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Review on Toxicity and Removal of Pharmaceutical Pollutants Using Immobilised Microalgae

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ABSTRACT

In recent years, global pharmaceutical consumption has increased, resulting in the increased release into the environment and endangering the entire ecosystem. These pharmaceuticals have attracted considerable attention due to their persistence, toxicity, and the appearance of resistance genes and development antibiotic-resistance bacteria. Furthermore, conventional wastewater treatment plants are ineffective in treating antibiotic-contaminated wastewater. Thus, algae-based technologies are sustainable, low-cost, and friendly to the environment. In this context, immobilization appears to be of particular interest to many researchers as they develop new, efficient, greener strategies for the elimination of toxic and hazardous pollutants. provide a critical overview of algal immobilization-based technologies, and a biotechnological tool that restricts cell movement by confining it within a polymer matrix or attaching it to a rigid support is a promising, and cost-effective alternative that does not necessitate the use of additional chemicals. This paper presents strategies for the systematic removal of pharmaceuticals based on algae immobilization techniques as an economical, effective, and feasible alternative technology for removing pharmaceuticals and environmental concerns from water bodies and discusses the benefits and drawbacks of these techniques.

Keywords: aquatic environments, environmental impact, immobilization algae, pharmaceuticals, removal mechanisms.

INTRODUCTION

Pharmaceuticals are a significant group of uncontrolled substances, either synthetic or derived from natural sources; they follow the emerging pollutants and are found in the aqueousc environment in varying proportions from ng/L to g/L (Almeida et al., 2020). It constitutes a smaller percentage contrasted to other contaminants existent in water and wastewater, Pharmaceuticals mostly enter the environment through a variety of sources, including homes, pharmaceutical industries, hospitals, aquaculture facilities, and runoff from fields (Majumder et al., 2019). To a lesser extent, they enter through emissions from production facilities, improper prescription disposal, and wastewater treatment plants. Among different sources, hospitals are the main contributors to the discharge of medications into the ecosystem (Samal et al., 2022).

More than 200,000 tons of pharmaceutical material are consumed each year in India, Russia, and China, according to estimates (Kovalakova et al., 2020). Pharmaceutical compounds are biologically active and designed to interact with particular physiological routes in the target organism (Mezzelani et al., 2020). Despite its low environmental concentrations, it can pose at hreat to humans health and the ecosystem due to its potential health effects, its dispersive nature, its survival in the environment for prolonged periods of time, its stable structure, and the difficulty of its removal by traditional methods (Patel et al., 2019). The presence of pharmaceuticals in the aquatic environment may disturb the growth of aquatic plants and animals, endangering human health (Kayode-Afolayan et al., 2022). Due to their low concentration, the drug molecules, according to several short-term toxicity studies, do not have an immediate harmful impact on aquatic creatures (Fernandes et al., 2021). Therefore, their continuous discharge into an aquatic environment has long-term (chronic) consequences. For example, in laboratory tests, the presence of estrogens has been observed to induce feminization in male Oryzias latipes (Japanese medaka), increase fish mortality, and alter the traits and behaviors of other aquatic species (Tijani et al., 2016). Antibiotics are one of the most extensively utilized pharmaceutical classes in medical and veterinary applications, and they are constantly being discovered in aquatic environment (Felis et al., 2020). Antibiotic use has increased globally recently, with an estimated 65% increase between 2000 and 2015, with a 200% increase projected by 2030 if nothing is done (Klein et al., 2018). There are two key causes for the rise in antibiotic usage worldwide, The first is the rise in consumption caused by an increase in the human population globally, additionally, the usage of antibiotics increased as a result of rising prosperity and easier access to medications, the second factor is the growing demand for animal protein, which increases the need for growth boosters and antibiotics in food production (Adeleye et al., 2022; Kovalakova et al., 2020). They will eventually end up in the aquatic environment and cause toxic damage due to their relatively slow biodegradability and constant availability; additionally, there has been increased worry about the emergence of bacteria and genes for antibiotic resistance in the environment (Zheng et al., 2021; Wang et al., 2020).

Fungus, and Antibiotic-resistant bacteria alone inflicted more than 35,000 fatalities and 2.8 million illnesses and in the United States in 2019 (Kadri et al., 2020). This endangers public health systems and raises mortality by at least 700,000 people annually. According to recent reports, if no action is taken to reduce it, the number of deaths may reach 10 million per year by 2050 (Yu et al., 2012). Because of the widespread awareness of their potential hazards, some measures to decrease their use as traditional biological therapy approaches have been investigated (Oberoi et al., 2019). Antibiotics are removed from the aquatic environment using a variety of technologies, including physical and chemical methods. These methods are usually effective, but they require expensive chemical reagents or catalysts and consume a lot of energy (Li et al., 2021), and potentially producing contaminants such as significant amounts of metal sludge (Leng et al., 2020; Rambabu et al., 2020). The technology based on microalgae is seen as apromising and important alternative to removing pharmaceutical compounds because it grows in an autotrophic, heterotrophic, or mixed way, is free from harmful chemicals, can grow faster, and can withstand challenging conditions of the environment like extreme heat, salinity and nutrient stress. It is also relatively resistant to a wide range of pollutants such as pharmaceuticals,heavy metals, and organic compounds (Xiong et al., 2018; Rempel et al., 2021).

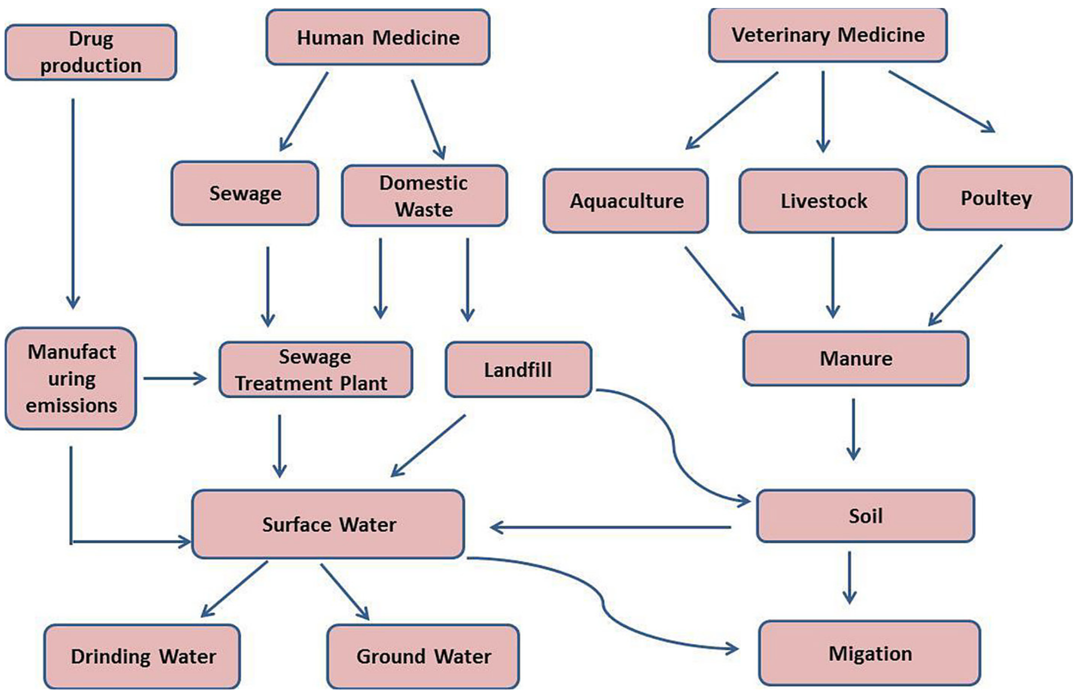

Figure 1. Principal sources of water pollution with pharmaceutical compounds

Microalgae cryo-immobilized technology has received increased attention in recent years; it has been utilized in a variety of fields, including the removal of organic pollutants, nutrients, hazardous textile dyeing compounds, pharmaceutical material from wastewater, heavy metal biosorption, and biofuel production (Cao et al., 2022; Kaparapu and Geddada, 2016). These techniques have several benefits, including efficient CO2 fixation, environmental friendliness, solar energy-driven activity, and the production of biofue (Nguyen et al., 2021). In general, microalgae have exceptional resilience to endure and flourish in challenging conditions, making them ideal candidates for enhanced wastewater treatment (Xiong et al., 2021).

Immobilization of algae is a technique in which,the cells mobility is restricts by attaching them to a solid support or entrapping them within a polymer matrix (Girijan and Kumar, 2019). Immobilizing algal cells has been suggested as a solution to the harvest issue, allowing the preservation of high-value algal bio-mass for further processing. Coimmobilization and microencapsulation are two recent advancements in the field that have demonstrated the outperform of immobilized cells over free cells (Mallick, 2020). Immobilized microalgae have been used in many bioprocesses such as the production of high-value products (e.g. Photopigments, biohydrogen, and biodiesel), the elimination of nutrients (e.g. phosphate, ammonium ions, and nitrate), the production of biosensors, and the control of stock culture, The most potential applications of immobilized microalgae seem to be in wastewater treatment (Vasilieva et al., 2016; Eroglu et al., 2015).

IMPACTS OF PHARMACEUTICALS ON AQUATIC ORGANISMS

Several scientific studies have shown that the bioaccumulation of pharmaceutical preparations in living things' tissues has negative effects on both their diversity and the existence of aquatic creatures that consume them (Kayode-Afolayan et al., 2022; Madikizela and Ncube, 2022) (Table 1).

PHARMACEUTICALS' FATE IN AQUATIC ECOSYSTEMS

Many processes influence drug dissipation in the aqueous system, including biodegradation (anaerobic and anaerobic) and abiotic transformation (e.g., UV decomposition, sediment adsorption, and hydrolysis), and depend on the physicochemical properties of drug compounds, such as antibiotic concentrations, half-lives, and environmental factors (Kalyva, 2017). Pharmaceuticals have three primary probable fates in the aquatic environment: first, pharmaceuticals are mineralized into carbon dioxide and water, for example, aspirin; second, the compounds are metabolized but remain in water-soluble forms of the parent component, so they move through the wastewater treatment

Table 1. Summary of the impacts of pharmaceuticals on marine species

Examples of pharmaceutical	Marine species	Impacts	Reference
Diclofenac	*Perna perna*	DNA damage was caused , impacted gene transcription , shell deformities, decreased COX activity ,and lysosomal membrane stability	Fontes et al., 2018
Losartan Fluoxetine	*Perna perna*	Showed cytogenotoxic impacts in hemocytes and gills of the mussel induced cytogenotoxic effects and had a negative influence on mussel health overall	Cortez et al., a2018; Cortez et al., b2019
Tamoxifen	*Mytilus galloprovincialis*	Showed Increased GST activity, LPO byproductsin the gills, neurotoxicity, and male endocrine disruption	Fonseca et al., 2019
Gemfibrozil and Propranolol	*Sparusaurata; Mytilus galloprovincialis, and Paracentrotus lividus*	Reduced fertilization in sea urchins, harms seabream larvae' survival	Capolupo et al., 2018
Ranitidine, Bisoprolol, and Sotalol	*Daphnia similis,* fish *Danio rerio*	Negative impacts on D. rerio larval locomotion and decreased fertilization in Daphnia similis	Godoy et al., 2020
Procaine penicillin (PP)	*Daphnia magna*	Influence the physiological parameters and swimming behavior of Daphnia magna	Bownik et al., 2019
Acetaminophen Ibuprofen	*Crassostrea gigas*	Alterations in gene transcription, biotransformation, and drug metabolism	Bebianno et al., 2017

facility and finish up in recipient waterways; if the metabolites are bioactive, they may impact aquatic life. Thirdly, the polymer is lipid-soluble and will not degrade fast; some of it will be retained in the sludge (Klaminder et al., 2014; Kayode-Afolayan et al., 2022). Among the most significant processes for eliminating pharmaceutical compounds from the aqueous ecosystem are summarized as follows:

1. Adsorption is one of the significant ways to eliminate or dilute antibiotics in the aqueous ecosystem; numerous studies on antibiotic absorption in soil and water have been conducted, and sediment adsorption is regarded as one of the most significant antibiotic fates in aquatic ecosystems (Cheng et al., 2022) The most often used adsorbents for removing antibiotics involve bentonite, ion-exchange resins, activated carbon ACs, CNTs carbon nanotubes, and biochar BCs (Ahmed et al., 2015). And have been used of carbon-based adsorbent materials for the eliminate of various groups of antibiotics, for example, activated carbon utilized for the adsorption of antibiotics such as quinolones and penicillin (Ahmed, 2017), and graphene oxide used for the adsorption of sulfonamides SAs and chloramphenicols CAPs (Yang et al., 2021).
2. Hydrolysis is a key mechanism for the breakdown of various organic compounds, particularly amides, and esters, The temperature as well as the pH level are the most important factors influencing antibiotic hydrolysis rates (Mitchell et al., 2014) Amoxicillin (AMX) is a beta-lactam antibiotic that hydrolyzes in this manner, it dissolves rapidly in aqueous circumstances due to lactam ring hydrolysis, generating two components, AMX penilloic acid and AMX diketopiperazine-2'-5' (Jin et al., 2017).
3. Photolysis is one of the major degradation processes for organic pollutants in in aquatic ecosystems and includes direct photolysis, sensitive photolysis, and photooxidation, there are many factors affecting the photodegradation process of pharmaceutical compounds, for example, water properties (e.g., pH and temperature), water content (e.g types inorganic compounds,and contents of dissolved organic), the composition and properties of organic pollutants, and photocatalysts (Cheng et al., 2022). For example, oxytetracycline undergoes direct photolysis and is considered the major disposal pathway in surface waters (Jin et al., 2017).
4. Photodegradation, both direct and indirect, is an important process in the abiotic transformation of pharmaceuticals in waterbodies,Indirect photolysis is brought on by natural photosensitizers, whereas direct photolysis is brought on by sunlight's direct absorption (Nikolaou et al., 2007). Its photolysis dissolution in water is impacted by several variables, such as the intensity of solar radiation, latitudinal, organic matter content,and eutrophication circumstances (Wang et al., 2021).

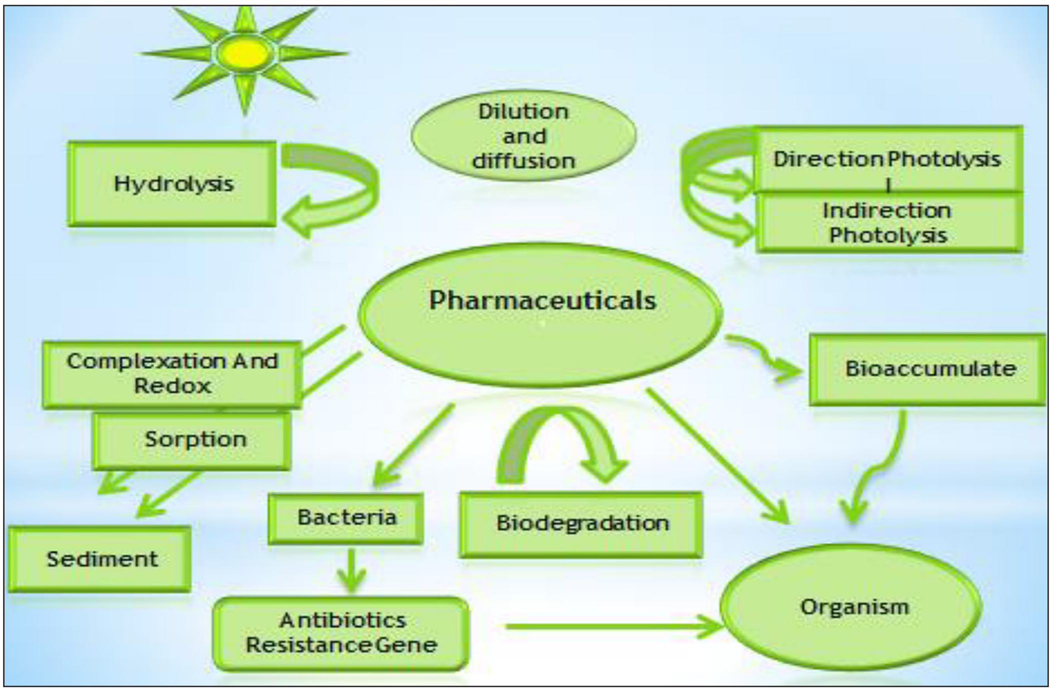

Figure 2. Pharmaceuticals' pathway in aquatic ecosystems

5. Antibiotic biodegradation is the elimination of antibiotics from the ecosystem through the utilize of microorganisms like bacteria, algae, and yeast, a variety of factors influence this process, including microbial species, anaerobic and aerobic conditions, antibiotic concentrations, precipitation, and temperature (Liu et al., 2021). Anaerobic and aerobic biodegradation are the two most common methods for removing medications from the dissolved (Mansouri et al., 2021).

Many environmental factors (abiotic and biotic) influence pharmaceuticals' fate in aquatic environments, including pH, temperature, sunlight and light intensity, hydraulic retention time, seasonality, microbial communities, sediment, natural organic matter, suspended particles, body water volume, turbidity, the hydraulic regime, weather conditions, etc (Carpenter et al., 2018). In aquatic environments, salinity has an even greater impact on the distribution and natural degradation of medicinal substances, when freshwater and saltwater meet, the role of salinity becomes more important. For instance, as salinity rises, the coefficient of separation between estrone and sediment rises, resulting in a drop in estrone's aqueous content and a favoring of further adsorption to the sediment (Patel et al., 2019). A further important factor influencing the fate of pharmaceutical preparations is pH, which can convert an ionic form to cationic, anionic, neutral, or zwitterionic. As a result, it will have an impact on the biological, chemical, and physical features of the medications, such as their toxicity, activity, photosensitivity, and absorption (Verlicchi 2012; Fernandes et al., 2021). It was discovered that the pH of a submerged membrane bioreactor (MBR) had a significant impact on the elimination of antibiotics like ibuprofen, diclofenac, ketoprofen, and sulfamethoxazole (between 5 and 9). At pH 5, the maximum elimination of these antibiotics was [58]. According to research by Baena-Nogueras et al. (2017), The photodegradation of many pharmaceutical compounds is influenced by pH, Acetaminophen photodegraded faster at pH 4 or 9 than at pH 7, whereas other medications such as diclofenac, ibuprofen, and ketoprofen showed no significant difference (Tiwari et al., 2021). Majumder et al. (2019) found that an acidic pH had a positive impact on the rate of -Blocker breakdown, with a pH of 6 producing the highest levels of degradation Figure 3.

MECHANISMS OF PHARMACEUTICAL REMOVAL BY MICROALGAE

Algae are autotrophic organisms found in a range of habitats; they are fast-growing and can withstand harsh environmental conditions; they have a wide variety of applications, including food or dietary supplements, pharmaceutical manufacturing, fish feed, fertilizer production, biofuel production, bioremediation, etc (Salem et al., 2021). When microalgae are exposed to pharmaceutical compounds, they exhibit a variety of responses,they employ a variety of biotic and abiotic methodologies to detoxify and stay alive, like hydrolysis, bioaccumulation, absorption, intracellular biodegradation, and photolysis, etc. (Leng et al., 2020; Liu et al., 2021). Table 2. summarizes the methods and effectiveness of the removal of several pharmaceuticals

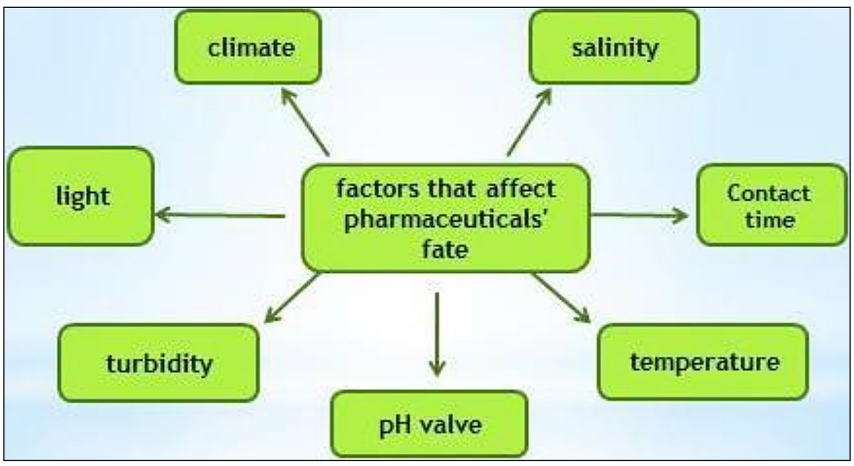

Figure 3. Environmental factors that affect pharmaceuticals' fate

using algae-based techniques. Since volatilization, photodegradation and hydrolysis routes are not universal and only happen occasionally under certain conditions, they normally make a minimal contribution to elimination (Li et al., 2022). Therefore, This review consequently focuses primarily on biodegradation, biosorption and bioaccumulation.

- Biodegradation: The term "biodegradation" refers to the process whereby algal cells, either within or outside, break down antibiotics into simpler, less harmful chemicals,, with some degraded derivatives being consumed by algal cells (Naghdi et al., 2018). Antibiotics are broken down by biodegradation into several metabolic intermediates or are mineralized into H_2O and CO_2 (Vo et al., 2020).This process depends on a group of enzymes inside and outside the cells; as glutathione-S-transferase and cytochrome P450, while P450 is associated with extracellular polymeric complexes (EPS), as a stage I enzyme, act P450 on catalyze a wide variety of chemical reactions, including glycosylation, hydroxylation, hydrogenation, carboxylation, cyclization, and oxidation. While glutathione-S-transferase is believed to be the phase II enzyme that facilitates the complexation of glutathione and electrophilic compounds, resulting in protection against oxidative stress by opening the epoxide ring [21]. The extracellular polysaccharides and enzymes contained in EPS can cause degradation of certain substances or compounds around the cells of the microalgae (Naghdi et al., 2018; Viancelli et al., 2020). Biodegradation process contributes to the removal of many antibiotics, including sulphonamides (i.e., sulfamethazine, sulfamerizine, and trimethoprim) (Xie et al., 2019; da Silva Rodrigues et al., 2020), macrolides (erythromycin, and roxithromycin) (Zheng et al., 2021); and B-lactams (Li et al., 2021). In this context, an investigation was made, Chlorella pyrenoidosa (intracellular degradation) of ceftazidime and the achieved antibiotic removal ratio of 92.70% and 96.08%, respectively (Yu et al., 2017). Garca-Galán et al. (2020) studed the utilization of a high-rate algae pond (HRAPs) to eliminate12 antibiotics,and their majority metabolic products, discovering that the majority of the compounds were removed at a rate of 40–60% (García-Galán et al., 2020).
- Bioadsorption: Pharmaceutical bioadsorption is a physical process that is reliant on microalgal extracellular features such as cell walls and EPS (Daneshvar et al., 2018). EPS is a type of biopolymer produced by microbes; 90% of its organic content is made up of proteins, polysaccharides, enzymes, lipids, and substituents, and EPS enhances digestive activities and mass transport functions as well as cell absorption capacity and surface features (Wang et al., 2018). Increased EPS content (especially protein content) is frequently associated with increased antibiotic adsorption, whereas decreased cellular negativity can result in decreased antibiotic adsorption because of impaired electrostatic interaction (Viancelli et al., 2021). Most of the time, the adsorption can take place via polymer groupings and function groups on the cell walls of as proteins, cellulose, and hemicelluloses, and it is consider as an extracellular operation (Xiong et al., 2018).
- Sorption: Sorption is important, but not dominant, in the removal of antibiotics. Potential mechanisms for antibiotic adsorption by microalgae include surface sedimentation, hydrogen bonds,hydrophobic effect, and surface sedimentation (Leng et al., 2020). Adsorption can effectively remove some drugs, like as the algae *Chlorella* sp. Cephalexin (at 50 mg/L) was removed by adsorption from modeled sewage with an efficiency of 82.70% and 71.20%, respectively (Angulo et al., 2018). Chlorella vulgaris can bio-adsorb metronidazole (with a starting concentration of 5 mM) with a 100% removal efficiency (Hena et al., 2020). Additionally, it was found that one of the major methods, for tetracycline elimination in HRAP is adsorption (Norvill et al., 2017). Adsorption is typically quick; for instance, 7-ACA (amino cephelosporanic acid) can be eliminated in 10 minutes via microalgal adsorption (Guo et al., 2016).
- Accumulation: Adsorption is an extracellular process used to eliminate contaminants from water, whereas accumulation is an intracellular method, Several antibiotics are capable of passing through algal cell membranes and being absorbed by the cell (Bai et al., 2017). Algae accumulation has been linked to the elimination of antibiotics such as sulfamethoxazole, trimethoprim and doxycycline (Partovinia and Rasekh, 2018; Bai

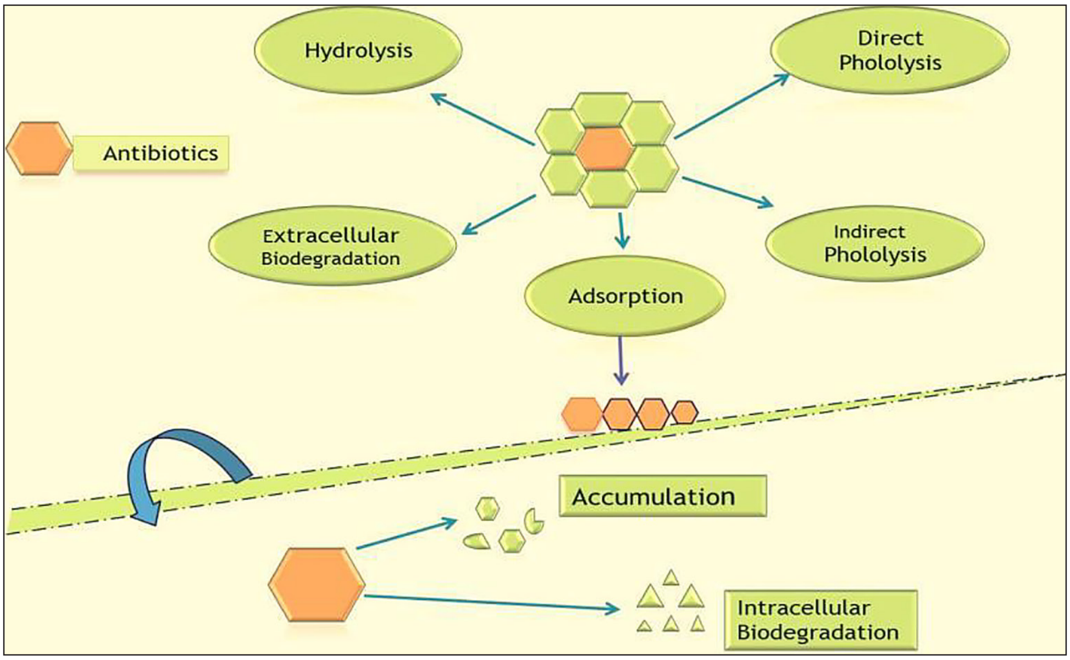

Figure 4. Removal mechanisms of Pharmaceutical by microalgae

Table 2. Mechanics used by algae to remove various antibiotics

Antibiotics	Algae	Processes	Removal	Ref.
Tetracycline	*Chlamydomonas* sp.	Photolysis, biodegradation, and hydrolysis	100%	Xie et al., 2017
	Spyrogira sp.	Photodegradation	89%	Garcia-Rodríguez et al., 2013
	Tetraselmis suecica	Biosorption	56.25%	Daneshvar et al., 2018
Sulfamethoxazole and Sulfadiazine	*Chlamydomonas* sp.	Biodegradation Biodegradation, photolysis, biosorption, and hydrolysis	~20% 54.52%	Xie et al., 2019
Sulfathiazole	*Spyrogira sp.*	Biodegradation, and indirection photodegradation	36.0%	Garcia-Rodríguez et al., 2013
Ciprofloxacin	*Chlamydomonas sp.*	Biosorption, photolysis, and biodegradation,	100 %	Xie et al., 2020
Ciprofloxacin	*Scenedesmus dimorphus*	Biotransformation, and bioadsorption	93.0%	Grimes et al., 2019
Erythromycin	*Scenedesmus obliquus*	Photolysis, biodegradation, and hydrolysis	97.0%	Wang et al., 2021
Norfloxacin	*Chlorella Vulgaris*	Photo-degradation	36.8%	Zhang et al., 2012
Levofloxacin	*Chlorella vulgaris*	Bioaccumulation, and biodegradation	82.34%	Kiki et al., 2020
Azithromycin	*Chlorella vulgaris* *Haematococcus pluvialis*	Biodegradation	92.77% 78%	Kiki et al., 2020
Amoxicillin Spiramycin	*Microcystis aeruginosa* *M. aeruginosa*	Biodegradation	33.6% 32.8%	Liu et al., 2012
Amoxicillin	*Chlorella pyrenoidosa*	Adsorption, and biodegradation	100%	Yu et al., 2017
Cefradine	*Chlorella pyrenoidosa*	Bio-degradation	41.47 %	Xiao et al., 2021
Ceftazidime	*Chlorella pyrenoidosa*	Biodegradation, and bioadsorption	93.0%	Xiong et al., 2021
7-amino cephelosporanic acid (7-ACA)	*Chlorella pyrenoidosa*	Biodegradation, and bioadsorption	96.07%	Yu et al., 2017
	Chlamydomonas	Photolysis, bioadsorption, and hydrolysis	100%	Guo et al., 2016

et al., 2017). Trimethoprim, sulfamethoxazole, and florfenicol,otherwise, the algae cell can counteract the consumption of the antibiotic by its metabolism, as it is broken down into simpler molecules (Song et al., 2019). In this state, accumulation is a precursor for biodegradation (Xiong et al., 2018). For example, *Chlorella vulgaris* cleared the antibiotic levofloxacin through subsequent intracellular biodegradation and accumulation (Xiong et al., 2018). Otherwise, the antibiotics accumulate in microorganisms, which would lead to further accumulation and be transmitted by the food chain, eventually leading to the development of antibiotic resistance (Sun et al., 2017).

- Hydrolysis and photolysis: Tow more primary abiotic elimination processes are hydrolysis and photolysis. According to Mitchell et al. (2014), hydrolysis rates can be significantly increased by adjusting the aqueous pH and temperature, which can be easily achieved throughout microalga growth. On the other hand, in microalgae-based systems, the contribution of photolysis to overall antibiotic elimination often decreases with treatment duration since an increase in cell density would result in shading impact, and reduces penetration of light (Pan et al., 2021) Whereas B-lactam compounds like amoxicillin and penicillin G are oversensitive to hydrolysis, and subsequent biodegradation starts after the B-lactam ring hydrolyzes, sulphonamide compounds like sulfamerazine, sulfadiazine, and sulfamethoxazole are less likely to be hydrolyzed (Chen et al., 2020). In general, photolysis is classified into two categories: direct and indirect photolysis, both of which depend on the ability of the drugs to absorb light,indirect photolysis occurs when antibiotics are unable to absorb light in the presence of photosensitizers, such as organic materials, carbonates, iron, and nitrates (Liu et al., 2021). Direct sunlight was found to be capable of removing 40% of the antibiotic tetracycline from water [75]. This method is effective, economical, easy to optimize, and ecologically friendly,after being incubated under 24 h of irradiation for seven days, Bai and Acharya (2017) found that triclosan and ciprofloxacin were fully eliminated from *Nannochloris* sp. – mediated culture via a photolysis mechanism.

IMMOBILIZATION

The use of microalgae in biotechnology has grown in recent years, as it is used in several applications such as food, pharmaceutical, cosmetics, aquaculture, biofuel production, and others (Salman et al., 2022). However, its small size and difficulty in harvesting made it difficult to apply biotechnology techniques to it; thus, cell immobilization techniques were developed to solve these problems, While the majority of early studies on immobilization focused on systems designed to release products produced by enzymes or enzyme complexes, recent developments have focused on immobilization of whole cells or cell aggregates (Kaparapu and Geddada, 2016).

An immobilized cell is described as a living cell that is prevented from moving independently from its original location to all parts of a system's aqueous phase by natural or artificial carriers (Xiong et al., 2021; Hejna et al., 2022). The basic idea is that immobilized microalgae in matrices, whether biological or inert, can help produce necessary biotechnological benefits from mass growth, such as the production of a specific metabolite or the removal of contaminants (De-Bashanand Bashan, 2010). Cell immobilization has several advantages over suspended cells, including making biomass harvesting easier; higher cell density; improved operational stability; avoidance of cell washouts; increased resistance to environmental stresses (temperature, acidity, and toxic compounds); and taking up less space, making it easier to handle and use regularly (Eroglu et al.,2015). According to Xie et al. (2020) immobilized *Chlorella vulgaris* demonstrated greater sulfamethoxazole tolerance than the suspended Thus, compared to a suspended reactor, the removal efficiency of living immobilized *Chlorella vulgaris* was 12% greater. The immobilized microalgae in a mixed culture could also shield the bacterial population against sulfamethoxazole while maintaining bacterial diversity and stability, thereby achieving better sulfamethoxazole removal, which in turn promoted a symbiotic relationship between the bacteria and algae (Ferrando and Matamoros, 2020). Immobilized systems have been utilized in several applications, including reducing contaminants, energy production, and wastewater bioremediation (Salman et al., 2022; Sarkheil et al., 2022; Yu et al., 2017; Eroglu et al., 2015).

MICROALGAE IMMOBILIZATION TECHNIQUES

These immobilization methods can be categorized as "passive" using microorganisms' propensity to cling to and grow on surfaces, whether natural or manufactured, and "active" using flocculant agents, and gel encapsulation (De-Bashan and Bashan, 2010). The six various types of immobilizations that have been identified include covalent coupling, affinity immobilization, adsorption, restriction in a liquid-liquid emulsion, capture behind a semi-permeable barrier, and entrapment in polymers (Partovinia and Rasekh, 2018; Vasilieva et al., 2016). In laboratory experiments, One of the most popular immobilization techniques is entrapment, which involves trapping the cells in a three-dimensional gel matrix comprised of either synthetic (polyacrylamide, polypropylene, polyvinyl, and polyurethane) or natural (alginate, cellulose, carrageenan, and agar) polymers (De-Bashan and Bashan, 2010; Mollamohammada et al., 2020). However, the most commonly used natural gels for algal immobilization are alginate and carrageenan (Kaparapu, 2017; Vasilieva et al., 2016). Selecting an appropriate carrier is one of the crucial steps in the immobilization process, there are two categories of carriers that can be employed for cell immobilization: natural and artificial (Vasilieva et al., 2016). A good carrier for cell fixation should have properties like a porous structure, low weight, mass transfer, non-biodegradability in test conditions, inertness, non-inhibition, and non-toxicity. Moreover, the carrier must be inexpensive, environmentally safe, and have excellent mechanical, chemical, and biological stability, as well as a rough, irregular structure for colonization (Emami Moghaddam et al., 2018).

IMMOBILIZATION'S EFFECT ON MICROALGAL CELLS

Immobilization effects on microalgal physiological activity Immobilized microalgae may operate differently than suspended microalgae, depending on the materials used for immobilization. For example, it has been proven that some artificial materials (polyurethane foam and resins) utilized for microalgal immobilization are highly hazardous and highly toxic, and immobilization techniques, like the immobilization of microalgae in polymers, have major consequences on microorganisms in furthermore to the immobilized material's toxicity on on microbes, also occur as a result of metabolite accumulation inside the matrix, The matrix thickness, light, accumulation of inner metabolic byproducts, and resistance for transfer the CO_2, are the potential key causes (Han et al., 2022). But in general, non-toxic natural polymers are used in algae immobilization, and multiple studies have shown that this immobilization process can shield microorganisms from challenging environmental conditions, Understanding how immobilization impacts microalgal physiological functions is essential to enhancing the use of microalgal immobilization for various treatments (Sánchez-Saavedra et al., 2019).

ADVANTAGES AND DISADVANTAGES OF IMMOBILIZED MICROALGAE.

Immobilization of different cells in (polymeric or biopolymeric) matrices, which has many advantages over free-cell suspension because immobilized cells take up less space, are simpler to deal with, have a higher cell density, and can be utilized repetitively for product creation, cell immobilization has also been suggested to improve adsorption ability and bioavailability of biomass (Carbone et al., 2020; Eroglu et al., 2015). Strengthening operational stability, avoiding cell drift, raising reaction rates brought on by higher cell density, and promoting growth and easy harvesting with promoting pollutant removal (Carbone et al., 2020; Soo et al., 2017), such as the efficiency of microalgae Scenedesmus sp. and Synechococcus elongatus to remove C, P, and N is higher when immobilized in chitosan capsules and loofa matrix compared to those in suspension (Rosales et al., 2018). Other advantages of immobilization processes include safeguarding cell cultures against harsh environmental factors like metal toxicity, salt content, pH fluctuations, and also any product inhibition (Han et al., 2022). protection of aging cultures from negative effects of photoinhibition; increased biomass concentrations; less-destructive cell recovery; Moreover, it can protect microalgae cell from outside threats including predators and growth inhibitors (Nair et al., 2019; Lee et al., 2020). However, there are several disadvantages to microalgal immobilization. immobilization of microalgae has some drawbacks. For instance, in immobilization systems, Polymers or carriers may also block mass transfer and material absorption, and the reagents and carriers for fixation on final treatment processes, for example (processing of bioenergy and production, acquisition) were affected (Lebeau and Robert, 2006). Moreover, the extra operating procedure of microalgae immobilization may lead to greater operating costs and requirements than a suspended system; a long period of operation may result in secondary environmental pollution and hazard from stabilization materials; and microalgae leakage may occur with a long period of operation (Han et al., 2022).

APPLICATION OF MULTIPLE IMMOBILIZATION ALGAE IN THE ENVIRONMENT

Recently, it has been discovered that immobilization microalgae could be used in wastewater treatment (Li et al., 2022; Salman et al., 2022). This is a result of their many biological traits, including the ability of microalgae to thrive in a variety of wastewaters with increased nutrient uptake and to successfully change these nutrients into a variety of advantageous biomolecules (Peter et al., 2022) Immobilization agriculture is currently seen as a potential strategy for increasing sustainable biological sewage treatment and repairing the aquatic environment (Han et al., 2022).

It is also simple to harves and highly resistant to harsh environmental conditions and immobilization of biomass protects cells from compound toxicity (Pang et al., 2020). It has also been used to remove multiple pollutants from aqueous systems, such as plastics (Chia et al., 2020), heavy metals (Sen et al., 2020), and dyes (Wu et al., 2020), pharmaceuticals, such as antibiotics and PPCPs (Couto et al., 2022; Chu et al., 2022; Chandel et al., 2022), and biocides and hydrocarbons (Mondal and Khan, 2021). Immobilized algae may be utilized to produce high-value metabolites, such as those used in the production of biofuel cells, photovoltaic solar cells for electricity generation, energy conversion, and so on (Emami Moghaddam et al., 2018).

FACTORS INFLUENCING MICROALGAL IMMOBILIZED SYSTEM PERFORMANCE

The most important factors affecting the effectiveness of immobilized algae are light intensity, temperature, pH, and fixation methods. Light intensity is critical because it limits the growth of microalgae due to their requirements for photosynthesis, Light intensity greater or less than the optimal range results in photoinhibition, or undermining of the activity of photosynthesis, affecting algae growth and thus the removal of pollutants (Han et al., 2022). The production of biomass is demonstrated to be improved by increasing light intensity (Hena et al., 2021). The second photosystem of microalgae's chloroplasts is damaged by exposure to much higher light, which lowers the metabolic activity of the algae and their capacity to remove PPCP (Hena et al., 2018). Additionally, it has been noted that during the exponential phase of cells, most nutrients and organic components are removed, and the amount of light determines whether biofilm adhesion increases or decreases in the connected microalgal immobilization system (Zhuang et al., 2020). Along with light intensity, other elements including light quality and light regime are crucial. For instance, purple light inhibits cell growth while enhancing organic carbon uptake and hydrogen synthesis, while blue light increases cell growth while decreasing hydrogen synthesis (Ruiz-Marin et al., 2020). Temperature has a direct impact on biochemical process pathways and the efficiency of pollutant clearance, making it a key element in determining how well microalgae develop. Low temperatures, for instance, can impede growth by lowering the activity of carbon uptake, which can impact photosynthesis. a high temperature. On the other hand, excessive temperature (often above 40 °C) hinders photosynthesis, slows growth, and causes heat stress by inhibiting photosynthetic proteins and disrupting the cell's energy balance, ultimately leading to culture failure (Khan et al., 2018) And temperature significantly influences cellular metabolism, enzymatic activity, electron transport in the respiratory and photosynthetic systems, membrane fluidity, and composition (Corredor et al., 2021). Temperature can influence biofilm creation; depending on the species, increased temperature can promote cell growth, EPS production, and surface adhesion (Moreno Osorio et al., 2021). Other factors influencing immobilization methods, include the effects of different immobilization systems, the chosen fixation technique, the matrix or carrier material, the effectiveness of the purification process, the major algal biomass species that make up the bulk of the immobilized microalgal system, and the ratio of the concentration of target pollutants to the number of microalgae beads (Emparan et al., 2018), and the admixture of various matrices at various volume proportion (Lee et al., 2020; Abu Sepian et al., 2010). Alginate Selection, and the choice of microalgal strains (Kube et al., 2021).

CONCLUSION

Currently, microalgae immobilization technology is a leading contender for green technology. In practice, microalgal systems utilise as solar power,at same time need small amounts of other operation inputs. Also, algae can easy to handle because are environmentally friendly and produce no secondary pollution, they have been utilized in industries; produce no health hazards; and their end products can be transformed into different byproducts (like biofuel or fertilizers) that could further lower costs.Immobilized microalgae are a good,and promising biotechnological tool for the remediation of extremely toxic contaminants, via the processes of bioaccumulation, biosorption, and biodegradation. Because these systems are compact, they produce less sludge and are simpler to maintain than large fluidized beds. The field of microalgal immobilization is vast, though, and there are still a lot of unanswered questions that need to be found and resolved by researchers.

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