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Highlights of biological activities, secondary metabolites, and Chaetomium morphology

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Introduction

Many researchers are interested in the use of microbial secondary metabolites in general and fungal metabolites in particular in various biotechnology fields because of their bioactive qualities, which have led to their use in pharmaceutical, industrial, and agricultural fields. Microorganisms known as fungal endophytes reside inside the tissues of living plants without causing any harmful effects [1–4]. In general, endophytes are abundant in new, physiologically active natural substances that have amazing therapeutic potential. Endophytic fungi have recently produced amazing pharmacological compounds [5, 6]. Endophytes have been shown to contain more than 50% of hitherto unidentified physiologically active compounds [7]. Endophyte-derived biopharmacological secondary metabolites have a variety of antibacterial, anticancer, antitumor, and anti-inflammatory properties [8]. Chaetomium, an endophytic fungus, is a great model that is employed as a biotechnological tool in many different domains. Known for producing secondary metabolites with essential biological functions, Chaetomium species are heterothallic fungi that are primarily found in soil and organic compost. More recently, they have been isolated from coral, soft coral, and marine algae. [9–14]. Chaetomium isolates have been shown to produce a number of antifungal compounds and to exhibit a variety of antagonistic mechanisms against other disease fungi [15, 16]. Chaetomium globosum Kunze Fr., for instance, has been found to be a promising biocontrol agent against a variety of plant diseases [17]. Highlights of the biology, ecology, description, and secondary metabolites of Chaetomium species were included in this review.

Chaetomium description and ecology

Microbes that colonize the inside living tissues of plants without immediately posing a threat are referred to as "endophytes" [1]. A dematiaceous filamentous fungus known as Chaetomium sp. may be isolated from soil, air, and plant waste [18, 19]. Chaetomium is a member of the Chaetomiaceae family, Order Sordariales, and class Pyrenomycetes (Ascomycotina). Around 95 species have been identified globally under the genus Chaetomium [20]. Chaetomium species are not just contaminants but also human pathogens. Certain organisms have neurotropic and thermophilic traits [21]. Although spore concentrations in outdoor air are not extremely high, Chaetomium sp. are common fungus species that are widely distributed around the planet. They are found in soil and on decomposing plant materials. Chaetomium can be found indoors on cellulose materials such as straw, wood, compost, and sheet rock. For hardwood and softwood timber, it is also referred to as a soft-rot fungus [22]. Chaetomium colonies grow quickly; they start off looking white and cottony before turning grey and olive as they age. The tint seems to be brownish black or reddish tan when viewed from the back [23]. Ascomata globose, ellipsoid to ovate or obovate, ostiolate or non-ostiolate in certain species, and typically consisting of walls made of textura intricata or epidermoidea in surface view, or textura angularis in certain species, are characteristics of chaetomium. In certain species, ascomatal hairs are smooth, hypha-like, flexuous, undulate, coiled to simple or dichotomously branched, or have a verrucose surface (Figure 1, 2). Evanescent ascospores that are fusiform or asci clavate and have eight biseriate or irregularly organized ascospores. Ascospores are bilaterally flattened,

limoniform to globose, or irregular in certain species, and typically longer than $7\mu\text{m}$. If they exist, asexual morphs resemble acremonium. A member of the Chaetomium genus



Figure 1. Chaetomium species with spiral setae and with oval ascospores. isolated and identified by Dr. Waill Elkhateeb (Photographs was taken by Dr. Waill A. Elkhateeb, Locality: National Research Center of Egypt).

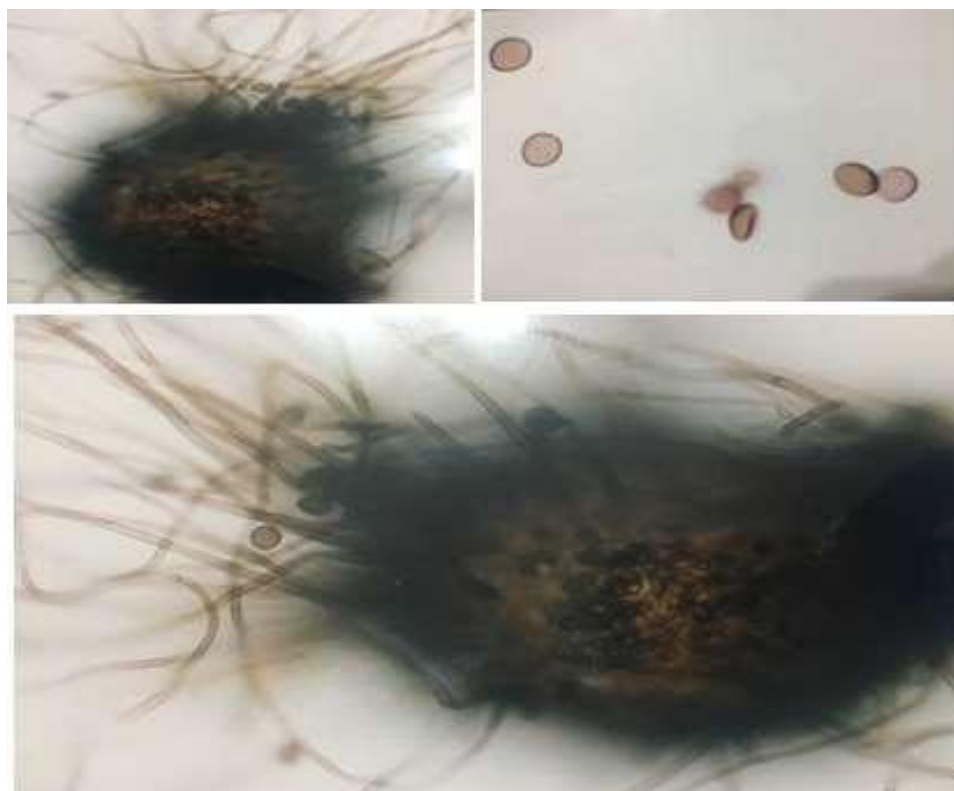
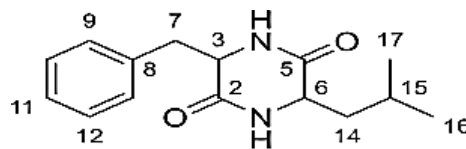
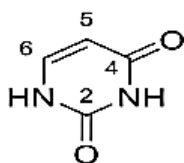
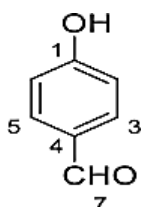


Figure 2. Chaetomium species with globosum ascospores isolated and identified by Dr. Waill Elkhateeb (Photographs was taken by Dr. Waill A. Elkhateeb, Locality: National Research Center of Egypt).

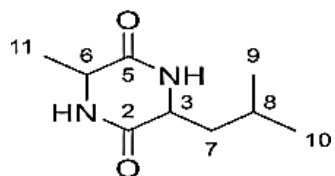
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Chaetomium secondary metabolites

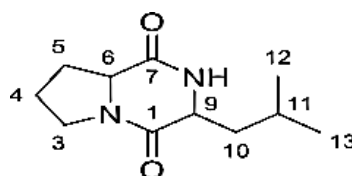
Terpenoids, chaetoglobosins, tetramic acids, steroids, xanthenes, diketopiperazines, bis (3-indolyl)-benzoquinones, azaphilones, anthraquinones, pyranones, and orsellides are among the more than 200 secondary metabolites that have been separated and identified from *Chaetomium globosum*. Some of these metabolites demonstrate various bioactivities such as cytotoxic, antiviral, anticancer, antimalarial, and antibacterial properties. Some compounds that have been studied for their antibacterial and anticancer properties were found by Tawfik et al. [25]. Five pure chemicals were obtained using metabolomics and bioassay-guided isolation: p-hydroxybenzaldehyde, uracil, 3-benzyl-6-isobutyl piperazine-2,5-dione, Cyclo (L-Alanin-L-leucin), and Cyclo-(L-proline-L-leucine) (Figure 3).



p-hydroxybenzaldehyde Uracil 3-benzyl-6-isobutyl piperazine-2,5-dione



L-Alanin-L-leucin



Cyclo-(L-proline-L-leucine)

Figure 3. Some bioactive compounds produced by *Chaetomium* species.

Some biological activities of *Chaetomium* metabolites

Studies were carried out to assess the biological activities of such compounds because of their abundant synthesis of secondary metabolites, including chaetoglobosins, xanthenes, anthraquinones, terpenoids, depsidones, and steroids [26, 27].

Because of their strong antibacterial properties, *Chaetomium* species have been used as biocontrol agents. Numerous studies have documented the effectiveness of many species, particularly *Chaetomium globosum*, against the apple scab pathogen *Venturia inaequalis* [28], as well as against *Macrophoma kuwatsukai*, *Rhizoctonia solani*, and *Sclerotium rolfsii* (*Corticium rolfsii*) [29, 30]. Additionally, *Chaetomium* exhibits encouraging antagonistic properties against *Drechslera sorokiniana*, the spot blotch pathogen [31, 32]. Additionally, *Chaetomium* shown antifungal properties against *Alternaria raphani*, *Cochliobolus sativus*, *Fusarium*, *Pyricularia oryzae*, *Helminthosporium*, *Pyrenophora*, *Pythium ultimum*, and *Sclerotinia sclerotiorum* [33, 34]. Additionally, using *C. globosum* as a biocontrol agent to prevent late blight in potato plants produced more tubers and showed encouraging results. Likewise, it was noted that *C. globosum* might inhibit *Pythium ultimum*-induced damping-off of sugar-beet [35, 36]. However, *Chaetomium* species demonstrated strong antibacterial activity against both gram-positive and gram-negative bacteria, particularly *Staphylococcus aureus* and *Escherichia coli* [37].

There have also been reports of *Chaetomium* species' cytotoxicity and anticancer effects. For instance, a panel of seven

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human solid tumor cell lines shown anticancer activity in response to a novel dihydroxanthone that was derived from *Chaetomium globosum* (Wijeratne et al., 2006). The

Chaetomium globosum CGMCC 6882 polysaccharides demonstrated anticancer properties against human lung cancer A549 cells [38]. With IC₅₀ concentrations of 9.89 µg/ml, 18 µg/ml, and 54 µg/ml, respectively, flavipin, which is produced by *Chaetomium globosum*, shown dose-dependent antiproliferative action against A549, HT-29, and MCF-7 cancer cells [39]. Methyl 9-dihydro-8-trihydroxy-9-oxo-Hxanthene-1-carboxylate, a member of the xanthenes, and (E)-methyl 2-hydroxy-6, 6-dimethyl hept-3-enoate, two novel compounds extracted from *Chaetomium globosum* isolated from Egyptian soil, demonstrated anti-proliferation activities against the human breast cancer cell line MCF-7 and the human liver carcinoma cell line HEPG-2 [40].

It should be mentioned that co-culturing particular bacterial species has been shown to cause *Chaetomium* to produce metabolites [41–44]. Additionally, *Chaetomium* species shown promising nematicidal properties, particularly against *Meloidogyne incognita*, *Heterodera glycines*, and *Meloidogyne javanica* [45–50].

In conclusion :

In addition to the increased knowledge of the harmful effects of employing chemicals for pest and fungus control, the emergence of antibiotic-resistant microorganisms and novel diseases that pose a threat to human life necessitate a constant search for powerful natural molecules.

Biocontrol of soil-borne diseases has garnered interest recently as a potential substitute or supplement to the hazardous pesticides now in use. *Chaetomium globosum*, in particular, and other *Chaetomium* species in general are promising biocontrol agents that can eradicate infections and raise the yield. Further research is necessary to fully comprehend the nutritional requirements, method of action, and quantification of fungi in soils. *Chaetomium*'s evolution, ease of isolation, and molecular identification have made it easier to find new species. Additionally, the development of sophisticated tools for chemical identification of compounds and advancements in chemical extraction techniques have made it possible to find new compounds with potential biological functions. Further research is needed to fully understand the interactions between *Chaetomium* and other microbes and their host plants using molecular markers. It is crucial to conduct more research on the outcomes of co-culturing *Chaetomium* with other bacterial species and how this affects the metabolites that are produced. Lastly, looking into the possible bioactivities.

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