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Review Article

Some Using Places of Marine-Derived *Aspergillus niger* in Biotechnology: A Mini Review

Zehra TORUN*

* Deparment of Pharmacognosy, Faculty of Pharmacy, Inonu University, Malatya, Türkiye

ABSTRACT: Marine animals and plants, as well as inanimate habitats such as saltwater, sediments, hydrothermal vents, mud, and mudflats, are all home to marine fungi. Marine fungi are resistant to harsh marine conditions and may adapt. These marine microorganisms are significant because they can be easily cultivated and used repeatedly, as well as being safely stored in a laboratory setting. Thus, they are included in many biotechnological applications. In this review, we aimed to sum up the use of marine-derived *Aspergillus niger* fungus in biotechnology. The use of fungi in biotechnological applications such as bioremediation of heavy metals, biosynthesis of nanoparticle and nanofluid samples, production of valuable enzymes was explained in the section of biotechnological applications.

Keywords: *marine fungi, eco-friendly applications, biotechnology*

1 INTRODUCTION

The marine environment is under investigation increasingly for various biotechnical applications and as a new source of discoveries of science. The extreme circumstances of the sea environment are resisted by marine creatures [1]. Among the marine microorganisms, marine fungi are particularly noteworthy because they coexist in symbiotic partnerships with marine plants, vertebrates, and invertebrates and also which are isolated from the marine inanimate areas are an environmentally friendly alternative for biotechnology applications while delivering the highest value compounds under these extreme conditions [2].

In biotechnology, marine fungi are typically assessed based on their ability to produce novel secondary metabolites and are also the production source of enzymes, vitamins, polysaccharides, pigments and lipids. Nearest research has demonstrated the significance of marine fungi in the fields of biotechnology, including the synthesis of several extracellular enzymes which have applications across various domains, including food, beverage, detergent and medicine, and use in the bioremediation such as hydrocarbon degradation, removal of heavy metals, and increasing secondary metabolite production with nanoparticle applications, and biosurfactant production [3].

Tieghem (1867) designated *Aspergillus niger* as a species belonging to the *Nigri* section from the *Aspergillus* genus [4]. This

*Corresponding Author: Zehra TORUN
E-mail: zehra.torun@inonu.edu.tr
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asexually spore-bearing saprophyte inhabits aerobic settings, including 13% soil, 10% mutant environments, 24% marine environments, 27% endophytes, and 26% other environments [5,6]. *A. niger* fungus which was explored to produce citric acid for the first time, is also demonstrated as a natural source of many active compounds. *A. niger* produces many extracellular enzymes, including cellulase, pectinase, oxidase, catalase, dehydrogenase, and α-amylase, as well as a wide variety of useful proteins by developing technology [7,8]. In addition to production of secondary metabolites, which is a unit of biotechnological applications, this fungus is also used in other biotechnological applications such as bioremediation of heavy metals, biosynthesis of nanoparticle and nanofluid samples, production of valuable enzymes.

In this paper, we aimed to brief the use of marine-derived *Aspergillus niger* fungus in biotechnology. Utilization of the marine fungus *Aspergillus niger* in biotechnological applications is explained according to using purpose.

2 USE OF MARINE DERIVED *ASPERGILLUS NIGER*

2.1 Bioremediation of Heavy Metals

Toxic metals, one of the biggest problems brought by industrialization, harm both nature and people. Fungi can transport extracellular metals into the cell by increasing their growth capacity and binding them to the cell surface by improving their access through mycelium branching [9]. Thus, the fungi are an important option as natural bioremediation agents. On this subject, studies on marine fungi are very rare compared to terrestrial fungi. Marine-derived *Aspergillus niger* was studied as a bioremediation agent.

When the researches on chromium (Cr), which is among the metals of concern by the World Health Organization (WHO) due to its high toxicity and carcinogenic properties, are examined, the marine-derived *A. niger* has shown significant biosorbent competence by biomass and micellar pellets. At 25, 50 and 100 ppm concentrations of Cr (IV), there was no significant change in the dry weight of *A. niger* associated with *Eucheuma* sp. red algae, while 3.5, 7.76, and 18.1 mg of Cr were found in their pellets, respectively. Both results showed that the fungus tolerated a wide range of chromium and accumulated more than 25% of chromium [10]. Marine-associated *A. niger* displayed the greatest absorption of Cr (VI) with 117.33 mg/g biomass at pH 1.0 in the presence of 400 mg/L Cr at 50 °C, according to a kinetic investigation on the Cr (VI) sorption of dead biomass [11]. Mycelial pellets of the fungus *A. niger* isolated from the East China Sea were prepared and the ability of Cr (IV) to reduce to Cr (III) and its bio-adsorbent properties were investigated. It has been estimated that micelle

pellets produce substances that reduce Cr (IV) to Cr (III) and that these substances can diffuse into the solution containing chromium. By confirming that the fungal cell wall also adsorbs Cr (IV), marine-derived *A. niger* can be used as a natural biosorbent in wastewater treatment was predicted [12].

In studies on tolerance to copper (Cu) and lead (Pb) and their uptake capacity, *A. niger* which occurred from the sediment of the Langat River, Selangor, Malaysia, tolerated 1000 mg/L of Cu (II) and 5000 mg/L of Pb (II). In addition, the fungus removed 20.910 ± 0.581 mg/g Cu (II) at 200 mg/L of Cu (II) and 54.046 ± 0.328 mg/g Pb (II) at 250 mg/L of Pb (II) [13]. *A. niger* isolates from the Mandovi estuary in Goa, India, tolerated concentrations of 12.5 mM Pb (II) and 5 mM Cu (II). The isolate from mangroves showed a good absorption capacity of 32 - 41 mg/g of Pb^{2+} and 3.5 - 6.5 mg/g of Cu^{2+} of mycelium dry weight [14].

In other studies on heavy metals, the spores or mycelial pellets of *A. niger* fungus isolated from *Padina* sp. algae were used for aluminum recovery from bauxite ore by utilized as substrates [15].

2.2 Decolorization

Dyes, which are toxic to human cells and organs, are one of the most dangerous industrial wastes that are difficult to treat [16]. In addition, dye-containing wastewater threatens aquatic life by preventing the passage of daylight, reducing photosynthesis and causing chemical toxicity [17]. Among many dye removal procedures such as advanced oxidation processes, solvent extraction, adsorption, coagulation, ion exchange and membrane separation, the adsorption method is effectively used [17,18]. The discussion revolves around issues like clogging, efficient separation of liquid and solid after adsorption, and the potential for reusing the adsorbent [19]. The immobilization of the adsorbent biomass allows the solution of these problems to be reported. Fungi such as *Aspergillus* sp., *Penicillium* sp. and *Rhizopus* sp. have been found to undergo self-immobilization forming stable mycelial pellets. Thus, fungal biomass is a good alternative for dye removal [20-23]. *Aspergillus niger* obtained from Gorgan Bay in the Caspian Sea performed the dye removal by its adsorption ability. One gram of fungal mycelium cell adsorbed the dye molecules in a temperature range of approximately 28-30 °C in 20 hours and achieved 97% colour removal [24].

Self-immobilizing mycelial pellets of halophilic fungus *A. niger* (ZJUBE-1 strain) acquired from the East China Sea were used as biosorbent and the removal of an azo dye, also known as Congo red, was investigated. As a result, *A. niger* mycelial pellets have the highest possible adsorption capacity of 263.2 mg/g of mycelium and also have effective decolourization capabilities of > 98.5

reported [25].

2.3 Nanotechnological Applications

While utilizing marine microbes in the biosynthesis of nanoparticles (NPs) is being increased, studies on the use of marine microorganisms are still limited. Especially silver (Ag) salts and elemental silver as antimicrobial agents induced great expectations with the nanoparticle form in medical applications [26]. The synthesis of extracellular silver nanoparticles (AgNPs) of *A. niger* which was obtained from the sea of Bhavnagar coast, Gulf of Khambhat, West Coast of India, was carried out for the first time by treated with different concentrations of silver nitrate (0.25–1 mM). The utilization of laser optical speckles derived from spherical and 5-26 nm AgNPs holds potential for applications in sensors and biomedical optics [27]. AgNPs of the same fungus were biosynthesized at different pH ranges (pH:5, 8, 9, and 10). This biosynthesis, which usually takes 24 hours, took place within 3 minutes in the alkaline pH range. Antimicrobial activities of AgNPs synthesized at different pH ranges against *Bacillus megaterium*, *Shigella sonnei*, *Staphylococcus aureus* and *Proteus vulgaris* bacteria alone and in combination with gentamicin (antibiotic) were investigated. It was reported that NPs are promising antimicrobial agents, both alone and in combination, and organisms are more susceptible in an acidic pH environment [26]. Gold (Au) nanoparticles (GNPs) that affect the properties of light are utilized in potential applications of biomedicine, imaging, catalysis, and photonics. In another study on the same marine-derived fungus, it was informed that *A. niger* synthesized extracellular GNPs by its biomass exposed to Au (III) solution with different pH (7, 8, 9, 10). The weak localization of light (approximately 225 nm) in the synthesized gold nanofluids was observed. Consistent backscattering experiments were performed at two particle sizes (15 nm and 35 nm) in a water-based suspension [28]. Aspernigrin A, Aurasperone A and fonsecinone A among substances of naphtopyrones derivatives which were isolated from *Aspergillus niger* attained from a tunicate *Phallusia nigra* obtained from a coral reef in the Red Sea near Hurghada, Egypt showed the inhibitory effects. These components are evaluated as AChE enzyme inhibitors for Alzheimer's disease, and increased their inhibitory activity 16, 84 and 13 times, respectively, with AgNP synthesis [29].

2.4 Enzyme Production

Marine organisms produce therapeutic enzymes such as oncolytics, thrombolytics, and anticoagulants, as well as biocatalytic enzymes such as oxidoreductases, hydrolases, transferases, isomerases, ligases and lyases [30,31]. One of the hydrolytic enzymes used to

break down biopolymers and produce biochemicals from renewable biomass is cellulose [32]. Cellulose, which causes environmental problems when not used efficiently, is hydrolyzed by the cellulase enzyme and converted into glucose. The hydrolysis effect of cellulase is due to the synergistic effects of enzymes from exoglucanase, endoglucanase and β-glucosidase which are included in cellulase. Endoglucanase and exoglucanase mainly depolymerize cellulose, while β-glucosidase converts depolymerized substrates to glucose. Necessary to produce stable and effective enzymes that can withstand this salinity rate for the hydrolysis of cellulose (exp., marine algae [33]) that causes water pollution in a high salinity environment. In this regard, the enzymatic activity and thermodynamic characteristics of β-glucosidase obtained from *A. niger* which was obtained from the East China Sea at different salinities were investigated. Activity of β-glucosidase was elevated 1.46 times in 6% NaCl (w/v) solution salinity, 66 ^{C} temperature and pH 5.0 optimum conditions [34]. Optimization of cellulase production of the same fungal strain was investigated using different substrates (*Eichhornia crassipes*, corn cob, rice straw, wheat bran), and natural seawater (a mineral salt source). In 96 hours of incubation, biomass is maximized, while production of cellulase is 17.80 U/g based on substrate dry weight in 144 hours of incubation. An eco-friendly process was developed for cellulase production using response surface methodology [35]. *A. niger* which was acquired from sediment in the East China Sea, contained cellulase enzyme composed of high amounts of β-glucosidase with endoglucanase and exoglucanase which show low activity for cellulose hydrolysis. To increase the activity of the marine *A. niger* cellulase enzyme on cellulose hydrolysis, a vector occurring *Bacillus amyloliquefaciens* cellulase enzyme which has endoglucanase and exoglucanase with high activities was integrated into this marine fungus. The promoter glaA-signal peptide sequence-B. amyloliquefaciens cellulase-trpC terminator synthesised sequence served as the vector. The endoglucanase and exoglucanase activities in the original strain were 0.21 U/mL and 4.51 U/mL, respectively, while the activities in the vector-transformed strain were 0.89 U/mL and 15.12 U/mL, respectively. The β-glucosidase activity was 17.86 U/mL and 18.21 U/mL for the transformant and the host strain, respectively. While the cellulase activity expressed in the filter paper assay (FPA) was 4.47 U/mL, the cellulase activity of the original strain was 0.63 U/mL. In this study, the functions of endoglucanase and exoglucanase from the marine *A. niger* can be increased without changing the β-glucosidase activity for

the hydrolysis of cellulose, which causes pollution, especially in salty waters explained by gene expression [36]. In another study, the vector which is occurred promoter glaA-signal peptide sequence-*Piromyces rhizinflata* cellulase−trpC terminator, is integrated into the same marine *A. niger* strain. While endoglucanase and exoglucanase activities in the original strain were 0.21 U/mL and 4.51 U/mL respectively, after the expression they increased to 0.81 U/mL and 19.10 U/mL respectively. FPA increased from 0.63 U/mL to 4.69 U/mL. The cellulase obtained from the transformant strain showed both high activity and preserved its halostable which was in the original strain [37]. In another study, the same team investigated the function of exoglucanase from the same *Aspergillus niger* strain at a range of salt-free to 18% salinity. Exoglucanase exhibited the highest activity at 12% NaCl solution. Exoglucanase can be used for the hydrolysis of cellulose in settings of elevated salinity [38]. Salt-tolerant β-glucosidases (BGL1 and BGL2) were obtained in a study using *A. niger* (ZJUBE-1 strain) isolated from East China Sea mud as a homologous expression host. Pure BGL1 and BGL2 enzymes exhibited the highest activity at pH 3.0-4.0 and 3.5-4.5, respectively. BGL1 is resistant to metal ions, while BGL2 is sensitive to Cu2+, Fe3+ and Ag+ ions. In addition, the activity of BGL2 enhanced by 44% in the existence of 4 M NaCl was found [39]. Cellobiohydrolase is another enzyme found in cellulase. To create cellobiose, cellobiohydrolase splits the cellulose chain from its ends. β-glucosidase also reduces this cellobiose to glucose. In the study performed by Cai et al. on the same *Aspergillus niger* (ZJUBE-1 strain), they used *Agrobacterium tumefaciens* AGL-1 for transformation and expressed two genes (cel7a and cel7b) for cellobiohydrolase homologously. The industrial uses of the obtained cellobiose hydrolases (AnCel7A and AnCel7B) under acidic, high salinity and high-temperature conditions were evaluated. AnCel7B was more thermostable than AnCel7A, exhibiting half-lives of 90, 35, and 15 minutes at 80, 90, and 100 °C, respectively. In addition, AnCel7B exhibited halotolerance at 0.9 M NaCl optimal salt concentration, while AnCel7A showed acidophilic properties with optimal pH 2.5-4.5 values [40].

Another hydrolytic enzyme, xylanase, is a hemicellulotic that disrupts the bond between lignin and xylan, which protects cellulose fibres [41]. Particularly in the bio-bleaching process, xylanases are preferred because they do not contain cellulase, are effective at alkaline pH, are stable at extreme temperatures, and are active in the presence of sulfated lignin. The fungus *Aspergillus niger* which was obtained from the detritus of rotting

mangrove leaves from mangrove swamps on Chorao Island, Goa, India, was investigated as a suitable source of alkaline xylanase for use in the biological bleaching of pulp. The culture filtrate showed optimum activity at 50 °C and a secondary activity at 90 °C for pH 3.5, while optimum activity was observed at 80 °C for pH 8.5. The crude enzyme containing 580 U/L xylanase without cellulase was thermostable for at least 4 hours at 55 °C and retained approximately 60% activity. In addition, b-xylosidase and a-L-arabinofuranosidase acted synergistically with xylanase in crude culture phytate. There were reports of their moderate activities [42].

L-asparaginase (L-asparagine amidohydrolase, LA) is an important oncolytic enzyme used in the treatment of pediatric acute lymphoblastic leukaemia. *Erwinia carotovora*, *Erwinia chrysanthemi* and *Escherichia coli* bacteria are the sources of trade LA products [43,44]. However, these bacterial sources also bring with them anaphylaxis, diabetes, leukopenia, neurological seizures, pancreatitis and coagulation abnormalities possibly leading to intracranial thrombosis or bleeding [45]. In the search for a new source of LA, the fungus *A. niger* (AKV-MKBU strain) was isolated from the *Avicennia marina* mangrove located on the Bhavnagar coast, Gulf of Khambhat, West Coast of India was found as the strongest producer with the LA activity 7.5642 U/mL [46]. Optimization of LA production was achieved by using models such as the response surface methodology (RSM) used in microorganism enzyme production and the artificial neural networks (ANNs) used for enzyme production optimization. LA production which was 15.78 U/mL at pH 4, was increased by 108.62%, while the ANN method was found to be superior to the RSM analysis [47]. In another optimization study, LA activity was increased by 22.0% with 9.2285 U/mL in the medium optimized with the Plackett-Burman design and 73.52% with 13.1252 U/mL in using the central composite design (CCD) of RSM [48]. The LA enzyme purified from the fungus is 90 kDa molecular weight, active at the pH 4-10, and stable in temperatures 20-40 °C. Purified LA demonstrated its potential antiproliferative activity against HepG2, A549, U87MG, JURKAT E6, and chronic myeloid leukemia cells obtained from bone marrow, showing IC_{50} values of 0.375, 0.399, 0.204, 0.22 and 0.2 U/mL, respectively [49].

3 CONCLUSION

Biotechnological disciplines encompass environmental, industrial, pharmacological, and clinical applications. Marine fungi, in particular, represent a significant resource that is assessed in various biotechnological domains. *Aspergillus* species are considered one of the most significant

marine fungal species that have been studied. The review demonstrates the significance of utilising marine-derived *Aspergillus niger* as a valuable alternative component in biotechnological applications. According to reports, hydrolytic enzymes derived from the fungus have shown increased activity. Therefore, it is imperative to consider *Aspergillus niger* fungus as a crucial candidate for future research on the synthesis of biocatalyst enzymes, which are essential for enhancing the sustainability and efficiency of industrial processes. The significance of marine *A. niger* in the field of grey biotechnology lies in its ability to effectively eliminate poisonous dyes and heavy metals from soil and water, hence addressing environmental pollution. This organism plays a crucial role as a natural symbiont, particularly in the elimination of hazardous heavy metals like chromium, copper, lead, and aluminium that tend to collect in water and soil contaminated with waste. Additionally, it is effective in removing dangerous dyestuffs that can negatively impact human cells and tissues. The marine *A. niger* fungi should be regarded as the foremost option in the realm of environmental biotechnology, specifically designed for the purpose of biological remediation, waste management, and purification applications. The *A. niger* fungus is assessed for its ability to produce bioactive chemicals for medicinal and therapeutic use within the field of red biotechnology. Moreover, the investigation of the therapeutic characteristics of nanoparticles derived from isolated substances and synthesised with elements such as Ag and Au is a new and promising field of research. This review serves as a guide to accessing biotechnological studies on marine *Aspergillus niger*. There is a need to enhance the assessment of marine-associated *Aspergillus niger* in the biotechnology domains indicated. Furthermore, it serves as a significant resource model for other biotechnological domains that have yet to be assessed. Further scientific investigations should incorporate marine *A. niger* to enhance the comprehensiveness of the research.

4 AUTHOR CONTRIBUTIONS

Hypotesis: Z.T.; Design: Z.T.; Literature review: Z.T.; Data Collection: Z.T.; Analysis and/or interpretation: Z.T.; Manuscript writing: Z.T.

5 CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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