eo)	[20]
	K. pneumoniae	16.1 (M); 13.7 (Eo)	
	C. albicans	10.2 (Eo)	
	B. subtilis	12.3 (M); 11 (Eo)	
	S. aureus	14.9 (M); 13.8 (Eo)	
	S. typhi	13.4 (M); 10.9 (Eo)	
	C. albicans	11.66 ± 0.4 (Cr); 14 ± 0.5 (Eo); 15.33 ± 0.2 (A)	[57]
	S. aureus	14 ± 0.4 (Cr); 23.5 ± 0.2 (Eo); 22.5 ± 0.8 (A); 12 ± 0.6 (M)	
	E. coli	11.5 ± 0.6 (Cr); 13.66 ± 0.2 (Eo); 16.5 ± 0.4 (A)	
	E. faecalis	13 ± 0.6 (Cr); 12 ± 0.2 (Eo); 13 ± 0.4 (A)	
	B. subtilis	17 ± 0.1 (Cr); 19.66 ± 1.2 (Eo); 26 ± 0.4 (A)	
	E. faecium	18.33 ± 1.1 (Cr); 21.66 ± 0.8 (Eo); 24 ± 0.4 (A); 10 ± 0.8 (M)	
Mixed culture species			
Coelastrum sp.*, S. quadricauda, Selenastrum* sp. (mixed culture)	*P. fluorescens*	ND	[58]

Table 1 (continued)

ND Not detected; *A* Acetone extract; *Aq* Aqueous extract; *M* Methanol extract; *C* Chloroform extract; *E* Ethyl acetate extract; *Eo* Ethanol extract; *P* Petroleum ether; *W* Water; *D* Dimethyl formamide; *DEth* Diethyl ether; *Dich* Dichloromethane; *H* Hexane; *Ela* Elatol; *Iso* Iso-obtusol; *B* n-Butanol; *tH* tris HCl

S. platensis, Spirulina platensis; M. aeruginosa, Microcystis aeruginosa; A. platensis, Arthrospira platensis; A. sphaerica, Anabaena sphaerica; A. oryzae, Anabaena oryzae; O. limnetica, Oscillatoria limnetica; O. limosa, Oscillatoria limosa; O. sancta, Oscillatoria sancta; L. birgei, Lyngbya birgei; P. tenue, Phormidium tenue; C. turgidus, Chroococcus turgidus; N. spumigena, Nodularia spumigena; S. pevalekii, Synechocystis pevalekii; R. mesenterica, Rivularia mesenterica; W. prolifica, Westiellopsis prolifica; R. gracilis, Romeria gracilis; P. tricornutum, Phaeodactylum tricornutum; C. vulgaris, Chlorella vulgaris; H. pluvialis, Haematococcus pluvialis; O. echinospermum, Oedogonium echinospermum; S. crassa, Spirogyra crassa; S. decimina, Spirogyra decimina; S. gratiana, Spirogyra gratiana; S. biformis, Spirogyra biformis; S. condensate, Spirogyra condensate; U. lactuca, Ulva lactuca; E. prolifera, Enteromorpha prolifera; E. linza, Enteromorpha linza; C. antennina, Chaetomorpha antennina; C. socialis, Cladophora socialis; V. pachynema, Valoniopsis pachynema; C. taxifolia, Caulerpa taxifolia; C. racemose, Caulerpa racemose; H. opuntia, Halimeda opuntia; C. onubensis, Coccomyxa onubensis; D. olivaceus, Desmococcus olivaceus; C. humicola, Chlorococcum humicola: A. spicifera, Acanthophora spicifera; L. papillosa, Laurencia papillosa; L. majuscula, Laurencia majuscula; L. brandenii, Laurencia brandenii; G. lithophila, Grateloupia lithophila; G. filicina, Grateloupia filicina; G. corticate, Gracilaria corticate; G. ornate, Gracilaria ornate; G. changii, Gracilaria changii; G. verrucosa, Gracilaria verrucosa; G. spinosum, Gelidium spinosum; A. fragilis, Actinotrichia fragilis; D. dichotoma, Dictyota dichotoma; P. tetrastromatica, Padina tetrastromatica; P. gymnospora, Padina gymnospora; S. marginatum, Stoechospermum marginatum; P. fascia, Petalonia fascia; T. ornate, Turbinaria ornate; T. triquetra, Turbinaria triquetra; C. myrica, Cystoseira myrica; C. trinodis, Cystoseira trinodis; E. kurome, Ecklonia kurome; E. cava, Ecklonia cava; E. stolonifera, Ecklonia stolonifera; S. latifolium, Sargassum latifolium; S. platycarpum, Sargassum platycarpum; S. vulgare, Sargassum vulgare; S. swartzii, Sargassum swartzii; S. wightii, Sargassum wightii; S. myriocystum, Sargassum myriocystum; S. crassifolium, Sargassum crassifolium; S. oligocystum, Sargassum oligocystum; S. hystrix, Sargassum hystrix; S. dentifolium, Sargassum dentifolium; H. valentiae, Hypnea valentiae; H. musciformis, Hypnea musciformis; C. elongate, Corallina elongate; C. tomentosum, Codium tomentosum; C. decorticatum, Codium decorticatum; C. fragile, Codium fragile; D. membranacea, Dictyopteris membranacea; S. quadricauda, Scenedesmus quadricauda

E. coli- Escherichia coli; P. mirabilis—Proteus mirabilis; P. aeruginosa—Pseudomonas aeruginosa; P. fluorescens—Pseudomonas fluorescens; K. pneumoniae—Klebsiella pneumoniae; C. albicans—Candida albicans; M. luteus—Micrococcus luteus; P. vulgaris—Proteus vulgaris; B. cereus- Bacillus cereus; K. aerogenes- Klebsiella aerogenes S. typhi—Salmonella typhi; S. enteriditis— Salmonella enteriditis; S. aureus—Staphylococcus aureus; G. ornata—Gracilaria ornate; V. cholera—Vibrio cholera; E. faecalis—Enterococcus faecalis; E. aerogenes—Enterobacter aerogenes; C. jejuni—Campylobacter jejuni; S. xylosus—Staphylococcus xylosus; A. hydrophilla—Aeromonas hydrophilla; C. tropicalis—Candida tropicalis; S. marcescens- Serratia marcescens

various cell line activities (Fig. 1) [13, 61]. In addition, the utilization of polysaccharides derived from microalgae in the field of biomedicine has been investigated for the fact that these polysaccharides are biocompatible, biodegradable, and nontoxic, in addition to exhibiting specific therapeutic capabilities [62, 63]. Moreover, cyanobacteria are photoautotrophic and prokaryotic bacteria that are known to grow in several habitats. Those can remove nitrogen from the atmosphere, make phosphate more soluble, and are an excellent source of high-quality chemicals, renewable biofuels, and bioactive substances [13, 64]. To avoid the need for synthetic antimicrobial substances or subtherapeutic doses of conventional antibiotics, microalgae biomass cell-free extracts have been evaluated as additions to food and feed composition (Table 1) [59]. Excessive use of antibiotics, as well as chemotherapeutics to treat infectious diseases, causes MDR variations. Microalgae are a safe, cost-effective bacterial infection treatment [13]. It has been reported that some green algae, *Microcystis* sp., *Chlorella* sp., *Chroococcus* sp., *Anabaena* sp., *Oscillatoria* sp., and *Spirulina* sp. have antibacterial properties [64].

Antibiotic-like compounds may be derived from seaweeds; the indicators of antimicrobial active chemicals in seaweeds include the synthesis/conglomeration of several metabolites. Indeed, antioxidants, antivirals, anti-inflammatories, and anticoagulants are just a few of the biologically active chemicals found in abundance in seaweeds [11]. As it is, seaweeds contain chemicals with comparatively high anti-proliferating and antioxidant action; those are low in fat but include a variety of vitamins and bioactive components, such as sulphated polysaccharides and terpenoids. Sulphated polysaccharides are a promising natural antioxidant without any cholesterol that is scarce in land plants [13]. These activities previously include anticoagulant, anti-hyperlipidemic, antiviral, antitumor, and antioxidant activity [65]. Because the brown alga *Sargassum swartzii* produces a natural product free of harmful side effects and displays antioxidant and antibacterial activity, this natural substance should be explored for synthesizing some newer medicines to control pathogenic microbes [13]. The bioactive compounds can be virulent factors or beneficial medications and chemicals that assist in creating industrial commodities. These metabolites play a role in determining how humans associate and value particular substances. Terpenoids comprise a significant portion of this category of natural products. They include thousands of structures involved in various biological process abnormalities [11].

Terpenes

Algae are the most common source of terpenes, a type of isoprenoid. These chemicals are responsible for controlling the aromas, flavours, and pigments that they produce. Terpenes have several different beneficial interactions within the body. These might be effective in warding off infections, predators, etc. Antibacterial terpenes are produced by cyanobacteria in low quantities [96]. *Microcoleus lacustri* has norbietane; *Nostoc commune* has noscomin and comnostin (A, B, C, D, E) had shown antibacterial activity against *E. coli*, *S. aureus*, *B. cereus,* and *S. epidermidis* (Fig. 5) [66, 67, 77, 89, 91]. Moreover, *Udotea flabellum*, *U. conglutinata*, *Halimeda* sp., and *Laurencia* sp. possess terpenoids (udoteafuran, flexilin, halimedatrial), and acetylmajapolene A, B, which were effective against *S. aureus*, *P. mirabilis* and *P. vulgaris* [75, 97].

Aromatic Compounds

Antibacterial activity was proven against *E. coli*, *S. aureus,* and *Micrococcus luteus* by aromatic bioactive compounds isolated from *Nostoc* sp., *Fischerella* sp., and *Eucapsis* sp., respectively. These compounds include carbamidocyclophanes and ambigol (A, B, C) [66, 67].

Alkaloid

Most of the antibacterial alkaloids that have been identified from cyanobacteria are compounds that contain indole. The antibacterial activity of alkaloids (ambiguine, hapalindole, laminarin, nostocarboline, and tjipanazole D) isolated from cyanobacteria *Fischerella* sp., *Hapalosiphon fontinalis*, *Nostoc* sp., and *Westiellopsis* sp., as well as brown algae, *Ascophyllum nodosum,* and *Laminaria hyperborea* were effective against pathogenic bacteria revealed the presence of brominated indoles and norharman. These two types of indole alkaloids were effective against harmful microorganisms (Fig. 5) [59]. Many compounds in the hapalindole class exhibit potent antibacterial action against Gram-positive and negative bacteria. It was revealed that the antibacterial activity of 12-epi-hapalindole E isonitrile was due to the ability of the compound to block the RNA polymerase of bacteria. It was found that the cyanobacterial alkaloid calothrixin A, which was isolated from the cyanobacterium *Calothrix* sp., blocked bacterial RNA polymerase [13].

Lipids

It was found that certain fatty acids derived from marine algae possessed antimicrobial properties. The lipids had antibacterial properties, and those also acted as QS inhibitors.

The fatty acids coriolic acid, -linolenic acid, and -dimorphecolic acid isolated from *Fischerella* sp. and *Oscillatoria* sp. could inhibit the growth of the pathogenic bacteria *M. flavus and S. aureu`s* [93].

Proteins

Some methods are mainly extracting proteins like conventional protein extraction methods, current protein extraction methods, and enrichment methods—membrane filtration, previously reported [99]. Moreover, marine algae are an excellent source of proteins, mainly green and blue-green alga, which have 40–60 percent proteins and offer various health benefits to men and animals. The proteins C-phycocyanin and phycobiliprotein derived from *Anabaena* sp., *Spirulina* sp., *Westiellopsis* sp., *Synechocystis* sp., and *Streptomyces* sp. were active against *E. coli*, *K. pneumoniae,* and *Pseudomonas* sp. [63].

Peptides

Peptides inhibit the growth of bacteria and are an essential functioning component of the immune system. Cyclic peptides are either ribosomally synthetically produced and post-translationally altered (RiPPs) or non-ribosomal peptides resembling a significant class of bioactive cyanobacterial bioactive molecules. RiPPs are made by ribosomes, and RiPPs are modified post-translationally. The cyanobactins constitute the most prominent family of RiPPs, and most of its members have undergone post-translational alterations, such as the formation of a macrocyclic core structure [89]. Kawaguchipeptins A and B, discovered from *Microcystis aeruginosa* are two particularly antimicrobial examples. Antibacterial properties were demonstrated by bioactive peptides such as tiahuramide (A, B, and C) and borophycin, which were derived from *Lyngbya* sp. and *Nostoc* sp. Respectively (Fig. 5). These peptides had promising activity on *M. luteus* and *E. coli*. Antibacterial activity was demonstrated by muscoride A, a linear peptide, as well as by schizotrin A and scytonemin A, lipopeptides derived from *Nostoc* sp., *Schizothrix* sp., and *Scytonema* sp. Respectively (Table 2). In addition, lyngbyazothrin, pahayokolide, scyptolin, and tenuecyclamide can potentially prevent bacterial infection growth in vitro [17, 80].

Polyphenols

Algae are responsible for the production of polyhalogenated compounds (PHCs), such as the chlorinated ambigols A, B, and C, which have been isolated from *Fischerella ambigua* and had potent activity against Gram-positive bacteria and mammalian cancer cell lines (Table 2). The cyanobacterium *Leptolyngbya crossbyana* was used to isolate

Table 2 Inhibition of UTI using of phycocompounds

Algal species	Compounds	Class	Activity on UTI pathogens	Reference
N. commune	Noscomin	Diterpenoids	*S. epidermidis, E. coli*	[62]
	Comnostin (A, B, C, D)	Terpene	*E. coli*	[63]
Nostoc sp.	Carbamidocyclophane	Aromatic	*S. aureus, E. coli, S. albus, P. aeruginosa, M. flavus,*	[62]
Fischerella sp.	Ambiguine I isonitrile	Alkaloids		
	Hapalindole T			
M. lacustris	Norbietane	Diterpenoid		
N. muscorum	Phenolic compound	Phenols		
O. redeki	Fatty acids	Lipids		
C. taxifolia	Endophytic actinomycetes		*E. coli, P. mirabilis, P. aeruginosa, K. pneumonia Enterobacter* sp.	[37]
Chlorella sp.	Chlorellin		*E. coli, P. aeruginosa*	[64]
Anabaena sp.	C-Phycocyanin	Protein	*E. coli, K. pneumonia*	[65]
F. ambigua	Ambigol A	Aromatic	*E. coli*	[66]
Fischerella sp.	Ambigol B	Aromatic	*M. luteus, E. coli, P. mirabilis, K. aerogenes, P. aeruginosa*	[63]
	Ambigol C	Aromatic		
	Tjipanazole D			
	12-epi-hapalindole E isonitrile	Alkaloids		
	γ-Linolenic acid	Lipid		
	Hapanidole A	Alkaloids		
H. fontinalis	Hapanidole A	Alkaloids	*E. coli, K. pneumoniae, P. morganii, M. luteus, P. vulgaris*	
	Hapanidole C			
	Hapanidole E			
	Hapanidole I			
Lyngbya sp.	Tiahuramide A, B and C	Peptide	*M. luteus, E. coli*	
N. harveyana	Norharmane-HCl (9H-pyrido(3,4-b) indole-HCl)	Alkaloid	*E. coli, P. aeruginosa*	
Scytonema sp.	Scytoscalarol		*E. coli*	
Spirulina sp.	C-Phycocyanin	Protein	*E. coli, K. pneumoniae, P. aeruginosa*	
Westiellopsis sp.	C-phycocyanin	Protein	*Pseudomonas* sp., *E. coli*	
	Hapanidole A (R)	Alkaloid		
A. nodosum	Laminarin	Alkaloid	*E. coli*	[67]
Amphidinium sp.	Amphidinodile Q		*E. coli*	[68]
S. fusiformis	Phycobiliproteins	Protein	*E. coli*	[69]
L. hyperborea	Laminarin	Alkaloid	*E. coli*	[67]
Synechocystis sp.	Phycobiliproteins	Protein	*E. coli*	[69]
S. platensis	C-phycocyanin	Protein	*K. pneumoniae*	[70]
Laurencia sp.	Acetylmajapolene A and B	Halogenated sesquiterpenes	*P. mirabilis, P. vulgaris*	[71]
L. majuscule	Halogenated compounds		*E. coli, K. pneumonia, Pseudomonas* sp., *Salmonella* sp., *S. epidermis*	[44]
S. cinereum	Methanol extract	Alcohol	*S. typhi, P. aeruginosa, Klebsiella* sp.	[72]
M. lacustris	Abietane	Diterpenoid	ND	[73]
F. ambigua	Ambigol (A, B) (R)	Aromatic	Biological activities	[74]
	Ambiguine	Indole alkaloid	*B. anthracis*	[75]
	Ambiguine (A, B, C, D, E, F, H, I, K, M) Isonitrile			
N. linckia, N. spongiaeforme	Borophycin	Peptide	ND	[76]
Calothrix sp.	Calothrixin A	Indolophenanthridine	Antibacterial activities	[77]

Table 2 (continued)

Algal species	Compounds	Class	Activity on UTI pathogens	Reference
Nostoc sp.	Carbamidocyclophane (A, B, C, D, E)	Cyclophane	Cytotoxic activities	[78]
O. redekei	Coriolic acid	Fatty acid	*B. subtilis, M. flavus, S. aureus*	[79]
L. crosbyana	Crossbyanol (A, B, C, D)	Polyphenyl ether	MRSA bacteria	[80]
M. aeruginosa	Kawaguchipeptin (A, B)	Cyclic undecapeptide	*S. aureus*	[81]
Lyngbya sp.	Lyngbyazothrin (A, B, C, D)	Cyclic undecapeptide	*B. subtilis, E. coli, P. aeruginosa*	[82]
L. majuscula	Malyngolide	Polyketide hybrid	Biological activities	[83]
N. muscorum	Muscoride A	Linear peptide	ND	[84]
M. lacustris	Norbietane	Diterpenoid	Pharmacological activities	[85]
N. harveyana	Norharmane	Indol alkaloid	Biological activities	[86]
N. commune	Noscomin	Diterpenoid	*E. coli, S. epidermidis, B. cereus*	[87]
Nostoc sp.	Nostocarboline	Alkaloid	ND	[88]
N. spongiaeforme	Nostocine A	Extracellular pigment	ND	[89]
Nostoc sp.	Nostocyclyne	Polyketide	Antimicrobial activities	[90]
Lyngbya sp.	Pahayokolide (A, B)	Cyclic peptide	ND	[91]
Schizothrix sp.	Schizotrin A	Lipopeptide	*E. coli, P. fluorescens*	[92]
S. hofmanni	Scyptolin A	Cyclic depsipeptides	*C. albicans*	[93]
S. pseudohofmanni	Scytophycin A	Marcrolide	ND	[94]
Scytonema sp.	Scytonemin A	Lipopeptide	ND	[95]
S. pseudohofmanni	Scytophycins C	Macrolide	Antifungal activities	[96]
N. spongiaeforme	Tenuecyclamide (A, B, C, D)	Cyclic hexapeptides	ND	[76]
F. ambigua	Tjipanazole D (R)	Alkaloid	*E. coli*	[74]
T. nodosa	Tolyporphin J	Porphinoid	Antibacterial activities	[97]
S. ocellatum, T. conglutinate	Tolytoxin	Macrolide	Biological effects	[98]
N. commune	1,8-dihydroxy-4-methyl anthraquinone	Polyketide	*E. coli, S. epidermidis, B. cereus*	[87]
O. redekei	α-dimorphecolic acid	Fatty acid	*B. subtilis, M. flavus, S. aureus*	[79]
N. commune	4-hydroxy-7-methyl indan-1-on	Indane	*E. coli, S. epidermidis, B. cereus*	[87]
E. cava	Eckol	Phlorotannins	*S. aureus*	[50]
E. kurome	Phloroglucinol Eckol Dieckol 8,8′—bieckol	Phlorotannins	*C. jejuni, S. aureus, E. coli* *B. cereus, S. enteriditis*	[49]
E. stolonifera	Dieckol	Phlorotannins	*E. coli, B. subtilis, K. pneumoniae*	[51]
E. kurome	Phlorofucofuroeckol A	Phlorotannins	*S. aureus, E. coli, B. cereus, S. enteriditis*	[49]
N. commune	Comnostin (E, D, C, B, A)	Diterpenoids	*E. coli, S. epidermidis, B. cereus*	[87]

Nostoc commune; Microcoleus lacustris; Nostoc muscorum; Oscillatoria redeki; Caulerpa taxifolia; Hapalosiphon fontinalis; Nodularia harveyana; Ascophyllum nodosum; Spirulina fusiformis; Laminaria hyperborean; Streptomyces platensis; Laurencia majuscule; Sargassum cinereum; Microcoleous lacustris; Nostoc linckia; Nostoc spongiaeforme; Leptolyngbya crosbyana; Microcystis aeruginosa; Lyngbya majuscula; Microcoleus lacustris; Nostoc spongiaeforme; Scytonema hofmanni; Scytonema pseudohofmanni; Nostoc spongiaeforme; Fischerella ambigua; Tolypothrix nodosa; Scytonema ocellatum; Tolypothrix conglutinate; Ecklonia cava; Ecklonia kurome; Ecklonia stolonifera; Laurencia brongniartii; Turbinaria ornate; Sargassum wightii

S. albus—Staphylococcus albus; *M. flavus*—Micrococcus flavus; *P. mirabilis*—Proteus mirabilis; *P. aeruginosa*—Pseudomonas aeruginosa; *K. pneumoniae*—Klebsiella pneumonia; *M. luteus*—Micrococcus luteus; *C. jejuni*—Campylobacter jejuni; *S. enteriditis*—Salmonella enteriditis; *K. aerogenes*—Klebsiella aerogenes; *P. morganii*—Proteus morganii; *P. vulgaris*—Proteus vulgaris; *B. cereus*—Bacillus cereus; *B. subtilis*—Bacillus subtilis,

polybrominated crossbyanols. Crossbyanol B, which has two sulfo substituents, was the only chemical that demonstrated substantial effectiveness in the brine shrimp lethality test and against MRSA [86].

Polyketides

The three different kinds of polyketide synthases (PKSs) contribute to the production of polyketides, leading to natural products with a wide range of chemical possibilities. Moreover, PKSs gene clusters responsible for producing these chemicals in cyanobacteria have been discovered. In a recent study, cyanobacteria were designed to create polyketides. The biosynthesis of alkylresorcinols is a chemical family that has received the most attention. Nostocyclyne A, 1,8-dihydroxy-4-methyl anthraquinone, carbamidocyclophanes, and cylindrocyclophanes are examples of other members of this chemical family with antibiotic activity (Table 2) [61]. The above compound could prevent the growth of several Gram-positive human pathogenic strains, such as *Streptococcus pyogenes*, *Staphylococcus aureus,* and *Bacillus subtilis*; it also had antiplasmodial activity. Malyngolide was the first polyketide antibiotic isolated from cyanobacteria in 1981 from *Lyngbya majuscule* [95].

The less recent research was focused on isolating alkyne-containing polyketides, synthesizing them, and determining whether these are effective against MRSA. These instances illustrate the possibility that cyanobacterial polyketides could be used to treat infections caused by resistant strains [97].

Other Classes

In addition to chlorellin from *Chlorella* sp., endophytic actinomycetes from *Caulerpa* sp., *Turbinaria* sp., and *Sargassum* sp., and halogenated compounds from *Laurencia* sp. demonstrated antibacterial action against *E. coli*, *K. pneumoniae,* and *Pseudomonas* sp. in vitro [11, 59].

Challenges for Phycocompounds

Microalgae are a rich source of valuable active bio-compounds such as carotenoids, C-phycocyanin, phenolics, amino acids, polyunsaturated fatty acids, sulphated polysaccharides, pigments, lipids, phlorotannins, polysaccharides, peptides, terpenes, polyacetylenes, sterols, indole alkaloids, these chemicals, which were associated with various pharmacological actions, such as the control of bacteria, viruses, tumors, inflammation, and allergies (Table 2) [30]. The fact that these compounds are only found in trace amounts in the extracts is one of the limitations. It is essential to study the many approaches that can be taken to boost the synthesis of these compounds [13].

Since algal slow-growth, periodicity, and low extraction yields are additional fundamental limitations, one of the significant issues in this area is the sustainable synthesis of these chemicals to supply enough for preclinical, clinical, and future commercialized drugs. By such a need, the whole chemical synthesis can ensure the long-term and steady production of the bioactive molecules, given the expansion of the scope of their uses [87].

Future Prospective

New methods in molecular biology, such as CRISP/ Cas9 and genomic research, could make it possible to obtain larger quantities of compounds without the need for many reagents or a significant amount of time, which would result in a reduction in the cost related to the mass production of these molecules [7, 59].

To design novel extraction processes, explore untouched marine sources with hidden medicinal values, and investigate structural interactions between active constituents from the same and multi-source. The elucidation of intermediate interactions of bioactive cofactors and their potential applications for marine-derived bioactive compounds shall be considered in the future [13]. As the source of several therapeutically beneficial chemicals, cyanobacteria have significant therapeutic potential. Numerous studies have been conducted on the pharmacological activities of cyanobacteria, including their bioactive components [62]. However, more in vivo and in vitro investigations employing various animal models and clinical studies will be required to bring cyanobacteria with their bioactive constituents into the translational mode for society.

Further research is required to assess the compounds in more intricate biological systems, such as in vivo models. The potential for 3D chemical structure modeling approaches to be used in the search for new biological targets for algae-derived chemicals has yet to be fully realized [11]. Furthermore, the potential of medicinal co-adjuvants generated from algae should be studied. Some algae-derived substances have limits that could be mitigated, and their efficacy could be enhanced by applying cutting-edge techniques like nanotechnology to create novel nano-formulations. However, more advanced technologies are required to verify whether their antimicrobial efficacy could be improved in nano-formulations [98].

Despite the literature addressing female UTIs and their risk factors, much remains to be learned. Methods to reduce the danger of UTIs are under scrutiny. Strategies for managing several essential issues, including pregnancy, diabetes, anaemia, etc., are still being researched and developed. Despite growing interest from public health groups, research into public education about UTIs and their causes has been

sparse. There should be more nontoxic antibacterial through which MDR microorganisms can be controlled [6].

Conclusion

The gargantuan types of secondary metabolites produced by algae have the potential to serve as a rich source of new entities that can lead to the formulation of new medications. Those metabolites can also have peptides, alkaloids, indole alkaloids, polyketides, and terpene chemical structures, and many of these molecules have a wide range of pharmacological properties. The enormous chemical diversity and biological activities of algal products have prepared those sources an appealing candidate for developing novel drugs for application in various therapeutic domains; nonetheless, the historical underappreciation of algae compared to other microbial sources of natural products. Thus, the pharmacological potential of algae advantages increased attention from the scientific community and research that draws from various fields. In addition, the diverse algal strains originating from environments that still need to be well investigated can be promising candidates for use in the pharmaceutical industry.

The oxygenic photosynthetic blue-green algae are found in various biological niches worldwide. Over the past two decades, researchers have recognized algae as a promising resource for developing novel therapeutic lead compounds due to the wide range of actions displayed by the bioactive molecules isolated from them. Because it can be grown with relatively inexpensive inorganics, cyanobacteria offer another benefit as the microbiological source for drug development. As a result, the blue-green algae may treasure broader application in drug research.

Data and Material Availability All data generated or analyzed during this study are included in this published article.

Code Availability Not applicable.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval Not applicable.

Informed Consent This article contains no studies with human participants or animals performed by authors.

Publication Consent Not applicable.

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