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Chaetomium globosum: A potential fungus for plant and human health

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ABSTRACT

***Chaetomium globosum* is a ubiquitous fungus that occurs on a wide variety of substrates, and is recognized as cellulolytic and/or endophytic. *C. globosum* has been also explored as a source of secondary metabolites with various biological activities, having considerable potential in agricultural, medicinal and industrial field. This species of *Chaetomium* is also well known for hydrolytic enzymes and plant growth promotion attributes including biocontrol against phytopathogens, and helping in phytonutrition. *Chaetomium globosum* has also been used extensively for cytotoxic and phytoxic drug discoveries. This review is focused on the research being carried out on biology and potential applications of *C. globosum* with emphasis on its role in plant and human health.**

Key words: *Chaetomium globosum*, biocontrol, phytonutrition, cytotoxic

INTRODUCTION

The need for new and useful compounds to provide protection and relief to crop plants from pests and thereby sustenance of food production for human consumption and new therapeutic drugs for well being of human health is ever growing. Nature has bestowed us with plenty of worthy microbes to take into account their assistance but still very limited work has been done in response to this quality. Based on the current need, research being carried out on a potent fungus *C. globosum* is reviewed here. Fungus *C. globosum* is a well known mesophilic member of the family *Chaetomiaceae* established by Kunze in 1817 (cited from Von, 1986). *Chaetomium* species are well known as coprophilous, seed and soil fungi (Somrithipol, 2004; Somrithipol *et al.,* 2004). The genus of this filamentous fungus (Phylum *Ascomycota*, Class *Sordariomycetes*) encompassing species that typically possess densely setose, ovoid to pyriform ostiolate ascomata, clavate asci and pigmented, one celled ascospores is known for its varied performance (Domsch *et al.*, 1993). *Chaetomium* is a dematiaceous, filamentous fungus belonging to a large genus of saprobic ascomycetes found in soil, air, plant debris, dung, straw, paper, bird feathers, and seeds (Guarro *et al.*, 1995).

More than 100 species of *Chaetomium* have been described, the most common ones being *C. atrobrunneum, C. funicola, C. globosum*, and *C. strumarium* (Aru *et al*., 1997). Wang *et al.*, (2016) reassessed *C. globosum* phyllogenetically by using β-tubulin (tub2) and RNA polymerase II second largest subunit (rpb2) as DNA barcodes for differentiating *Chaetomium* species; twenty-eight species were reduced to synonymy under *C. globosum*, and two additional species, were tentatively maintained: *C. cruentum* as an albino form of *C. globosum*, and *C. spirochaete* slightly deviating from *C. globosum* by more regularly coiled and thicker ascomatal hairs. Several species, including *C. elatum* and *C. subaffine*, were also considered as close relatives of *C. globosum*.

Chaetomium globosum is frenquently encountered and is a very common species in indoor environments. The fungal colonies show rapid growth, initially white in colour with a cottony appearance and on maturation becomes grey to olive, tan to red or brown to even black. Microscopically, *C. globosum* has distinctive small brown 'lemon' or 'football'-shaped ascospores. The spores, formed inside the fruiting bodies, are forced out of openings and spread by wind, insects, and water splash (**Fig.1**). This species causes biodeterioration of paper and other cellulosic material. It is considered as a "weed" of mushroom beds, where it inhibits the growth of cultivated mushrooms. *C. globosum* is important to human health as a contaminant in indoor environments by producing mycotoxins and allergic reactions (Dalmont *et al*., 2017) and by producing many of crucial pharmaceutical drugs. It also contributes to plant health as plant growth promoting fungus (PGPF). The fungus has recently been introduced in the world of nanobiotechnology by Singh *et al.* (2018). These authors synthesized and characterized antibacterial silver and gold nanoparticles using aq. cell-free filtrate (CFF) of endophytic *C. globosum* and found enhanced antibacterial activity

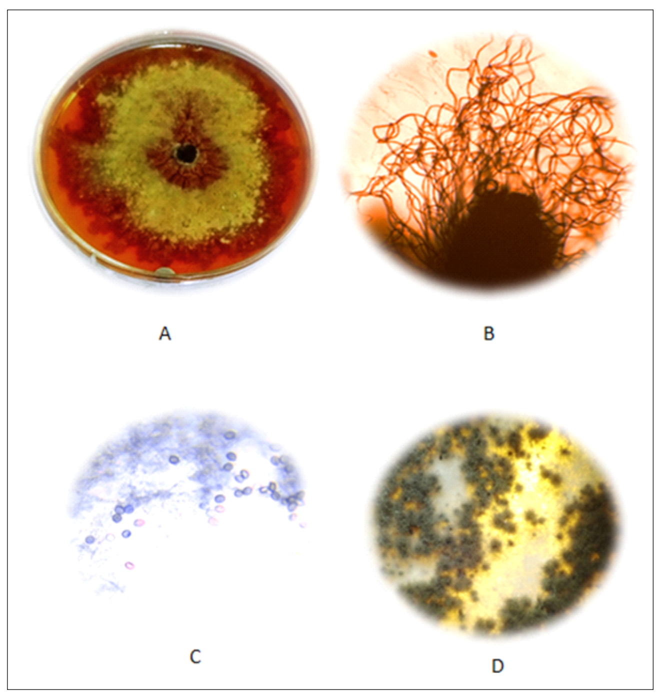

Fig.1. Colony of *Chaetomium globosum* on PDA medium (A). Perithecia and ascospores of *C. globosum* (B and C). Colony texture and ascomata of *C. globosum* on PDA medium (D).

against *Staphylococcus aureus* and *Klebsiella pneumoniae* compared to $AgNO_3$.

OCCURRENCE ON VARIOUS SUBSTRATES

Chaetomium globosum, is one of the commonest species growing saprophytically in rhizosphere and phyllosphere. It can be isolated easily from decaying plant material, seeds and other cellulosic substrates. It is the most frequently isolated and cosmopolitan species out of the over 150 species of *Chaetomium* described to date (Domsch *et al.*, 1993). This fungus is frequently isolated in water-damaged buildings (Arreche *et al.*, 2017). They are habituated from deserts to mountain soils across various ecosphere, inhabiting in several organic and inorganic materials such as compost, dung, seeds, cereals, card board, foam and fabrics, soil, straw, paper, sheetrock, wallpaper, ceiling, tiles and on wooden products (Flannigan and Miller 2011; Miller *et al*., 2008; Cuomo *et al*., 2015). It has also been isolated as an endophytic fungus from non-symptomatic tissues of plants of terrestrial and aquatic regions by several researchers for their noble properties in plant and human welfare (Longoni *et al*., 2012; Kumar *et al*., 2013; Park *et al*., 2005). Spores of *Chaetomium* species have not been detected in air samples of sick buildings but from moisture damaged building materials; it could be on account of unavailability of favorable water activity required for growth (>0.90) (Fogle *et al*., 2007; Andersen *et al.*, 2011). Data in **table 1** describes the various sites of occurrence of *C. globosum.*

Chaetomium globosum has been recovered as an endophyte from several different tissue types of gymnosperms, dicots and monocots including *Ginkgo biloba* (Li *et al*., 2014) *Vitis vinifera* (Longoni *et al*., 2012), *Oryza sativa* (Naik *et al*., 2009) and lichen, *Everniastrum nepalense* (Zheng *et al.*, 2014) (**Table 2**).

Dissemination of the fungal spores occur through air, wind, water, insects, etc. On culturing *Chaetomium* can produce an *Acremonium* **-**like state (imperfect stage) on growth media. The fungus is mainly characterized by superficial flask

Table1. Various sites of isolation of *Chaetomium globosum*

S. No.	Sites of isolation	Reference
1	Soil samples a) Soil of pineapple plantation b) Cucumber rhizospheric soil c) Egyptian soil	 Pornsuriya *et al.* (2008) Awad *et al.* (2014) Hani and Eman (2015); Hamed *et al.* (2016)
2	Organic compost	Soytong *et al.* (2001)
3	Wood , ceiling & tiles	Flannigan and Miller (2011); Miller *et al* .(2008)
4	Gypsum wallboard	Anderson *et al.* (2017)
5	Moisture damaged building materials	Andersen *et al.* (2011); Provost *et al.* (2013)
6	Wall paper, mattresses, & carpets	Summerbell (1998)
7	Rising damp	Gravesen *et al.* (!999)
8	Atmosphere of Karachi city	Afzal and Mehdi (2002)
9	Bedroom, drawing room, living room etc	Bokhary and Parvez (1995)
10.	Dust of Aircondiner	Bagy and Gohar (1998)
11	Asthematics patient	Vesper *et al.* (2007)
12	Black pepper, white pepper & Brazil nuts	Freire *et al.* (2000)
13	Cashew kernels	Pitt *et al.* (1993)
14	Harvested wheat and shorghum du st (air of hey sites)	Abdel *et al*. (1990)
15	Anise & fennel seeds from Egypt	Moharram *et al.* (1989)
16	Tobacco samples	El- Maghraby and Abdel- Sater (1993)
17	As endophytes (From different plants)	Listed in table 2.

Table 2. Different plant host used for isolation of *C. globosum* as an endophyte

S. No.	Name of the host	bioprospects	Authors
1	*Ginko biloba*	Antioxidant Herbicidal Antifungal Phytotoxic & cytotoxic effect Anticrustaceans	Ye *et al.* (2013) Wang *et al.* (2017) Xue *et al.* (2012); Zhang *et al.* (2013) Li *et al.* (2014) Qin *et al.* (2009)
2	*Imperata cylindrica*	Antitumor	Ding *et al.* (2006) ; Shen *et al.* (2015)
3	*Ulva pertusa*	Antitumor	Cui *et al.* (2010)
4	*Viguiera robusta*	Antibiotic	Borges *et al.* (2011)
5	*Amaranthus viridis*	Phytotoxic	Piyasena *et al.* (2015)
6	*Curcuma wenyujin*	Antifugal & cytotoxic	Wang *et al.* (2012)
7	*Everniasvum nepalense*	Insecticidal Anticancer	Shi *et al.* (2013) Zheng *et al.* (2014)
8	*Gossypium hirusutum*	Antiparasitic	Zhou *et al.* (2016)
9	*Adiantum capillus*	Anti-inflammatory	Haider *et al.* (2013); Selim *et al.* (2014)
10	*Wikstroemia uva-ursi*	Cancer chemo preventive	Youn *et al.* (2015)
12.	*Nymphaea nouchali*	Antibacterial	Dissanayake *et al.* 2016
13	*Salvia miltiorrhiza*	Elicitor	Zhai *et al.* 2017
14	*Houttuynia cordata Thunb*	Antifungal	Pan *et al.* 2016

shaped perithecia which are clothed with dark, stiff hairs and the ascospores are released inside the perithecium and squeezed out through an ostiole. Ahammed *et al.* (2005) reported that different isolates show different shapes of perithecia as studied under light microscope. *C. globosum* requires acidic condition for favourable growth but has pH tolerance from 4 to 12 on potato dextrose, (Fogle *et al*., 2008; Kharwar *et al*., 2011). Cellulose is found crucial for sporulation at 26º C in dark and it exhibits cellulolytic activity on lignocellulosic substrates (Rathinam and Sumati, 2017). It also obtains its energy for growth and sporulation from different carbon sources such as sugars like glucose, mannitol, fructose, sucrose, etc; but acetic acid is reported to enhance its growth rate. It stores energy in cell in the form of glycogen and trehalose (Domsch *et al*., 1980). Mycotoxins from *C. globosum* are optimally produced at neutral pH (Fogle *et al*., 2008). Ascospores of *C. globosum* can withstand higher temperatures but not more than 55 ºC (Chapman and Fergus, 1975). The species forms germ tube for germination which subsquently develops into pale aerial mycelia. Species of *Streptomyces* and tannin has been found to inhibit spore germination in catabolism (Aspiroz *et al*., 2007) and calcium propionate, methylparaben and propylparaben results in its complete growth inhibition (Sequeira *et al*., 2017).

AS A SOURCE OF BIOACTIVE METABOLITES

1. Role in Pharmaceutical Industry

Chaetomium globosum is a contaminant in indoor environments found in buildings and act as an allergen as it produces mycotoxins and usually cause skin and nail infections and rarely cerebral and systemic infections in humans, particularly in immune compromised patients (Madsen *et al*., 2016; Cuomo *et al*., 2015. Shi *et al*., (2016) reported the first case of onychomycosis caused by *C. globosum* with periungual inflammation that was confirmed by clinical findings, repeated fungal isolation, light microscopy and sequencing analysis of the rDNA internal transcribed spacer (ITS) region. It is known to produce the highly cytotoxic chaetomins and chaetoglobosins that inhibit cell division, locomotion, formation of cell surface projections and glucose transport (Nielsen *et al*., 1999; Ueno, 1985). Recently two new azaphilone derivatives, chaephilones A and B were evaluated for cytotoxic activities against five human cancer cell lines (HL-60, SMMC-7721, A-549, MCF-7, and SW480) (Chen *et al*., 2016b). Chaetoglobosin U produced by endophytic fungi *C. globosum* IFB-E019, residing inside the stem of healthy *Imperata cylindrica* exhibited cytotoxic activity against the human nasopharyngeal epidermoid tumor KB cell line with an IC_{50} value (Ding *et al*., 2006).

Chaetomium globosum was found to produce flavipin as an oxidant under optimized culture conditions (Ye *et al*., 2013). *C. globosum* TW1-1 a symbiont derived from the medicinal terrestrial arthropod *Armadillidium vulgare* was reported to be a rich source of cytochalasans chemically investigated from the methanol extract of solid rice culture (Chen *et al.*, 2016a). Eight rare pyrrole-based cytochalasans, termed armochaetoglobins KR (18), along with three known analogues (911), it was evaluated for their anti-HIV activities in vitro, and compounds 24, 7, 8, and 10 showed significant anti-HIV activities. *C. globosum* has been reported as a remarkable producer of bioactive natural products that include globosumones (Bashyal *et al*., 2005) benzaldehyde derivative chaetopyranin (Wang *et al*., 2006), chaetoglobosins (Ding *et al*., 2006), polyhydroxylated steroids (Qin *et al*., 2009), and a novel fungal enzyme glucocerebrosidase. This unique enzyme can hydrolyze glycosphingolipid called glucosylceramide (GlcCer) to glucose and ceramide; this could be helpful to develop novel strategies to deliver glucocerebrosidase to lower the load of glucosylceramide and ameliorate Gaucher's disease in man. *C. globosum* strain L18, isolated by Wang *et al*., (2012) from the medicinal plant *Curcuma wenyujin*, produced chaetoglobosin X (1) which exhibited a broad antifungal spectrum and showed the strongest cytotoxic activity against H22 and MFC cancer cell lines.

A recent research by Hani and Eman (2015) resulted in isolation and purification of two potential anticancer compounds namely, methyl 9-dihydro-8-trihydroxy-9-oxo-hxanthene- 1-carboxylate as a member of xanthones and (E)-methyl 2-hydroxy-6, 6-dimethyl hept-3-enoate from *C. globosum* isolated from Egyptian soil. The two compounds were tested against Michigan Cancer Foundation-7(MCF-7) breast cancer cell lines and hepatocellular carcinoma, Human (HEPG-2) a human liver carcinoma cell line and showed inhibitiory effect on the proliferation of two cell lines. Endophytic *C. globosum* was isolated from aquatic origin by Ruan *et al*., (2017) for the production of aureonitol and cytochalasan as anti- acetyl cholinesterase, anticoagulant and anticancer effect. *C. globosum* SNSHI-5 derived from extreme environment produced two new cytochalasan derivatives, isochaetoglobosin D_b (1) and cytoglobosin A_b (2) Cytotoxic against H292 human lung cancer cell (Wang *et al.*, 2017).

C. globosum isolated from lichen produced Chaetoglobosin Y (1) an amorphous powder ($C32H38N_2O_5$) which was cytotoxic to colon cancer HCT-116 cell line. *C. globosum*, from the leaves of *Ginkgo biloba* produces a novel cytotoxic chlorinated azaphilone derivative named chaetomugilin D (1); this together with three other known metabolites displayed significant growth inhibitory activity against the brine shrimp (*Artemia salina*) and *Mucor miehei* (Qin *et al.*, 2009). *C. globosum* (CG6) isolated by Haider *et al*., (2013) from China produces anti-inflammatory substances in its host *A. capillus-veneris;* presence of several anti-inflammatory substances could be attributed to its long period of co-evolution (Zhao *et al*., 2010; 2011). It was also isolated from healthy leaves of the same host plant from Egypt. For the first time inhibitory activity of endophytic *C. globosum* secondary metabolites to butyrylcholinesterase, one of the neuro hydrolase enzymes that play a major role in development of Alzheimer's disease was reported (Selim *et al*., 2014).

Chaetoglobosin Fex (Cha Fex), a cytochalasan-based alkaloid, was isolated from marine-derived endophytic strain of *C. globosum* QEN-14; it was found to be a mediator in inflammatory responces via toll-like receptor 4 (TLR4) signaling in macrophages (Dou *et al*., 2011). *C. globosum* isolated by Youn *et al*., (2015) from leaves of *Wikstroemia uva-ursi* led to the isolation of two new azaphilones, chaetoviridins J and K (1 and 3), along with five known derivatives (2 and 4-7). The isolated compounds were evaluated for their cancer chemopreventive-potential based on their abilities to inhibit tumor necrosis factor alpha (TNF-α)-induced nuclear factor-kappa B (NF-κB).

2. Role in Agriculture

A number of endophytic fungi and their metabolites have been reported to exhibit insecticidal, fungicidal and plant growth promoting activity (Kumar *et al*., 2008). Cell wall degradation caused by beta-glucanases and carboxymethyl cellulases is one of the possible modes of action of *C. globosum* against phytopathogenic fungi (Aggarwal, 2015). Recently parameters of induced resistance in wheat (*Triticum aestivum*) against *B. sorokiniana* and *Puccinia triticina* using biocontrol agent *C. globusum* were investigated by Aggrawal (2015). Enhanced activities of defense related enzymes polyphenol oxidase, peroxidase, phenyl alanine lyase and catalase revealed the role in induction of systemic resistance. Role of endophyte *C. globosum* Lk4 was reported in growth of *Capsicum annuum* by production of gibberellins and indole acetic acid by Khan *et al*., (2012). Microorganisms of the genera *Trichoderma*, *Aspergillus* and *Chaetomium* are thought to be cellulase producers, and crude enzymes produced by these microorganisms are commercially available for agricultural use (Kumar and Thippeswamy, 2013).

The use of microorganisms or their enzymes for the conversion of cellulose into simple carbohydrates is receiving increased attention. *C. globosum* as Biophos produces phosphatases and phytases, which mobilize P and enhance the production of castor, wheat and pearl millet crops (Vaghasia *et al*., 2017; Tarafdar and Gharu, 2006). Dhingra *et al.*, (2003) reported successful competition of *C. globosum* with major interfering fungi such as, *Trichoderma*, *Nigrospora*, and *Fusarium* in colonizing the soybean stems above and under the soil surface. Investigation into the mechanism of biosynthesis of such natural products in *C. globosum* was carried out by Nakazawa *et al*., (2013) which led to the discovery of aureonitol, with two new compounds, mollipilin A and B; aureonitol acts like a transcriptional regulator for the biosynthesis of other secondary metabolites. Chaetoglobosin C produced by *C. globosum* can act to stimulate plant immunity against several diseases by inducing a localized and sub-systemic oxidative burst in carrots, potatoes, sweet potatoes, tomatoes, and tobacco (Kaewchai *et al.*, 2009)

Chaetomium globosum strain TAMU 520 has been reported for reductions in herbivory, negatively affecting the fecundity of both cotton aphids (*Aphis gossypii*) and beet armyworms (*Spodoptera exigua*). Endophytic, *C. globosum* inhibited root-knot nematode (*Meloidogyne incognita*) infection and reduced female reproduction below ground (Zhou *et al.*, 2016). Kharwar *et al*., (2008) discussed the possibility of use of *C. globosum* for its anti-stress property in leaf tissues of the 'sadabahar' plant. *C. globosum* isolate CgA-1 can reduce soybean stem canker disease caused by *Diaporthe phaseolorum* f. sp. *meridionalis* (Dhingra *et al.*, 2003) *C. globosum* has also been found to mobilize organic and poorly soluble phosphates resulting in enhanced yield in the field of wheat and pearl millet by releasing phytases and acid phosphatases (Tarafdar and Gharu, 2006). A combination of copper sulphate and *Chaetomium* increased seedling dry weight, osmotic solute content and antioxidant enzyme activity compared to copper sulphate alone, while lipid peroxidation levels were also decreased. The fungal scavenger system might be important for supporting the ability of maize seedlings to resist copper toxicity (Alhamed and Shebany, 2012). The fertilizer prepared by Zhou (2016) having the microbial composition of *Bacillus licheniformis*, *Trichoderma reesei*, *Chaetomium globosum*, and *Bacillus cereus* was found to be effective in growth, yield and dry grain wt. of wheat also reduced aphid damage. The fungus isolated from rhizospheric soil of Cucumber, produced some antioxidant and antimicrobial secondary metabolites against *B. subtilis*, *E. coli* and *R. solani* (Awad *et al.*, 2014). Two new indole alkaloids chaetocochin J (1) and chaetoglobinol A (8), along with chetomin (2), chetoseminudin A (3), cochliodinol (9), and semicochliodinol (10), were isolated from the rice culture of the fungus *C. globosum* which exhibited antibacterial activities against *Bacillus subtilis* (Xu *et al*., 2015). Wang et al. (2017) isolated the fungus from same plant for seven azaphilones, including Chaetomugilin A (1), D (2), S (3), I (4), J (5), Q (6) and O (7), applied for glyphosate control as a broad-spectrum systemic herbicide

Extracts of *C. globosum* EF18, isolated as endophytic fungus from *Withania somnifera*, were found to be effective against *Sclerotinia sclerotiorum* an omnivorous plant pathogen causing white rot in many crops (Kumar *et al*., 2013). This fungus has also been isolated from the leaves of the allelopathic plant *Amaranthus viridis* of the family *Amaranthaceae* (Piyasena *et al*., 2015). This fungal strain was found to produce chlorine-containing azaphilone derivatives, chaetomugilin D (1) and chaetomugilin J (2) showing phytotoxic activity in lettuce (*Lactuca sativa*) seed germination bioassay. In this review, we focus on the advantages of using mycofungicides for plant disease control and fungal biofertilizers to increase crop production.

3. Role as Biocontrol agent

Chaetomium globosum has been reported to be a potential antagonist against soilborne and seedborne phytopathogens, (**Fig. 2**) (Biswas *et al*., 2012). The antagonism of *C. globosum* against these pathogens is exerted through three modes of action: competition, mycoparasitism, and antibiosis (**Fig 3.)** chaetoglobosin A from *C. globosum* inhibits the growth of *F. sporotrichioides* causing potato dry rot (Jiang *et al*., 2017) and Chaetoglobosin-C from *C. globosum* inhibits colony, sporangia, and growth of oospores of *Phytophthora parasitica* the causative agent of root rot of citrus (Nguyen *et al*., 2016) Di Pietro *et al*., (1992) reported that the ability of *C. globosum* strains to produce chaetomin in liquid culture is correlated with their activity against damping-off of sugar beet caused by *Pythium ultimum*. Fu *et al*., (2017) prepared a simple and environmentally friendly wettable powder by using *C. globosum* for a better control effect, and industrial production with broader application. Foliar spray of purified culture filterate of *C. globosum* and high antifungal metabolite production by *C. globosum* results in potent *in vivo* antifungal activity against spot blotch of wheat under laboratory and glasshouse conditions (Biswas *et al*., 2000). *C. globosum* No.04 was isolated by Zhang *et al*., (2013) from the medicinal plant *Ginkgo biloba* and the crude extract of the fungus fermentation was used in agar-diffusion tests against phytopathogenic fungi *Rhizopus stolonifer* and *Coniothyrium*

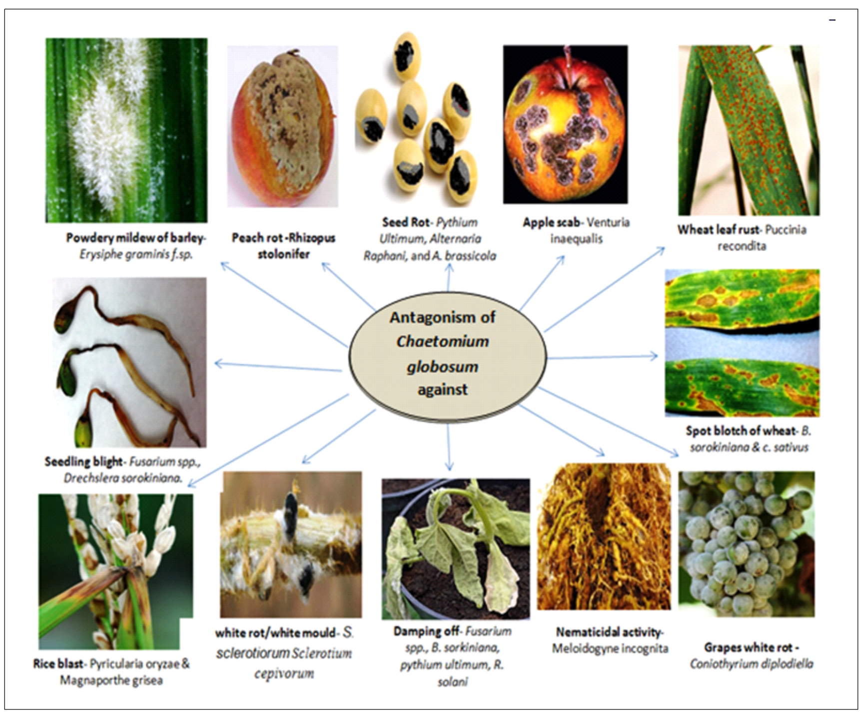

Fig. 2. Antagonistic effect of *Chaetomium globosum* against different plant pathogens (images for disease symptoms are taken from google images)

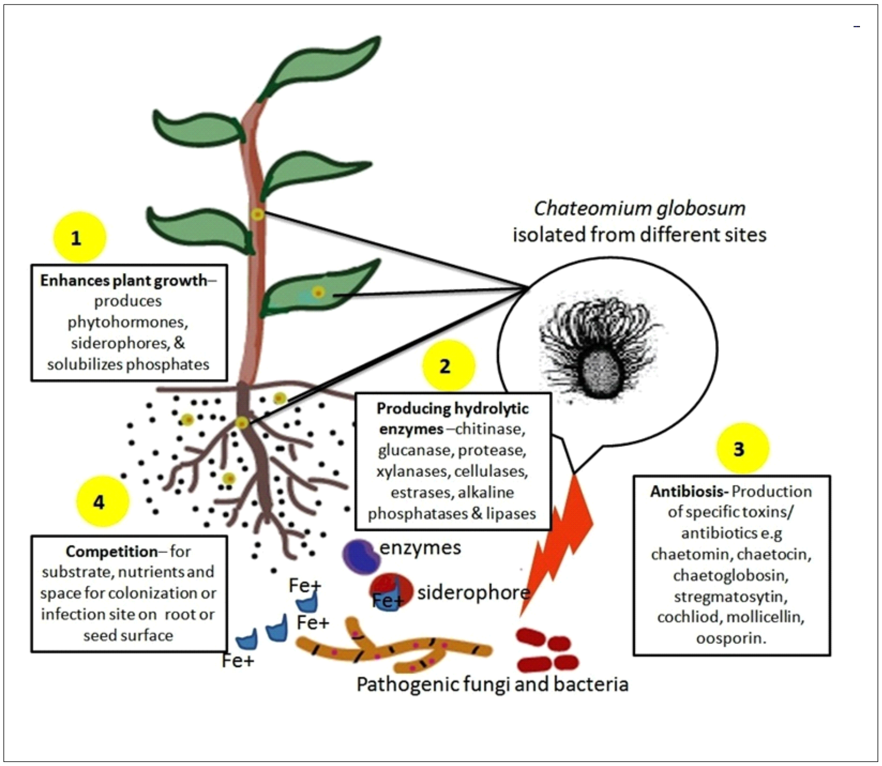

Fig. 3. Different mechanism of action for antagonistic effect and plant growth enhancement of *Chaetomium globosum*

diplodiella causing peach rot and grape white rot found active against pathogen used.

Chang and Kommedahl, (1968) revealed that, competition for nutrients and space led to physical exclusion of *Fusarium graminearum* by biopriming maize seed with *C. Globosum*. Cullen *et al.* (1984) reported evidence of antibiosis by *C. globosum* against *V. inaequalis*, which causes apple scab. The positive relation between the production of antifungal metabolites by *C. globosum* isolates in liquid culture or soil and efficacy in suppressing *P. ultimum* causing damping off has been reported by Di Pietro *et al*., (1992). Antagonistic effect of *C. globosum* against rice blast pathogen was reported by Soytong and Quimino, (1989). *In vitro* and *in vivo* studies by Mandal, (1995) have shown that cell-free culture filterate of *Trichoderma reesei* and *C. globosum* inhibited the growth of spot blotch pathogen, *B. sorokiniana*. *C. globosum* also has been reported to be effective against other seed- and soil-borne plant pathogens like *Alternaria raphani, A. brassicola,* and *Fusarium* spp. (Aggarwal *et al.*, 2004; Chang and Kommedahl, 1968; Mao *et al*., 2017).

Seed infestation with *Chaetomium* spp., has been successful in controlling seedling blight caused by *R. solani* (Baker, 1968). Kommedahl and Mew (1975) observed increased field stands of maize hybrids when seeds were coated with *C. globosum*. Strain, F0142 of *C. globosum*, which was isolated from barnyard grass, showed potent disease control efficacy against rice blast (*Magnaporthe grisea*) and wheat leaf rust (*Puccinia recondita*). Two antifungal substances were purified from culture of broth from this organism and identified as chaetoviridins A and B. Chaetoviridin A exhibited higher antifungal activity than chaetoviridin B against plant pathogenic fungi both *in vitro* and *in vivo*. Treatment with chaetoviridin A at 62.5 mg/mL suppressed the development of rice blast and wheat leaf rust by over 80%. The molecule also exhibited moderate control of tomato late blight, resulting in 50% control following the application of 125 mg/mL chaetoviridin A (Park *et al*., 2005).

Chaetomium globosum as a biocontrol agent against the late blight pathogen *Phytophthora infestans* was evaluated in potato plants by Shanthiyaa *et al*., (2013). From the culture of an endophyte *C. globosum* found in *Ginkgo biloba*, 12 metabolites, including 3 diketopiperazines, 2 cytochalasins, 2 sterols, 2 simple phenolic compounds, one complex aromatic compound, a nonprotein amino acid and a linear triterpene were isolated. Among them, eight compounds were reported for first time in the genus *Chaetomium*. Gliotoxin (8) has good antifungal activity against plant pathogenic fungi (Li *et al.*, 2011). *Chaetomium* as biopellets and biopowders are introduced and implemented in several Asian and Europian countries by using new broad spectrum biological fungicides registered as Ketomium® mycofungicide against *Phytophthora palmivora* (Thailand Patent No. 6266, International Code: AO 1N 25/12) (Kaewchai *et al*., 2009)

It has been found that by using specific strains of *C. globosum* it is possible to obtain good control over many plant pathogens; *C. globosum* is able to suppress plant pathogens such as *Curvularia lunata, Pyricularia oryzae* and *Rhizoctonia oryzae in vitro* (Soytong, 1992). It was found that Ketomium-mycofungicide was most efficient in suppressing raspberry spur blight caused by *Didymella applanata* and could also reduce potato disease caused by *R. solani*, increasing potato yield (Shternshis *et al*., 2005). Six new azaphilones, 50 -epichaetoviridin A (7), 40 -epichaetoviridin F (9), 12β-hydroxychaetoviridin C (10), and chaetoviridins GI (1113), and six known azaphilones, chaetoviridins AE (15) and 40-epichaetoviridin A (8), were isolated from the endophytic fungus *C. globosum* isolated from the leaves of *Viguiera robusta*. These showed strong antiparasitic activity against *Caenorhabditis elegans* infection model (Borges *et al*., 2011). *Chaetomium globosum* was isolated for its insecticidal effect as an endophyte from Drunken horse grass, *Achnatherum inebrians* an important perennial bunchgrass in China associated with the narcosis of grazing animals by endophyte infection (Li *et al*., 2009; De Oliveira *et al*., 2010).

Looking it as a potential biocontrol agent Aggarwal *et al*., (2014) developed a PCR-based marker which will help to detect the fungus at the place of its application and to ensure of its proper use in agriculture.

4. Significance of the work

The present review was undertaken for the investigation of the biological and chemical aspects of the fungus *C. globosum*, for various purposes including the drug discovery process and biocontrol of phytopathogens in aspect in agricultural field holds considerable promise. *C. globosum* isolated from many sources, as an endophyte from different host plant, from soil, marine samples, sick buildings, etc; the fungus possesses a great and diversed group of novel bioactive properties and has lots of attributes towards plant growth promotion by conferring the plants with for antibacterial, antifungal and antinematocidal effects. It also provides plant protection through induced systemic resistance (ISR) and plant nutrition by phytohormone secretion and phosphate (organic & inorganic) solubilization. Many mentioned anticancerous, ant-oxidant and anti-inflammatory drugs have been isolated and successfully experimented for encouraging results. So in this way, the study pave a lot of dignified information regarding the importance of the *C. globosum* species in human and plant health's benefits.

5. Gaps in the work

There is still much more that is unknown about the role of the *C. globosum* species complex in human disease and plant health. Current scientific world is interested in medicinal plants harboring endophytic fungi that are believed to be associated with the production of same metabolites as their hosts (Jia *et al*., 2016). So if the endophytic microorganism is not a biotroph and the bioactive compound unique to it is not produced by the host, its exploitation would not only reduce the need to harvest slow growing and possibly rare plants but also preserve the world's ever-diminishing biodiversity. Furthermore, it is recognized that a microbial source of a valued product may be easier and more economical to produce, effectively reducing its market price which creates a need to find an alternative way to control farm pests and pathogens. Too little work has been reported for the enhanced production of the therapeutically useful phytomolecules in large scale by this potential fungus.

Using controlled fermentation conditions by altering the accessible culture and process parameters, the compounds produced by fungal endophytes might be optimized (Kusari and Spiteller, 2011). *C. globosum* was isolated for its insecticidal effect as an endophyte from Drunken horse grass, *Achnatherum inebrians* an important perennial bunchgrass in China associated with the narcosis of grazing animals by endophyte infection (Li *et al*., 2009; De Oliveira *et al*., 2010).

Recently, Selim *et al*., (2016) designed fermentation experiments using a Taguchi orthogonal array (OA) design and found that the production of antioxidants was more favourable under static conditions with 25 g potato extract/100 mL broth. The extract obtained from the optimized medium was investigated to posses' moderate antimicrobial activity, strong anticancer activity against HepG-2, UACC62 cell lines, antiviral activity against HSV-2 virus and strong inhibitory activity to butyrylcholin esterase enzyme (Selim *et al*., 2014). Ye *et al*., (2013) reported *C. globosum* from *Ginko biloba* as a remarkable producer of 1,2-benzenedicarboxaldehyde-3,4,5-trihydroxy-6-methyl (flavipin) an antioxidant; optimized culture condition included 25 °C, 100/250 mL flask, 12 discs/flask, 150 rpm, pH 6.5 for 14 days) for its high production (315.5 mg/L). So many more significant compounds are still to be extracted and optimized for commercial purpose.

6. Future prospects

Despite being identified in the last half of the 21st century and more recent associations with human disease, and plant health the role of the *C. globosum* complex in human health and disease remains largely unexplored. So, an additional work on the genomics, molecular microbiology, and host immune response to the *C. globosum* species complex will provide insight into the roles of these fungi. Whole genome sequencing and comparison served as an important reference for further studies of the basis of its cellulose specificity, for genes that enable human infection and for further comparative studies with other fungi as it's a medically important fungus as a contaminant in indoor environments and known to produce mycotoxins. Mycoses lead to high death rates and seldom cause cerebral and systemic infections. The mechanisms underlying this connection have not been studied so far. The fungus *C. globosum* is reported to be accidentally associated with human hosts through contamination especially in immune compromised individuals.

As the fungus *C. globosum* be full of noble products, may eventually be available via industrial fermentation. The biggest problem of using fungi for fermentation to produce novel compound is its very low yield and unstable production compared with that of other sources, the short generation time and high growth rate of fungi make it worthwhile to continue our investigation of these species. The physical and chemical parameters play a major role on production of bioactive compounds and antimicrobial agents. Virtually very few reports are available on screening endophytic fungi from tropical medicinal plant species and its co-cultivation. Therefore, study must take into account to acquire advanced information on metabolite production by medium optimization and formulation of isolated fungal endophytes against phytopathogens. Use of *C. globosum* as biocontrol agents has become cynosure in current scenario, because of their ability to suppress plant pathogens through different mechanism. So, the characterization, optimization, formulation and elucidation of this potential biocontrol agent produced by the species may contribute to resolve mentioned problems.

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