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MEDICINAL BENEFITS OF ALGAE

Author's Name: Zainulabdeen H. A. Al-Khafaji[1] , Israa N.Al-Asady[2]

Affiliation:

1. Department of Biology, College of Education for Pure Science, University of Mosul, Mosul, Iraq
2. Department of Biology, College of Education for Pure Science, University of Mosul, Mosul, Iraq

Corresponding Author Name & E-Mail: Zainulabdeen H. A. Al-Khafaji[1], zainulabdeen.hamzah@uomosul.edu.iq

Abstract

Algae contain various components those that have shown a great potential to be used for human health and medical. The therapeutic properties of algae exhibit vast range of applications like cardiovascular health, anticancer, anti-inflammatory, anticoagulant, antiviral, antibacterial, antifungal, and others in human medicinal products. Algal components are used to enhance immune system and to reduce blood cholesterol and are effective against hypercholesterolemia. Algae contain effective components that can remove harmful elements from the human body and have properties of antitumor, stomach ulcer, and wound healing. The extract of microalgae enhances blood hemoglobin concentration and decrease blood sugar level. Some algal species are extensively used to form analgesic, broncholytic, and antihypertensive medicines. Large quantities of bioactive components obtained from microalgae have strong beneficial properties which reduce the production of inflammatory compounds, effective against muscle degradation. Algal bioactive components play a potential role in disease-inhibiting and health-promoting medicines like capsules, tablets, powders, and gels. This article also reviews the health risks regarding algae intake.

Keywords: **Algae, active compound, antimicrobial**

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INTRODUCTION

Algae are organisms that resemble plants but lack roots, stems, and leaves. They use the photosynthetic process to transform light energy into chemical energy. The divisions of lower plants that include chlorophyll in plant cells are known as algae, which are one of the main producers. They may be broadly categorized into macro-algae and micro-algae. There are 30,000 species of algae in the world, which provide the biosphere with oxygen, food for fish and humans, phytochemicals, medicines, and fertilizers, as well as being a source of naturally occurring compounds with distinctive structural properties [1].

Spirogyra, a filamentous green algae of the order Zygnematales, is a freshwater macroalga that has unique physiologically active chemicals for use as an antibiotic, an antiviral, an antioxidant, and an anti-inflammatory . With 400 species, primarily free-floating algae, the genus *Spirogyra* is a member of the Chlorophyceae family of algae. With very few exceptions, they are often found in freshwater ponds and lakes with sluggish moving water[2] . The anti-viral, anti-bacterial, and anti-fungal characteristics of *Spirogyra* species also have a number of biomedical uses that could benefit human health. Musk grass, also known as *Chara vulgaris*, is a type of freshwater green alga that can be found throughout the world in a variety of habitats. A submerged species known as *C. vulgaris*, it can adapt to survive in ponds, streams, and rivers, among other types of environments. Extracts from *chara* algae have demonstrated some antibacterial and bactericidal properties. Additionally, the pharmaceutical industry received approval for the *C. vulgaris* isolates [3].

People of all ages are affected by urinary tract infections (UTIs), which are typically characterized by inflammation of the urinary system, which includes the kidney, ureters, bladder, and urethra. are a common issue that are brought on by microbial invasion of various urinary tract tissues [4]. While kidney and ureter infections are a sign of an upper urinary tract infection, bladder and urethral infections are referred to as lower urinary tract infections. The infection linked to kidney damage is a major concern, whereas cystitis is a frequent sort of infection. The catheter-acquired urinary tract infection is the most prevalent medical device infection, and this amount of time is sufficient for bacterial development in the catheter. It has been demonstrated that the growth of antibiotic-resistant bacteria is contributing to the problem of infectious diseases that are potentially fatal, which has a negative effect on the health of human populations [5]. It is vitally necessary to find new antibacterial medications with a potential innovative mechanism of action to overcome this obstacle. Unfortunately, the rate of discovery of new, effective antibiotics is steadily dropping despite the enormous effort made by various research groups and pharmaceutical corporations worldwide. which is significantly lowering our chances of coming up with a solution to this ongoing dilemma. Because of the side effects of the antibiotics and microbial resistance, specialists have been encouraged to use extracts and bioactive compounds derived from different plant-based varieties used in herbal medicine [6].

Scientists and researchers in the field of drug and pharmaceutical production have been working on alternative therapies for natural products, which may have a more specialized effect on conventional treatments, the active compounds produced from intracellular extracts and extracellular extracts were powerful alternatives that imposed themselves strongly on the therapeutic arena. In general, these compounds have many therapeutic properties, such as antibacterial, antifungal and anti-algae, as well as antimicrobials and antibiotics Cancer or cancer-protective and many other indications [7].

Algal extract is commonly used as an antibacterial due to its natural nature and little risk of

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microorganisms gaining resistance. Compared to their synthetic alternatives, they might cause fewer negative side effects in humans and animals and less environmental dangers. Because of interactions between several molecules with antioxidant characteristics, algae have an intriguing antioxidant system that is thought to be more effective. The pigments, phenols, flavonoids, and vitamins present in algae are the most potent antioxidants [8].

Due to their potential for cancer and mutagenesis consequences, consumption of synthetic antioxidants has recently been banned. Consequently, the use of natural antioxidants has garnered a lot of attention. Natural antibacterial and antioxidant capabilities of plant extracts have been documented, and their functional qualities are related to the presence of secondary metabolites like phenolic compounds [9].

2. Review

2-1. Algae

Algae are a large variety of autotrophic organisms that have the ability to polarize light through the process of photosynthesis and the conversion of inorganic materials from water and carbon dioxide into organic matter, where energy is stored [10]. Algae is characterized by a variety of appearance, ranging from small unicellular kelp to huge kelp, which is more than 70 meters long.The first appearance of algae goes back to the Precambrian era 3.5 billion years ago, and it has their role in maintaining the balance of all ecosystems, whether on the sea or on land, as it is an essential source of food[11].

Neighborhoods Green algae is one of the most widespread types of algae around the world, living in many environments such as fresh water. They are also found in saline water, which represents about 10%, and grow vigorously, or adherent to rocks (endolithic) or wet soil (endaphic) or plants (epiphytic). Some algae live in the sulfuric hot spring waters, which range between 50-70 ° C. Some species have been identified in Polar Regions such as *Phormidium*. the plastids of green algae show a great variety in their shapes and sizes, they may be goblet or hydrangea [12].

The cell wall contains cellulose, and it may contain total betaine, (pectin) (chitin) the representative stability represented by chlorophyll a, b and xanthophyll dyes. These include neoxanthin, (b-carotine) Zeaxanthin and lutein. neoxanthin as for the stored food, it consists of carbohydrates represented by [13]. There are thousands of species of algae. Although each researcher classifies algae according to various criteria, marine algae are typically separated into microalgae and macroalgae, or seaweed, despite the fact that the taxonomic categorization of algae is a delicate topic. For the sake of this discussion, macroalgae are further divided into the following three major groups: green (Chlorophyta), brown (Phaeophyta), and red algae (Rhodophyta). These three categories contain thousands of species, many of which are edible [14].

Additionally, they have long been utilized in traditional medicine to treat a variety of illnesses (tuberculosis, arthritis, colds and influenza) [15]. Many cultures, notably those in Asia where they have a high nutritional value, include seaweeds in their diets. In addition to their concentration in micronutrients (such as salts, minerals, and vitamins) important for the proper and healthy functioning of the organism, algae are a valuable source of protein (5–14%), fiber, lipids (3%), and carbs (13–19%) [16].

A number of secondary metabolites, including phenolic substances, phycobiliproteins, carotenoids, alkaloids, terpenes, sulfated polysaccharides, and phytosterols, are also abundant in them [17]. Numerous algae are capable of producing a respectable amount of protein relative to their dry weight, making them excellent sources of protein for organic fertilizer, animal feed, and human nutritional supplements [18].

2-2. Freshwater Environments

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Oceanography and limnology, which study water bodies within continental limits, are the two main subfields of aquatic biology (dealing with oceans and seas, occurring between continents). Aquatic algae found inside continental limits, where the water is normally fresh (not salty), and where there are primarily two types of water bodies [19]:

1- Standing waters particularly lakes and wetlands.
2- Running waters including streams and rivers.

2-2-1. Planktonic Algae

Where the light is bright enough for them to make food through photosynthesis, phytoplanktonic algae predominate on the surface of standing waters. Green algae, blue-green algae, diatoms, and euglenas often make up the planktonic algae community. Depending on the trophic level of the lake, these blooms are desirable since they mark the start of the food chain. Algal blooms involve a wide variety of species, and these species evolve throughout time in response to changes in temperature, light, nutrition, and other variables [20].

2-2-2. Benthic Algae

Benthic algae, which are found at the base of the water column in lakes and rivers and are closely related to sediments like rocks, mud, and organic material. Mixed biofilms frequently contained them (with bacteria, fungi and invertebrates). High light levels may cause massive growths of filamentous algae to dominate the biofilm and establish a periphyton ecosystem. Bigger connected algae, larger attached algae, and giant planktonic colonial algae are all examples of attached algae that can be glued to living things as epiphytes. There are stages in the life cycles of many algae species that are both planktonic and benthic. In some instances, they started out as actively photosynthetic benthic creatures before separating and becoming planktonic [21].

2-3. Some groups of macroalgae which found in fresh water

2-3-1. *Spirogyra* spp

In shallow waters, a genus of filamentous, unbranched green algae called *Spirogyra* spp. creates free-floating mats. It frequently grows in shaded littoral zones of lakes, meandering streams, and stagnant waters like ponds and canals [22]. Approximately, there are around 400 species of *Spirogyra* found. They have a vegetative structure that is most easily identified by the stunning spirally coiled chloroplast found in algal cells. The photosynthetic genus Spirogyra makes a significant contribution to the overall carbon dioxide fixation process. They raise the oxygen content in their environment. Numerous aquatic species consume them [23].

The cell wall, which gives the algae their slippery texture, is made up of an exterior layer of pectin and an inner layer of cellulose . Spirogyra blooms underwater in the spring. the filament's length The height of Spirogyra varians is (125-200 m) and its breadth is (28-30 m). Only the middle of the gametangia's shape is inflated. Pyrenoids, which are found in large numbers and store protein and starch in the chloroplast [24].

The green color of *Spirogyra varians* is mostly due to the presence of chlorophyll-a and chlorophyll-b. The macroalga, however, appears yellow or orange in some culture/stress settings because of the presence of secondary pigments (carotenoids). Since it absorbs light energy, chlorophyll is crucial for photosynthesis since this energy is later transformed into chemical energy that is bound up in biomass. Biologists, ecologists, and industrialists typically take biomass measurement into consideration. According to the algal species, taxonomic makeup, and physicochemical and biological parameters, the amount of algal Chl/carotenoids and its efficacy varies [25].

Due to its significant antioxidant properties, spirogyra is now a common element in cosmetic, food supplement, and medicinal goods. A review of the nutritional values showed that protein,

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magnesium, and manganese were all in high concentrations [26]. Previous studies have shown that *Spirogyra* spp. extract has additional biological functions. freshwater green algae ethanol extracts When examined using the DPPH radical scavenging activity test, Spirogyra gratiana demonstrated strong antioxidant activity [27].

The approved *Spirogyra* genus classification according to (prescott, 1979) is:-

Kingdom: Plantae Division: *Chlorophyta*
Class: *ygnematophyceae*
Order: *Zygnematales*
Family: *Zygnemataceae*
Genus: *Spirogyra*
Species: *Spirogyra varians*

The life cycle of *Spirogyra* occurs via one of the three ways; vegetative, asexual, and sexual. Vegetative reproduction under the favorable conditions occurs by fragmentation that develops into a new filament , while asexual reproduction happens when the protoplast shrinks and develops a wall around it under adverse conditions, resulting in the creation of zygospores, akinetes, or aplanospores. Because both A planospores and Akinetes are non-motile spores, their formation is comparable. However, Akinetes has a thicker cell wall made of cellulose and pectin [28].

Last but not least, sexual reproduction occurs through conjugation, which is defined as "two threads of Spirogyra come together and lie side by side." Scalariform conjugation and lateral conjugation are the two types of conjugation. The male gamete of one filament fuses with the female gamete of the other, leaving one filament empty and the other containing zygotes. After the parent filament decomposes, these zygotes are freed and germinate in a favorable environment , the male and female gametes in *Spirogyra* fuse to generate zygospores, which are diploid (2n) zygotes. Zygospores are the sole stage of the Spirogyra life cycle that is diploid. When appropriate conditions are present, the zygospore conducts meiosis to create 4 haploid (n) nucleuses, only one of which survives, and the others disintegrate [29]. The organism's life cycle was seen to alternate between the haploid filament and the diploid zygospore during sexual reproduction (alternation of generation) [30].

2-3-2. *Chara* spp

The complexity of Chara's morphological traits, such as the structure of its gametangia and its axis that is differentiated into nodes and internodes, makes it a distinctive genus of algae (Nishiyama *et al.*, 2018). These algae are thought to be the land plants' closest living cousins (Meurer *et al.*, 2012). As their assemblages are positively connected with water transparency, they are effective nutrient sinks and crucial to nutrient cycling, and they have an impact on zooplankton and phytoplankton biomasses, characeans play an important ecological role in aquatic habitats[31].

The most common classification of this macroalgae according to (Prescott, 1962)

Kingdom: Plantae Division: Chlorophyta

Class: Charophyceae

Order: Charales

Family: Characeae

Genus: *Chara*

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Species: *Chara vulgaris*

Chara vulgaris

Chara vulgaris is a submerged aquatic alga that thrives in bodies of water with benthic vegetation, such as lochs and ponds, though they can also be found in rivers and streams. They can also live in a variety of wetland habitats and freshwater or brackish environments, and they typically stick to the muddy, soft bottom near the edges of ponds and pools with the help of rhizoids. *Chara vulgaris* is known as "Stonewort" because it produces a calcium carbonate crust on its surface as a byproduct of photosynthesis, which makes the plant feel crunchy to the touch [32]. Moreover, are sensitive to water pollution and eutrophication. Their susceptibility to water pollution allows them to be used effectively as environmental bioindicators [33].

Instead of genuine leaves or roots, *Chara vulgaris* has branchlets grouped in whorls around the stem in place of leaves. They also have fine rhizoids that anchor the plant in the sediment, and each branchlet, rhizoid wall, and internode is one cell thick. While some nutrients can be taken in through the rhizoids, most nutrients are taken in directly from the water through the outer cells of the branchlets and stems. As a result, stoneworts are extremely sensitive to water quality, especially the presence of metals (Lambert, 2009). They divided into rhizoids and the main axis, which produces four different kinds of appendages from each of its nodes. While asexual reproduction is completely missing in *Chara vulgaris*, there is vegetative reproduction available through the following methods: Amylum stars, secondary protonema, and bulbils [34].

2-4: Some biological importance of Algae

Numerous studies have been prepared for ingesting algae for these objectives because it is well known that algae contain a wide variety of bioactive chemicals, many of which have economic potential in the pharmaceutical and medical industries. General antioxidant, anticancer, antibacterial, antiviral, anti-obesity, and biomaterial uses are among the biomedical ones. (Wan *et al.,* 2021). Compounds of algae that interest in medicine include phycocolloids ,phenolics, pigments, peptides and proteins, lipids , halogenated compounds and terpenoids [35].

Phlorotannins, another group of phenolic compounds found in algae, are essential structural elements of cell walls. They have also been studied for their potential therapeutic uses in addition to their secondary ecological roles, which include UV radiation protection, reproduction in algal reproduction, and defense against biotic factors (anticancer, antioxidative, antibacterial, anti-allergic, anti-diabetes, anti-aging, anti-inflammatory and anti-HIV activities) [36].

Algae contain a pigment called fucoxanthin, which has exceptional biological qualities. The antioxidant, anti-inflammatory, anticancer, anti-obesity, antidiabetic, antiangiogenic, and antimalarial properties of fucoxanthin, as well as its protective effects on the liver, blood vessels of the brain, bones, skin, and eyes, have all been demonstrated in numerous studies to have significant potential and promising applications in human health [37].

Natural anti-oxidants, which are present in a variety of algae, protect cells from oxidative damage, which helps them fight off many diseases and slow down the aging process. The anti-aging, nutritional, anti-inflammatory, antibacterial, antifungal, cytotoxic, anti-malarial, anti-proliferative, and anticancer activities of the antioxidant chemicals found in algae are prospective. In mammals, the hot-water extract of the alga *Sargassum hemiphyllum* demonstrated immune-stimulating and antioxidant properties reported that Gracilaria verrucosa, a marine red macroalga, shown antioxidant properties in an ethanol extract [38].

Fucoxanthin, alginates, fucoidans, and phlorotannins are four major bioactive compounds from algae that have the potential as anti-obesity agents. Obesity is a major epidemic that poses a global threat to human health as it is also associated with metabolic syndrome, type 2 diabetes, and cardiovascular disease. These substances' anti-obesity effects result from a number of

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mechanisms, including the suppression of fat metabolism and absorption [39].

Due to the growing number of diabetic patients and the dearth of antidiabetic medications, numerous aquatic organisms have been screened to determine their potential anti-diabetes activities. These include microalgae and macroalgae. The scientific community has shown a great deal of interest in the search for new compounds, particularly from marine sources. It has been demonstrated that marine bio resources can build a variety of unique scaffolds, frequently with strange skeletons. Terpenoid compounds are effective antiulcer agents, and the algae Sargassum polycystem and Ecklonia stolonifera have hepatoprotective properties against acetaminophen-induced liver damage in rats. Algae have been shown to be potential sources of novel and biologically active natural compounds for antiulcer, wound healing, and hepatoprotective activities. Fucoidan, laminarin, cellulose, alginates, and mannitol are polysaccharides found in algae. Fucans, galactans, and alginates have been demonstrated to have anticoagulant, anticancer, and hypocholesterolemic properties [40].

Algae have been found to have anticancer properties, and it has been hypothesized that the biochemical process by which fucoxanthin inhibited tumor cells was apoptosis induction (Jang *et al.,* 2021). The first antibiotic was created from Chlorella and is known as chlorellin. A variety of algae have been screened for antibiotics, and some pharmacologically active compounds with antiviral activity have been isolated from Chlorella spp., Chlamydomonas spp., Scenedesmus spp., Dunaliella primolecta, and *Cladophora* sp. (Hassan *et al.,* 2022).

Plouguerné *et al.,* 2010 and Karthikaidevi *et al.,* 2009 reported that the commercial drug was less effective than the methanol and ethanol extract of several widely found green algae against *Escherichia coli* and *Staphylococcus sp.*[41]

2-5: Antibacterial activity of algae extracts

Since the widespread use of antibiotics, there have been significantly fewer deaths from infectious infections. The overuse of these medications has recently resulted in a significant public health issue since microbes have developed antibiotic resistance as a result. Additionally, there has been a rise in the frequency of fungal infections, particularly in patients with weakened immune systems, such as those with HIV and those who have undergone chemotherapy, among others[42].

Many of the antibiotics produced from known microorganisms have become useless in our time due to the emergence of severe resistance to these pathogens as well as their high cost and side effects, such as hypersensitivity and the death of beneficial microorganisms of the gut [43]. Low antibiotic efficiency and increased bacterial resistance necessitated new alternatives to antibiotics. Due to this circumstance, researchers are looking for novel antimicrobial chemotherapeutic agents from a variety of sources. However, the development of synthetic medications is expensive and has negative side effects when compared to drugs generated from plants. Antibiotic-resistant microbes are a growing problem, hence novel natural medication sources have being looked into to combat this issue. Researchers have become interested in algae because they are abundant sources of novel, structurally complex, and physiologically active metabolites. Algae have been thoroughly investigated and have demonstrated their enormous potential as a source of both primary and secondary metabolites[44].

There are a number of variables that can affect an algae's antibacterial activity, including the environment, the time of year it was collected, its various growth phases, the experimental techniques used, etc. However, variations in antibacterial activity can be caused by the extraction process and solvent (Zerrifi *et al.,* 2018).

Methanolic and ethanolic extracts of three different algae from Baghdad University (Iraq) were tested against Gram positive and Gram negative bacteria by Almula (2018), who came to the conclusion that the ethanol extracts had a greater impact on the microorganisms tested, particularly on Gram-positive bacteria.

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Several scientists have developed an antibacterial assay for green algae against Gram positive and Gram negative microorganisms (Bhuyar *et al.*, 2020).
Chloroform was shown to be the best solvent to extract active chemicals with antimicrobial activity when Lefta (2015) examined chloroform, ethanol, and ethyl acetate extracts from algae for antimicrobial properties.

Gram positive and Gram negative bacteria isolated from burns and wounds were tested using acetonic and hexanic extracts of the algae *Cladophora glomerata* from Baghdad University (Iraq). 7 (2018) came to the conclusion that the hexane extracts had a greater impact on the microorganisms tested, particularly on Gram positive bacteria[45].

Bouhlal *et al.*, (2021) noted that the methanol alcohol extract of six marine algae, which belong to the red algae, the structure and the green, has a high inhibitory effect against the *S.aureus* bacteria other than the red algae *Corallina officinalis*, which showed no inhibitory effect. The highest inhibitory activity against the bacteria *Enterobacter aerogenes* of *corallina officinalis*, and the brown alga Cystoseira barbata has a wide-ranging inhibitory effect against all tested bacteria. The diameter of the *E.coli* inhibitor diameter is 22 mm. There was a difference between the dry and soft extracts of *Ulva rigida*, which did not record the dry extract with any inhibitory effect against *S.aureus* bacteria while high efficacy was observed towards *S.aureus*, *E.faecali* and *E. coli* when using the soft extract [46].

2-6: Antioxidant Activity

Free radicals are unstable substances that can participate in chemical processes. They are defined as any molecular species with an unpaired electron in an atomic orbital. Superoxide anion, hydroxyl radical, hydrogen peroxide, and nitric oxide are produced by free reactive oxygen, nitrogen, and sulfur species. By causing oxidative stressors, cell damage, and death, these substances may contribute to diseases as diverse as cancer, diabetes, Alzheimer's disease, and Parkinson's disease. Numerous natural substances have been shown to have antioxidant activity and to be useful in the treatment of disorders linked to oxidative damage. Numerous plants, fungi, and algae, including *Ecklonia cava*, *Stoechospermum marginatum*, and *Silybum marianum*, are regarded as key sources of natural antioxidants [47].

Because of interactions between several molecules with antioxidant characteristics, algae have an intriguing antioxidant system that is thought to be more effective. The pigments, phenols, flavonoids, and vitamins present in algae are the most potent antioxidants. Critical biomolecules including nucleic acids, lipids, proteins, and carbohydrates can suffer significant damage when these damaging radicals build up in the body (Halliwell and Gutteridge, 1990; El-Tablawy *et al.*, 2020).

Due to their mutagenic and carcinogenic properties, the consumption of synthetic antioxidants has recently been prohibited. As a result, the use of natural antioxidants has received a lot of attention. Natural antibacterial and antioxidant capabilities of plant extracts have been documented, and their functional qualities are related to the presence of secondary metabolites like phenolic compounds [48].

2-7: Urinary tract infections (UTI)

The kidneys, ureters, bladder, and urethra make up the urinary tract. An infection in any of the urinary tract's structural components brought on by pathogenic organisms (such as bacteria, fungi, or parasites) is known as a urinary tract infection. The presence of microbial pathogens surrounding the urinary tract is what UTIs are defined as, and they are typically categorized by the site of infection as either the bladder (cystitis), kidney (pyelonephritis), or urine (bacteriuria) (Robinson *et al.*, 2014). Urinary tract infections (UTIs), which are caused by microbial invasion of altered urinary tract tissues, are a persistent issue around the world. UTI is a significant global driver of antibiotic consumption as the second most frequent justification for empirical antibiotic treatment. [49].

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According to Colgan and Williams (2011), ladies have bacterial infections more frequently than males do (Salvatore *et al.*, 2011) Most often, they strike between the ages of 16 and 35, with 10% of females developing an infection annually and 60% developing one at some point in their life (Salvatore *et al.*, 2011).

The incidence of UTI in males in their fifth decade rapidly rises as benign prostatic hyperplasia progresses, obstructing the urethra. A shorter urethra in women than men makes them more susceptible to urogenital tract infections (UTIs). depending on normal or faulty underlying anatomy, and while they may be symptomatic, they frequently are not. Numerous pathogens that cause UTI, including *E. coli*, *Klebsiella*, *Proteus*, *Pseudomona*s, and other microbes, are described in prior investigations conducted around the globe [50].

2-8: Epidemiology

Recently, UTI is one of the most common diseases and one of the most widespread health problems (Öztürk and Murt, 2020). UTI is estimated about 150 million per year (Mangai *et al.*, 2019). High rate of morbidity and mortality had occurred because of community-acquired infection (Abaas, 2018). About eight million UTI cases are reported annually in emergency management, clinics, and outpatient clinics in the United States, with respiratory infections ranking second in terms of incidence. This number includes more than two million visits for cystitis [51].

In the United States of America, 15% of the population receives an antibiotic prescription for UTI. Due to anatomical and physiological factors, women experience UTI instances more frequently than men (30:1). In particular, in the second and third decades of sexual activity, aging is linked to an increased incidence of UTI in females. Nearly 1 in 3 women will experience at least one UTI attack by the time they are 24 years old, and between 40% and 50% of women experience UTI at some point in their lives. A small percentage of males aged 15 to 50 have acute, simple cystitis. According to earlier studies, between 3-8% of girls and 1% of boys experience fibrosis illnesses as a result of UTIs (Sharkey *et al.*, 1996). Additionally, between 25 and 40 percent of UTI patients get recurrent UTIs within a few weeks or months [52].

2-9: Pathogenic bacteria causes urinary tract infections

90% of UTI infections are caused by gram-negative bacteria, while gram-positive bacteria are responsible for 10% of cases. *Escherichia coli* is the most often isolated uropathogen (Serretiello *et al.*, 2021). The main causal agent of uncomplicated UTI is Escherichia coli, is followed in prevalence by *Klebsiella pneumoniae*, *Staphylococcus saprophyticus*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida* spp. [53].

Organisms like Enterococcus faecalis and highly resistant Gram-negative rods like *Pseudomonas* spp., *Klebsiella* spp., *Proteus* spp., and other organisms are more common in complicated urinary tract infections and hospitalized patients. *Pseudomonas* spp. Are comparatively more common in patients with complicated UTI as mentioned by [54]. Age, sex, catheterization, and hospitalization all have an impact on the relative frequency of the pathogens (Seifu and Gebissa, 2018). While *E. coli*, *Proteus mirabilis*, *P. aeruginosa*, and *Streptococcus faecalis* are the pathogens most frequently linked to catheter-associated UTIs, other pathogens, such as *Candida*, *Staphylococcus aureus*, *Klebsiella pneumonia*, and others, can also result in UTI [55].

Biofilm, a complex organic compound made of microorganisms living in colonies within an extracellular mucopolysaccharide substance, is a characteristic of bacteria associated with catheters (Bjarnsholt *et al.*, 2013). One of the key variables in the development of a urinary tract infection is the capacity of bacteria to adhere to or not [56].

2-10: Antibiotics therapy of UTIs

Antibiotic therapy is advised for the treatment of symptomatic UTIs in order to achieve

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notable outcomes in terms of clinical resolution and bacterial elimination (Wagenlehner *et al.*, 2020). The first line of antibiotic regimens includes: (fosfomycin trometamol 3 g) single oral dose; (nitrofurantoin 100 mg) twice daily for 5 days; (pivmecillinam 400 mg) twice daily for 3 days; and (trimethoprim and sulfamethoxazole 160/800mg) twice a day for 5 days. These regimens are only indicated in areas with low incidence of antibiotic resistant E. coli strains. Fluoroquinolones like ciprofloxacin, prulifloxacin, and levofloxacin should only be used as substitutes, not as major-line antibiotics, in the treatment of uncomplicated cystitis due to their negative effects [57].

Fluoroquinolones are the first choice of antibiotics in cases of complicated UTIs because they are also active against *Pseudomonas* spp. However, depending on the local pattern of antibiotic resistance, piperacillin plus blactamase inhibitors or third-generation cephalosporins can also be used successfully.

After collecting urine samples for testing and culture, antibiotic treatment should be combined with efforts to rule out complicating factors that, in many cases, need actual clinical trials [58].

Amoxicillin-clavulanate (500/125 mg, twice daily, for 3–7 days), amoxicillin (500 mg, twice daily for 5-7 days), cephalexin (500 mg, two times daily, for 3–7 days), nitrofurantoin (100 mg, twice daily, for 5-7 days), and fosfomycin are among the antibiotics that are recommended for use in pregnancy (Glaser & Schaeffer, 2015). Although trimethoprim-sulfamethoxazole (TMP-SMX) may be used, it should be avoided in the first trimester due to its competition with folic acid and the risk for kernicterus [59].

The selection of antimicrobial agent is determined following several criteria like the spectrum and susceptibility patterns of the certain etiological agent towards antimicrobial agents, the efficacy of the certain indication in clinical studies, acceptibality and adverse reactions of the drug, adverse ecological effects within human body, cost and availability [60].

Owing to the expected time required for microbiological results to be completed for 24-72 hours, the clinician prescribes an ampirical antibiotics for early therapy depending of clinical presentation of the infection. The insufficient therapy for critically ill, hospitalized patients results in increased morbidiy and mortality. When the antimicrobial susceptibility results for microbial infection cases becomes available, it is important to narrow the spectrum of antibiotics used to avoid toxicity and development of microbial antibiotic resistance. Due to the increasing rate of antimicrobial resistance of urinary pathogens the Knowledge of the common uropathogens in addition to local susceptibility patterns is important in determining suitable empiric therapy of UTIs (Bader *et al.*, 2020). Therefore, additional research is advised in Iraq to identify the indigenous urinary pathogens and their patterns of antibiotic susceptibility in order to slow the development of bacterial resistance and improve clinical results [61].

2-11: Drug–resistance in pathogens of UTIs.

Antibiotic resistance, which has increased 66% since 2000, is a serious danger to global health. Due to the frequent occurrence of a variety of antibiotic resistance mechanisms, treating UTIs is becoming increasingly challenging . *E. coli* and *K. pneumoniae* are of special concern because they both carry plasmids that encode extended-spectrum -lactamases (ESBLs), which spread resistance to third-generation cephalosporins as well as other antibiotics swiftly [62].

Since enterococci are undoubtedly resistant to trimethoprim, clindamycin, cephalosporins, and penicillins, multidrug resistance (MDR), which occurs when bacteria show resistance to one or more classes of antimicrobial drugs, is also common among enterococci (Jubeh *et al.*, 2020).

Enterococcus species have recently developed high levels of resistance to glycopeptides, including vancomycin, one of the last lines of defense against multidrug-resistant organisms [63].

Global strategies for the treatment of uncomplicated UTIs recommend several agents, such as, trimethoprim-sulfamethoxazole, nitrofurantoin monohydrate, fosfomycin trometamol,

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fluoroquinolones, pivmecillinam and beta-lactams (Bonkat *et al.*, 2019). However, there is a disturbing level of antimicrobial resistance emerging in urinary pathogens as a result of haphazard and extensive use of antibiotics. Bacteria generating extended spectrum beta-lactamases (ESBLs), displaying resistance to most antibiotics excepting the carbapenem group [64]. The increased incidence of MDR pathogens, restraining existing treatment choices for infections triggered by these organisms, and the lack of a novel antibiotics provide good reasoning for using older antibiotics, such as fosfomycin, that have been shown to maintain some activity against MDR pathogens [65].

The development of additional control strategies and therapeutic options has been prompted by the alarming trend toward a high incidence of multidrug-resistant uropathogens.

2-12: Alternative therapy for UTIs.

The antibiotic therapy became less disireable in clinical practice due to global problem of microbial antibiotic resistance, the effects of antibiotic prophylaxis on normal microbiota and the adverse effects of antibiotics on human body. The search for alternative therapy for microbial infections has a high priority in global research interest. Numerous studies approved the effectiveness of different alternative therapies in treatment of UTI, including probiotic therapy, phage therapy and Algae therapy and phytotherapy.

2-12-1: Algae therapy and phytotherapy

Numerous medicinal plants can be used to extract phytochemicals, whose active ingredients have been shown to treat diseases and alleviate their symptoms while occasionally having negative side effects (Boukhatem and Setzer, 2020). These phytochemicals, which include alkaloids, flavonoids, tannins, terpenoids, glycosides, saponins, and anthraquinones among others, have demonstrated promising microbiostatic and microbiocidal activity against a variety of pathogenic microbes [66].

Different researchers have proposed a variety of mechanisms for how phytochemicals exert their antimicrobial effects. These include inhibiting microbial growth, causing cellular membrane distresses, interfering with specific microbial metabolic processes, modulating signal transduction, or altering specific gene expression pathways. UTIs have long been treated using herbal remedies. By battling the germs, minimizing inflammation, and healing urinary tract tissues, herbal remedies can treat UTIs. Some herbs also function as preventative measures [67].

In excess of 5000 plant polyphenols have been recognized, and numerous of them reveal a wide spectrum of biological properties, comprising antiinflammatory, antimicrobial, and anti-carcinogenic properties. Some of them have been also used in the management and control of UTIs. These comprise cranberry, berberine, blueberry, bearberry, cinnamon and other herbs [68].

Conclusion

Cyanobacteria have active chemical compounds and they are mostly Alkaloid, Glycosides, Resins, Terpenes and Steroids. Different cyanobacteria have a lot of active chemical compounds by using the GC-Mass Spectrometry technology.

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