



ANTIFUNGAL ACTIVITY OF AU, AG, TiO₂, CH, PD, SE, AND ZNO NANOPARTICLES AGAINST *CANDIDA ALBICANS*: A REVIEW

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Abstract

Candida albicans is the most important, prevalent fungal pathogen in humans. They colonize gastrointestinal tract, skin, mucosal membranes, and genital, it may responsible for many diseases. This mainly depends on with immunological status of the host. Because of their resistance towards antibiotics, has represented a challenge for the scientific community to develop new bioactive compounds. Today attention was drawn to the use of materials nanoparticles to control the infection *C. albicans*. In this study, has been reviewed nanoparticles activity of action against *C. albicans*. Conclusions: The gold nanoparticles exhibit excellent antifungal activity by causing DNA damage and mitochondria dysfunction in *C. albicans*. Nano-Ag has shown considerable antifungal activity, these nanoparticles showed no significant cytotoxicity, Using TiO₂ nanoparticles has been found to have an effective effect in the prevention of fungal biofilms especially biofilms formed on the surface of medical devices. The ChNPs inhibited *C. albicans* biofilm, results showed the essential change in the external morphology of *C. albicans* after therapy with ZnO NPs it has been found to cause cell membrane damage Selenium nanoparticles easily adhere on the biofilm, and cause damage the cell structure by substituting with sulfur. Also, studies revealed PdNPs cause cell wall damage and cellular morphology changes, in *C. albicans*.

Key words : Antifungal, *C. albicans*, Au, Ag, TiO₂, Ch, Pd, Se, ZnO, Nanoparticles.

Introduction

Candida albicans is a commensal yeast that in greatest people lives in their gastrointestinal tract, mouth or vagina. *Candida albicans* is an opportunistic organism when it appears in a place in the body that is not normal where causes infection in immune individuals, such as transplant receptors, intensive care, surgery, cancer patients and people living with HIV. The excessive use of antibiotics can also stimulate *C. albicans* by cause excessive growth (Douglas, 2002; Seneviratne *et al.*, 2008; Wetenschappenn, 2010). It was found that the genus of *Candida* is one of the main causes of infection acquired from hospitals (Chandra *et al.*, 2001; Douglas, 2003; Seneviratne *et al.*, 2008). During the period 1980-1990, hospital data recorded a steady increase in the rate of fungal infection, including *Candida albicans* infection from 2.0 to 3.8 per 1000 discharges (De Rosa *et al.*, 2009; De Rosa *et al.*, n.d.; Ha *et al.*, 2011). Among the multiple factors likely to increase infections are changing

in clinical practice, for example, the excessive use of long-term venous catheterization, widespread use of antibacterial agents and improved laboratory techniques to determine the types of unusual candidiasis (Epstein *et al.*, 1980; Review, 2007). Patients with AIDS are more likely to infect oral and esophageal candidiasis. This type of infection is usually associated with oral cancers, the use of dentures and patients with heart disease and who have failed to produce saliva in sufficient quantities (Soll, 2002; Sudbery, 2011). Patients who get burned as well as newborns (born early) are also subject to white skin infections. In vulnerable groups of patients and patients in intensive care units in hospitals, candidaemia is a bloodstream infection that can be the result of *C. albicans*, which can develop into renal candidiasis when internal organs become infected. Candidaemia and Candidiasis are very serious medical cases, with surveys showing mortality rates ranging from 30-50%; these studies have been found to be the second most common cause of death from hospital injuries (Beck-Sagué and

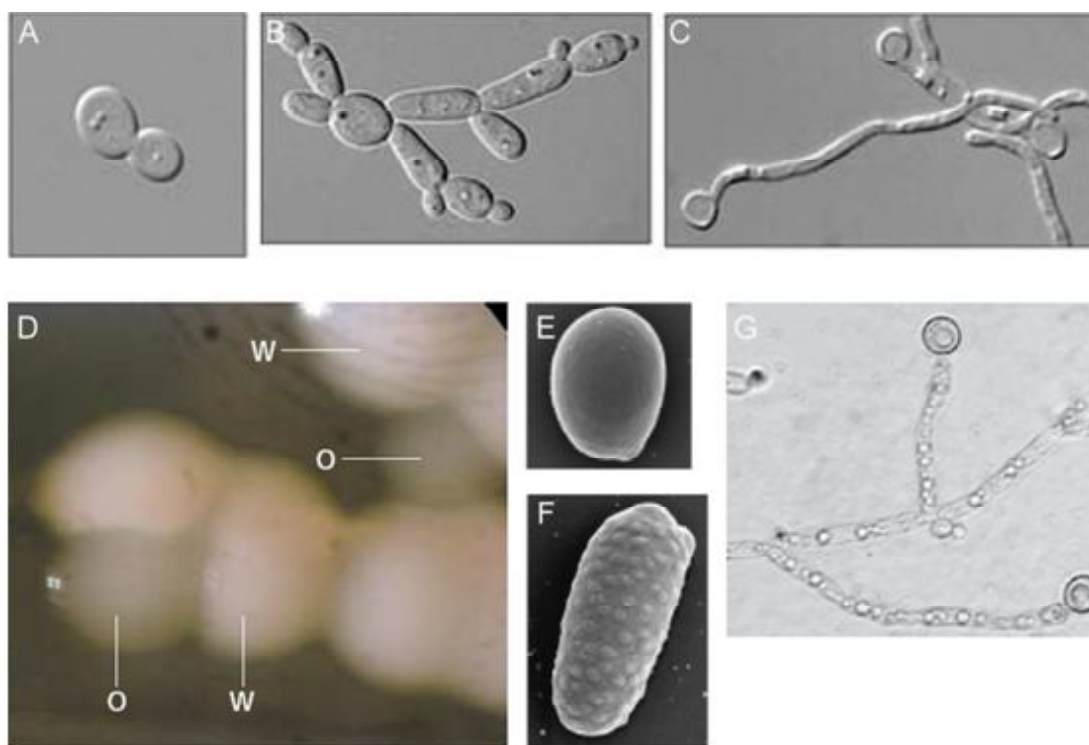


Fig. 1 : Morphological forms of *Candida albicans*.

Yeasts (A), pseudohyphae (B), and hyphae (C). Budding yeast cells are similar to diploid *S. cerevisiae* cells. Pseudohyphal cells have constrictions at the mother-daughter junction and at the positions of septa. Hyphae have parallel cell walls and no constrictions. (D) White-opaque phenotypic switching of the *C. albicans* WO-1 strain, grown on salt-dextrose at 23°C for three days. White (W) and opaque (O) colonies are seen. The cellular phenotype of white (E) and opaque cells (F). The white cell is round with a relatively smooth surface while the opaque cell is twice the size of the white cell and has unique wall pimples. (G) Chlamydospores are thick-walled spherical cells that are ~3 to 4 times larger than normal yeast cells. Adapted from Brown *et al.* (2007); Berman & Sudbery (2002); Staib & Morschhauser (2007)

Jarvis, 1993; Wisplinghoff *et al.*, 2004). It is characteristic in *C. albicans* that it can grow either as a ferocious single-celled bud or in false and dangerous filaments (Sudbery *et al.*, 2004). Pseudohyphae are morphologically distinct from the hyphae because the pseudohyphae have limitations in the spacing locations, which are wider than the filaments. In contrast, long filament-like threads are perfectly parallel and there are no restrictions in the dumping site, shown in Fig. 1 (Sudbery, 2011). *C. albicans* that grow yeast and filamentous cells cause oral and genital infections in humans (Dijck and Mathe, 2013; Guisbiers *et al.*, 2017). New drugs should therefore be developed to combat these diseases. Nanotechnology may have a promising future in this field where nanoparticles are less than 100 nanometers specifically derived for interaction with bacteria (Zhu *et al.*, 2014), fungi (Lara *et al.*, 2015). Interest has recently increased by combining Pure Se NPs for medical nano applications due to its surface ratio to its large size (Shi *et al.*, 2010; Liu *et al.*, 2012). *Candida* spp. is one of the pathogens responsible for fungal infections, which often cause hospital-acquired infections with a mortality rate of up to

40% (Panacek *et al.*, 2009). The effective antifungal currently available depends on polyenes (amphotericin B.), or triazoles (fluconazole, or itraconazole, voriconazole, posaconazole) or echinocandins (caspofungin, micafungin and anidulafungin). Although these antimicrobial agents are often associated with complications such as amphotericin B toxicity and adverse effects of certain strains, including toxic and drug interactions (Levin *et al.*, 2007; Venkatakrishnan *et al.*, 2000), yeast is also resistant to antifungal agents (White *et al.*, 2002; Wang *et al.*, n.d.). As a result, other treatments must be found to avoid the above-mentioned adverse effects (Panacek *et al.*, 2009). Among the well-studied materials nanoparticles with unique physical and chemical properties that make them promising for therapeutic agents without the intrinsic toxicity of human cells are the gold nanoparticles (AuNPs) (Wang *et al.*, n.d.; Alkilany *et al.*, 2012; Conde *et al.*, n.d.; Seong and Lee, 2018). At present, nano-materials are widely accepted for use as an antimicrobial effect due to different physical, chemical and electrical properties that are very small and are not available in larger forms (Zhang *et al.*,

2008; Jiang *et al.*, 2009; Haghighi *et al.*, 2013). In some studies, the effect of TiO₂ was studied (Haghighi *et al.*, 2013). Because of its unique features include high chemical resistance, non-toxic, long-lasting nature, and the lowest cost (Gao *et al.*, n.d.; Enyashin and Seifert, 2005; Liao, 2007). Silver and its compounds are known to be effective antimicrobial agents (Silver, 2003; Klasen, 2000; Woo *et al.*, 2009). Due to recent advances in research on nanoparticles, Nano-Ag has received special attention as a potential agent for microbes (Baker *et al.*, 2005; Melaiye *et al.*, 2005; Sondi and Salopek-Sondi, 2004).

Other *Candida* infections

Urinary *Candida* in this type of *candida* it is difficult to distinguish between the cases of colonization and the real infection, so it is the most confusing forms of *candida*. *C. albicans*, which is found in the urine is believed to be colonized or contaminated. Canduria can also be a sign of blood lipid or invasive kidney disease. It can cause candidemia during invasive urologic procedures (Hollenbach, 2008; Singhi and Deep, 2009). Gastrointestinal candidiasis can be diagnosed in children, adults with immunodeficiency disorders, cancer after surgery, and persons with a disability. Gastrointestinal candidiasis may involve the stomach, intestine or hepatobiliary system (Wetenschappenn, 2010). Respiratory candidiasis may include respiratory tracts from the pharynx and epiglottis to bronchi. In the case of patients in hospitals, *C. albicans* is a recurrent colonizer of the upper respiratory tract. Symptoms can be hoarseness, low fever, tachypnea, and sometimes no specific results in physical examination (Singhi and Deep, 2009). The most common infection in the vulva and vagina is vaginal candidiasis (VVC). Three out of four sexually active women will be infected by VVC at least once in their lifetime (Ferrer, 2000; Taguti Irie *et al.*, 2006; Li *et al.*, 2008). Vulvovaginal candidiasis may affect up to 75% of women at least once in their lives (Vulvovaginitis, 1997). A small group of women (5-10%) may experience frequent recurrent episodes that significantly affect their quality of life (Sudbery, 2011). Oral infection was first described in the 18th century (Barnett *et al.*, 2008; Wetenschappenn, 2010). *C. albicans* is one of 200 organisms of the genus *Candida* (Kobric and Kobric, 2012). This organism exists as a benign commensal entity in a variety of sites in the human host. These sites, in particular, the oral cavity, skin, genitals and digestive system. These species contain 75% of fungal species that have been sampled from the oral cavity (Cannon *et al.*, n.d.), but are only a small fraction of total oral microflora. *C. albicans* can be diagnosed as a

commensal microbial organism from the oral cavity in 30% to 90% of healthy adults but in many cases, the colony does not show signs or symptoms of infection (McCullough and Savage, n.d.; Diagnosing and Managing, 1992). *C. albicans* is a type of fungus that is often a benign member of the skin and mucous flora, but *C. albicans* can cause disease of mucous membranes (Sudbery, 2011). Symptoms of infection of *C. albicans* often include stomach complaints, constipation, abdominal cramps, discomfort, white patches on the tongue, inflammation of the skin that turns red and becomes rough, metallic taste and burning (Epstein *et al.*, 1980; Review, 2007). There are several types of *Candida* infections, for example invasive candidiasis, including candidemia and disseminated candidiasis with deep organ involvement, candiduria, *Candida* infection of gastro-intestinal tract and *Candida* infection of the respiratory tract and throat. Candidemia is a bloodstream infection with *Candida*. When the *Candida* types spread in the body after entering via the bloodstream, the named it is invasive candidiasis (Ha *et al.*, 2011).

Biofilms of *Candida*

That 65% of all human infections are related to the formation of biofilms by the causative or pathogenic microbes (Thein *et al.*, n.d.) and more importantly, up to 40% of the adult population are carriers of *C. albicans* in the oral cavity (Jenkinson and Douglas, 2002). With respect to *C. albicans*, formation of a biofilm begins with adhesion of the microbe to a suitable surface (biotic or abiotic), shown in fig. 2 (Lynch *et al.*, 2008). Adhesion occurs via non-specific factors (cell surface hydrophobicity/electrostatic forces) and specific factors (cell surface receptors that recognize serum proteins/fibrinogen). These particular, factors promote retention of the organism in the oral cavity or elsewhere in or on the body (esophagus/vagina). Further, *C. albicans* can adhere to other microbial biofilms that are already present (e.g. Dental plaque) (Ramage *et al.*, n.d.). In the oral cavity, *C. albicans* has been found to congregate with other oral pathogens, such as *Actinomyces*, *Streptococcus* and *Fusobacterium* (Jenkinson and Douglas, 2002). The formation of hyphae usually occurs 3-6-hours following the yeast cells initial colonization. Adhesion is followed by colonization, proliferation, and maturation of the biofilm structure. The adherent yeast cells form a basal layer that attaches firmly to the biofilm substrate (*i.e.* palatal epithelial cells, denture acrylic, etc.), a mature biofilm typically contains cells with hyphae and pseudohyphae (Nickerson *et al.*, n.d.). The mature biofilm is a well-organized and spatially structured complex surrounded by an extracellular polysaccharide matrix

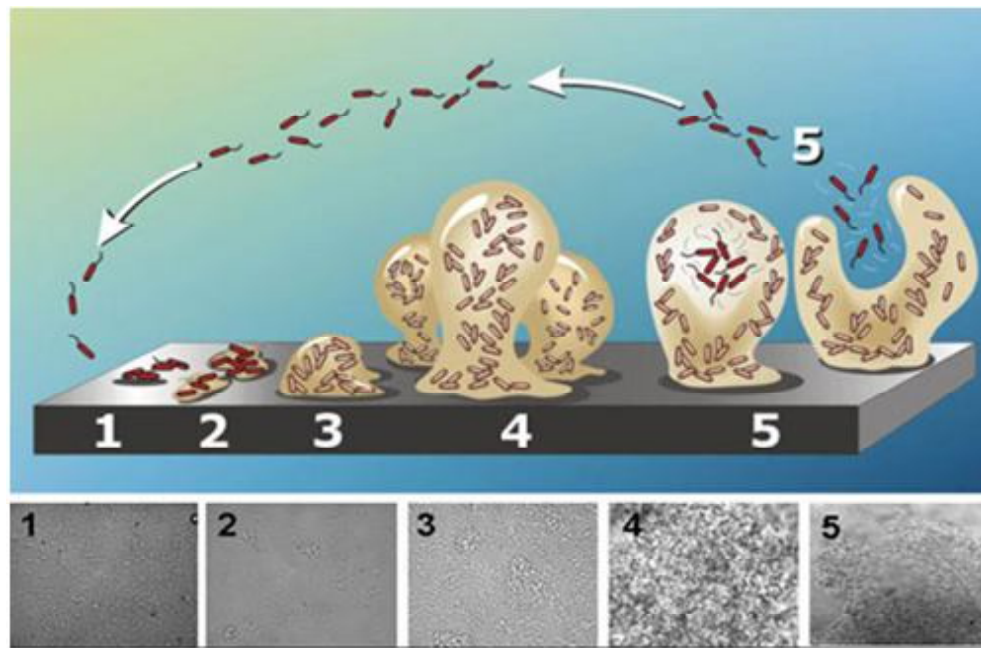


Fig. 2 : The different steps in the evolution of biofilm formation 1- the individual cells populate the surface, 2-extracellular matrix is produced and attachment becomes irreversible, 3-4-biofilm architecture develops and matures, 5-single cells are released from the biofilm.

(Thein *et al.*, n.d.). The extracellular matrix is composed of proteins, hexosamine, as well as phosphorus and uronic acid (Williams *et al.*, 2018). The last step, detachment of cells, is followed by colonization of distant sites and can be triggered by a process known as quorum-sensing (Kobric and Kobric, 2012). Some of studies have also shown that architecture of *C. albicans* biofilms is influenced by the nature of the substrate surface (Chandra *et al.*, 2001; C. K.-C. opinion in microbiology and 2002 n.d.; Tsang *et al.*, 2007). Biofilms have been significantly less susceptible to antifungal agents (L. D.-T. in microbiology and 2003 n.d.; Kuhn *et al.*, 2018). Presently *C. albicans* has more effective role than other nosocomial pathogens because this fungus has suitable potential for biofilms formation (Kojic, 2004; Venkatakrishnan *et al.*, 2000).

Nanotechnology

Nanotechnology is emerging as a rapidly growing field with applications important in science and technology for the aim of making new materials at the nanoscale level (Rai *et al.*, 2009; Pişkin *et al.*, 2018). That nanoscience and nanotechnology have massive potential to bring benefits in areas as diverse as drug development, information, water decontamination and communication technologies, and the production of stronger, lighter materials. It can be considered a blessing for human healthcare (Sahoo *et al.*, 2007). Nanomaterials may also be used for special medical purposes such as to produce novel

drug delivery systems, to enhance the performance of medical devices, or to produce diagnostic imaging materials (EXPRESS STATEMENT* Developing Safe Products Using Nanotechnology 2016). It has been found that nanotechnology has many benefits in the food sector (Slewa, 2018). Resistance to conventional drugs is rapidly emerging, and the decreased activity of these drugs against *C. albicans* was observed at some levels for each type of medication used at present (Biology, 2017; Seong and Lee, 2018). Therefore, the development of new effective and anti-breakfast material against *C. albicans* has gained wide attention. Nanoparticles, ranging from 10 to 100 nanometers, are promising because of their wide variety of several areas such as biological, biomedical, catalytic, optoelectronic, and pharmaceutical applications (Mohanraj and Chen, 2006). Previous studies have shown that nanoparticles can act as antimicrobial agents because of their ability to interact with microorganisms (Albanese *et al.*, n.d.). Because of these characteristics, various metal nanoparticles have been studied to determine their unique antimicrobial properties and their potential usage in a wide range of fields such as medical instruments, textiles, and purification (Sondi and Salopek-sondi, 2004; Judith and Espitia, 2012). AuNPs are well studied and their unique physical and chemical properties make them promising for therapeutic agents without intrinsic toxicity to human cells (Alkilany *et al.*, 2012; Conde *et al.*, 2018). AuNPs had been significantly used in cancer treatment as a drug delivery system and

thermal therapy (Seong and Lee, 2018; Huang *et al.*, 2008; Brown *et al.*, 2010). Previous studies have shown that AuNPs have antimicrobial activity against various pathogens, including *Escherichia coli*, *Streptococcus mutans* and *Candida* species (Hernández-sierra *et al.*, 2008; Lima *et al.*, 2013; Wani and Ahmad, 2013). Due to recent developments in research on nanoparticles, nano-Ag has received special attention as a potential antimicrobial agent (Woo *et al.*, 2009; Baker *et al.*, 2005; Melaiye *et al.*, 2005; Sondi and Salopek-sondi, 2004). Therefore, it has been found that the preparation of uniform nano sized silver particles with specific requirements in terms of size, shape and physical and chemical properties is of great importance in the formulation of new pharmaceutical products shown in fig. 3 (Merisko-liversidge *et al.*, 2003; Peer *et al.*, 2007). The selection of TiO₂ nanoparticles because of its unique features including: - high chemical resistance, non-toxic, long lasting nature, availability and low cost, shown in Fig. 4 (Gao *et al.*, 2018; Enyashin and Seifert, 2005; Liao, 2007). Using a novel method to inhibit attachment of cells to the surface and eliminate of fungal mass over surfaces is a valuable way to control infections (Butterfield *et al.*, 2002; Haghighi *et al.*, 2013). At present, chitosan has been used in many biomedical applications (Gondim *et al.*, 2018; Kong *et al.*, 2010). Chitosan has been characterized by anti-activity, especially against *C. albicans*, in the free form of the polymer (Ing *et al.*, 2012), or its derivatives (Kulikov *et al.*, 2014; Miranda *et al.*, 2013). Interest in the development of nano-systems of natural polymers, including chitosan, for use as biomarkers within biofilms, has increased because the biopolymer nanoparticles can be spread across biofilm structures and shown antimicrobial effects (Gondim *et al.*, 2018; Ing *et al.*, 2012). Chitosan-based zinc oxide NPs have been synthesized and evaluated for antimicrobial and antibiofilm potential against various microbial strains involve *C. albicans* (Panwar *et al.*, 2018; Singh and Surinder, 2014). Studies have found that selenium nanoparticles readily attach to biofilm, and then penetrate the pathogen, thus causing cell structure damage by replacing sulfur. 50% of the biological inhibition of white *candida* is at only 25 ppm (Guisbiers *et al.*, 2017). In other studies, the potential antifungal properties of Au @ CD nanoconjugates had been evaluated against the common fungal pathway *C. albicans*. This type of nanoparticle represents a new class of nanomaterials with the combined properties of gold nanoparticles and carbon points (Eepsita Priyadarshini *et al.*, 2018; Manuscript, 2017). These associations also have excellent optical and fluorescent properties, a new type of nanomaterial that whose

applicability appears and has a promising future. The carbon dots are of great importance because of its remarkable water solubility, compatibility with life, size and wavelength-based lighting properties (Chem, 2012; Zhang *et al.*, 2014). Also, Surface Plasmon Resonance (SPR) optical property, which was based on the size and shape of gold nanoparticles, was successfully used in catalysis, sensing, detection, and biomedicine (Essner *et al.*, 2015). At present, the benefits of metal/ carbon-nanohybrids have been reported on metal nanoparticles due to the exceptional ability of carbon points to reduce mineral salts and also act as stabilizers of nanoparticles after their synthesis (Sajid *et al.*, 2018).

Results

The gold nanoparticles have shown an excellent antioxidant activity. The small nanoparticles (7 nm) showed a higher innate activity than those with large ones (Ahmad *et al.*, 2013). In fungi, breathing occurs through the mitochondrial membrane, and small amounts of NPs cannot enter fungal cells to target the mitochondrial membrane, which leads to low antifungal activity (Rapid biosynthesis of antimicrobial silver and gold nanoparticles by in vitro callus and leaf extracts from *Lycopersicon esculentum* (Mill - Google n.d.). It was also found that AuNPs had no effect on membranes. Where the cell membrane plays an important role in regulating activities within and around the cell (Madeo *et al.*, 1997). Cell death is established by the sudden collapse of the plasma membrane permeability barrier (Lemasters *et al.*, 1987). To show whether AuNPs cause membrane disruption. the permeability had been measured the membrane using PI, a membrane-impermeable dye that only enters cells that have damaged membranes (Sansonetty *et al.*, 2001). These results suggest that AuNPs may not have an effect on membrane permeability in *C. albicans*. Therefore, the particles did not directly destroy the membrane of *C. albicans*. Because the antifungal activity of AuNPs is not associated with membrane disruption (Seong and Lee, 2018). The studies showed that the gold nanodiscs inhibit the fungal growth to the larger extent than the gold nanocrystals. Because the gold nanodiscs are having the higher surface area than the gold nanocrystals. Hence, the increase in surface area may result in the greater enhancement of interaction of the gold nanodisc with the binding sites of the plasma membrane proteins (Ballottin *et al.*, 2017). The growth of yeasts is inhibited at concentrations low using the non-stabilized silver NPs comparison with SDS-stabilized silver NPs (against *C. albicans*). Silver NPs stabilized by polymers and surfactants exhibited big antifungal activity as the result

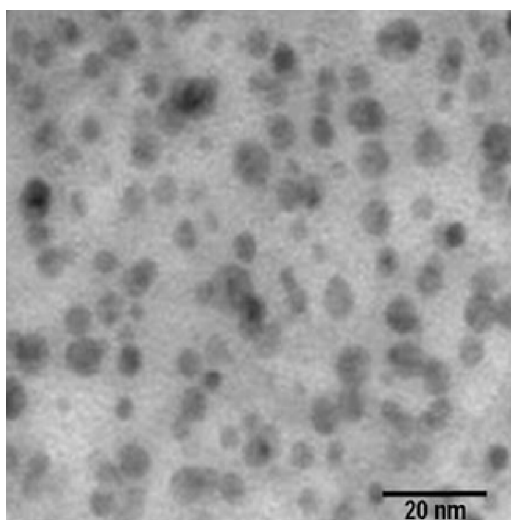


Fig. 3 : Transmission electron micrograph of the silver nanoparticles (nano-Ag). The bar marker represents 20 nm.

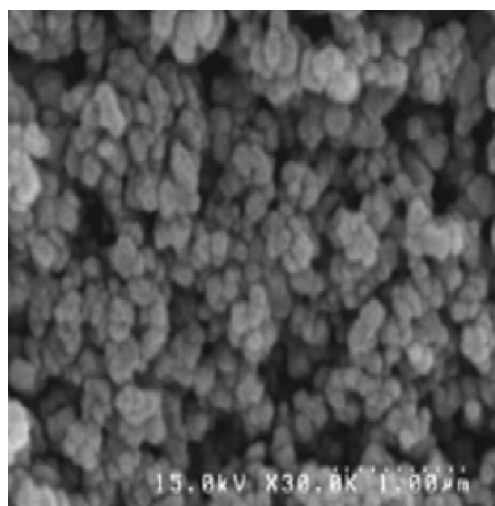


Fig. 4 : SEM images of TiO₂ nanoparticles.

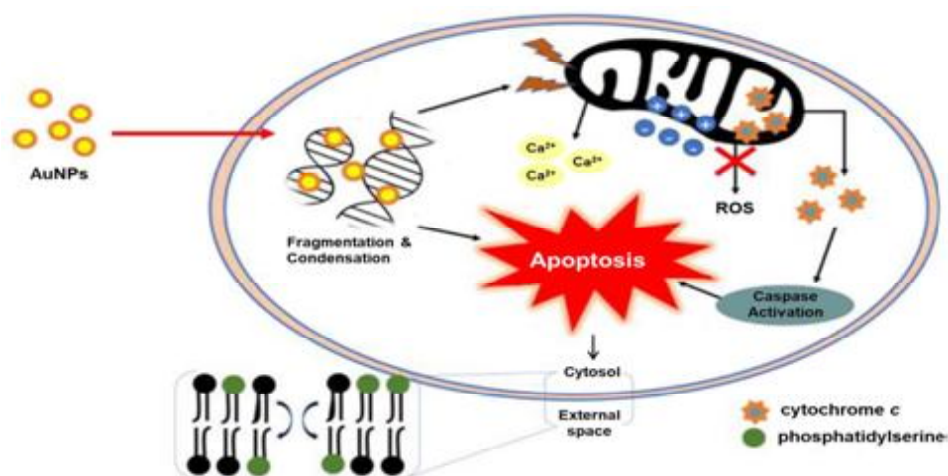


Fig. 5 : AuNPs exert ROS-independent apoptosis effects against *C. albicans* through intracellular disruption, including destruction of nucleus and nucleic acid and attenuation of mitochondrial homeostasis.

of their enhanced aggregate stability (Panacek *et al.*, 2009). It has been found in some studies, the report that stable and green silver nanoparticles with protein capping have low cytotoxicity and have interesting antimicrobial efficiency against *C. albicans*. When AgNP1 underwent a pre-treatment, they have presented more pronounced antimicrobial effects due to the lower concentration of stabilizing agents (proteins). AgNP1 without a pre-treatment presented higher cytotoxic effects when compared to the AgNP2 that underwent a pre-treatment, probably due to the differences in the nanoparticles' capping furthermore, AgNP1 without a pre-treatment have Found significantly higher damage to the DNA when compared to AgNP2 that underwent a pretreatment, and thus can be considered more genotoxic. Further, the textile impregnation by padding method was efficient and the cotton fabrics were able to inhibit microbial growth (Ballottin *et al.*, 2017). The increase has been in Ag NPs

concentration to 100 ppm leads to 50% inhibition of *C. albicans* (Roberto *et al.*, 2014). When the interaction between nano-Ag and membrane structure *C. albicans* cells, during nano-Ag exposure, exhibit important changes to their membranes, which are recognized by the formation of (pits) on their surfaces, result in the formation of pores and cell death, when cytometric flow analysis of the cell cycle was performed. It was found that the nano-Ag cell cycle was stopped in the G2 / M phase in *C. albicans*. This means that nano-Ag inhibits some cellular processes that are involved in normal bud growth (Endo *et al.*, 1997). It has been reported that growth inhibition of bud is associated with membrane damage (Endo *et al.*, 1997). It can be said that nano-Ag inhibits the natural budding process, maybe during the destruction of membrane integrity. Nano-Ag exhibited strong anti-fungal effects (Woo *et al.*, 2009). AgNPs have shown anti-fungal activity against *Candida albapsilosis*, AgNPs

have shown strong activity against fungal strains. Concentrations were different. AgNPs have shown that spherical activity is strong against *C. albicans* compared with commercially available antifungal agents. Antimicrobial activity of nanoparticles may be well associated with its low size and shape due to the increased surface area with improved antimicrobial effect (Muciformis *et al.*, 2014). TiO₂ nanoparticles have shown an appropriate anti-fungal property against *C. albicans* (Sc *et al.*, 2012). In addition, both TiO₂ and silver nanoparticles have shown significant activity specific to fungal strains (Martinez-gutierrez *et al.*, 2010). Yeast cells of *C. albicans* due to possess thick cell wall consist of glucan and chitin are more resistant than bacteria. It was reported that TiO₂ nanoparticles by producing intracellular reactive oxygen species (ROS) induce destructive effects inside the microbial cells, oxidation of intracellular Coenzyme A and peroxidation of the plenty of lipids, which decrease respiratory activity and subsequently cause death cell (Battin *et al.*, 2018; Foster *et al.*, 2011). The chitosan nanoparticles at all concentrations inhibited 25-50% of the initial adhesion of *C. albicans*, also found that chitosan nanoparticles exhibited activity on inhibition of *C. albicans* biofilm formation (Gondim *et al.*, 2018). The studies on CSNPs reported their effective interaction with the negatively charged plasma membrane of fungal cells because of their small and compact particle size as will rise surface shipments (Panwar *et al.*, 2018; Qi *et al.*, 2004; Tan *et al.*, 2013). Upon entering the fungal plasma membrane, FACSNPs could either inhibit *C. albicans* biofilm formation or damage its structural integrity chitosan would link to the trace elements and make the major nutrients unavailable inhibiting the natural fungal growth (Roller and Covill, 1999). Some studies have indicated that Au @ Carbon Dots the change in composition (carbon vs Au@CDs) show a deep effect on the susceptibility of *C. albicans* cells. A size-dependent toxicity was observed for the nan conjugates, CDs were found to be quite toxic owing to their little size which simplify their entry into the cells (Priyadarshini *et al.*, 2018). The interaction of Se NPs with *C. albicans* can be qualified as being the sequence of three mechanisms: 1.) adhesion, 2.) breakthrough and 3.) Sulfur substitution. It has been displayed that the size and crystallinity of the generated Se NPs are the key parameters in the inhibition of *C. albicans* biofilm (Guisbiers *et al.*, 2017). PdNPs were synthesized by chemical decrease method, obtaining spherical NPs. PdNPs showed inhibitory against *Candida albicans* reveal significant cell growth inhibition (Athie-garcía *et al.*, 2018). The antifungal activity of ZnO NPs and ZnO-

C NCs against *C. albicans* was studied. The analysis was showed the substantial change in the external morphology of *C. albicans* after therapy with both ZnO NPs and ZnO-C NCs perform the fungal cell membrane injury (Dananjaya *et al.*, 2018).

Conclusion

In this study, the emphasis was placed on the modus operandi of AuNPs on *C. albicans*. It has been found that AuNPs induce destruction of the nucleus, nucleic acids and attenuation of mitochondrial homeostasis, shown in Fig.5, causing apoptosis and small-sized nanoparticles with high innate efficacy compared to larger volumes. Gold nanodiscs showed the strongest activity of fungi compared to nanoparticles of polyhedral gold. Nanoparticles Gold is an excellent anti-oxidant activity against *Candida* isolates. It is characteristic of AuNPs that it has no toxicity in human cells (Wang *et al.*, 2018; Conde *et al.*, n.d.; Seong and Lee, 2018). Finally, it can be concluded that nanoparticles can be used as an effective and effective agent against human fungal pathogens. In other studies, silver NPs have been shown to inhibit yeast growth at very low concentrations compared to common antifungal agents. In addition, silver NPs do not show any cytotoxic effects on human fibroblasts at these low concentrations. Thus can conclude that Silver nanoparticles (Ag-NPs) are a new type of material with different applications, the most important used as antimicrobial against bacteria, fungi (Rahi, 2018). Photocatalyst TiO₂ nanoparticles showed a suitable antifungal property against *C. albicans* biofilms nanoparticles such as TiO₂ has antimicrobial efficacy. Which can be considered as a new strategy for the prevention of fungal biofilms, in particular, that are formed on the surface of medical devices. As for the nanoparticles, the chitosan nanoparticles had antagonistic activity against the planktonic *C. albicans*, and has prevented initial adhesion and the development of the mature biofilm of *C. albicans*. That FA-CSNPs reduced cell metabolism activity to *C. albicans*. That Au @ CDs can work an antifungal agent against the fungal pathogen, so the results demonstrate that the change in composition (carbon vs Au @ CDs) shows a significant impact on susceptibility for the infection of ovarian cells. PdNPs act as antifungal and yeast. In fact, these studies have indicated that the main toxicological mechanism of PdNPs includes cell wall damage and oxidative stress generation. Finally, ZnO C NCs showed a stronger antibody activity against *C. albicans* compared with ZnO NPs.

References

- Ahmad, Tokeer (2013). Antifungal Activity of Gold Nanoparticles Prepared by Solvothermal Method. *Materials Research Bulletin* **48**(1): 12–20. <http://dx.doi.org/10.1016/j.materresbull.2012.09.069>.
- Albanese, Alexandre, Peter S Tang and Warren C W Chan (....). The Effect of Nanoparticle Size, Shape and Surface Chemistry on Biological Systems.
- Alkilany, Alaaldin M, Samuel E Lohse and Catherine J Murphy (2012). The Gold Standard/ : Gold Nanoparticle Libraries To Understand the Nano Å Bio Interface. **XXX(Xx)**.
- Athie-garcía, Martha Samira (2018). Cell Wall Damage and Oxidative Stress in *Candida Albicans* ATCC10231 and *Aspergillus Niger* Caused by Palladium Nanoparticles. *Toxicology in Vitro*, (2017). <https://doi.org/10.1016/j.tiv.2018.01.006>.
- Baker, C. (2005). Synthesis and Antibacterial Properties of Silver Nanoparticles. **5**(2).
- Ballottin, Daniela (2017). Antimicrobial Textiles/ : Biogenic Silver Nanoparticles against *Candida* and *Xanthomonas*. *Materials Science & Engineering C*, **75** : 582–89. <http://dx.doi.org/10.1016/j.msec.2017.02.110>.
- Barnett, James A, Fredrik Borg, Charles Robin and Rhoda Benham (2008). A History of Research on Yeasts 12/ : Medical Yeasts Part 1 , *Candida Albicans* Keywords/ : History of Yeast Research/; *Candida Albicans*/ ; Pathogenic Yeasts/ ; Dimor. : 385–417.
- Battin, T. J. and F. Kammer and A Weilhartner - Environmental and Undefined (2009). Nanostructured TiO₂: Transport Behavior and Effects on Aquatic Microbial Communities under Environmental Conditions. *ACS Publications* <https://pubs.acs.org/doi/abs/10.1021/es9017046> (August 22, 2018).
- Beck-Sagué, C. and W. R. Jarvis (1993). Secular Trends in the Epidemiology of Nosocomial Fungal Infections in the United States, 1980-1990. National Nosocomial Infections Surveillance System. *The Journal of Infectious Diseases* **167**(5) : 1247–51. <https://ci.nii.ac.jp/naid/10014696251/> (August 17, 2018).
- Biology, D. Sanglard - *Candida albicans*: Cellular and Molecular, and undefined (2017). Mechanisms of Drug Resistance in *Candida Albicans*. *Springer*. https://link.springer.com/chapter/10.1007/978-3-319-50409-4_15 (August 20, 2018).
- Brown, Sarah D. (2010). Gold Nanoparticles for the Improved Anticancer Drug Delivery of the Active Component of Oxaliplatin. **8** : 4678–4684.
- Butterfield, Phillip W., Alex M. Bargmeyer, Anne K. Camper and Joel A Biederman (2002). Modified Enzyme Activity Assay to Determine Biofilm Biomass. **50** : 23–31.
- Cannon, R. D., A. R. Holmes and A. B. Mason (1995). *Journal of dental, and undefined* 1995. Oral *Candida*: Clearance, Colonization, or Candidiasis? *journals.sagepub.com*. <http://journals.sagepub.com/doi/abs/10.1177/00220345950740050301> (August 20, 2018).
- Chandra, Jyotsna (2001). Biofilm Formation by the Fungal Pathogen *Candida Albicans*/ : Development. *Architecture and Drug Resistance*, **183**(18) : 5385–5394.
- Chem, J. Mater (2012). One-Pot Synthesis of N-Doped Carbon Dots with Tunable Luminescence, **1**(100) : 16714–16718.
- Conde, J. (2018). Gold-Nanobeacons for Gene Therapy: Evaluation of Genotoxicity, Cell Toxicity and Proteome Profiling Analysis. *Taylor & Francis*. <https://www.tandfonline.com/doi/abs/10.3109/17435390.2013.802821> (August 17, 2018).
- Dananjaya, S. H. S., R. S. Kumar and M. Yang (2018). International journal of and undefined 2018. “Synthesis, Characterization of ZnO-Chitosan Nanocomposites and Evaluation of Its Antifungal Activity against Pathogenic *Candida Albicans*.” *Elsevier*. <https://www.sciencedirect.com/science/article/pii/S0141813017328349> (August 22, 2018).
- Diagnosing and Managing (1992). 123(January).
- Dijk, Patrick Van and Lotte Mathe (2013). Recent Insights into *Candida Albicans* Biofilm Resistance Mechanisms. 251–64.
- Douglas, L. Julia (2002). Medical Importance of Biofilms in *Candida* Infections. : 139–43.
- (2003). *Candida* Biofilms and Their Role in Infection. *Trends in Microbiology*, **11**(1): 30–36.
- Endo, Masahiro, Kazutoh Takesako and Ikunoshin Kato (1997). Fungicidal Action of Aureobasidin A, a Cyclic Depsipeptide Antifungal Antibiotic, against *Saccharomyces cerevisiae*. **41**(3) : 672–676.
- Enyashin, Andrey N. and Gotthard Seifert (2005). Structure, Stability and Electronic Properties of TiO₂ Nanostructures. *Physica status solidi (b)*, **242**(7): 1361–1370. <http://doi.wiley.com/10.1002/pssb.200540026> (August 20, 2018).
- Epstein, Joel B., Nancy N Pearsall and Edmond L Truelove (1980). Quantitative Relationships Between *Candida albicans* in Saliva and the Clinical Status of Human Subjects, **12**(3): 475–476.
- Essner, Jeremy B., Charles H. Laber and Gary A Baker (2015). Carbon Dot Reduced Bimetallic Nanoparticles/ : Size and Surface Plasmon Resonance Tunability for Enhanced Catalytic Applications. : 16354–60.
- EXPRESS STATEMENT* *Developing Safe Products Using Nanotechnology*. 2016. www.toxicology.org www.facebook.com/societyoftoxicology (August 20, 2018).
- Ferrer, J. (2000). Vaginal Candidosis/ : Epidemiological and Etiological Factors. 21–27.
- Foster, Howard A., Iram B. Ditta, Sajnu Varghese and Alex Steele (2011). Photocatalytic Disinfection Using Titanium Dioxide/ : Spectrum and Mechanism of Antimicrobial Activity Photocatalytic Disinfection Using Titanium Dioxide/ : Spectrum and Mechanism of Antimicrobial Activity (June).
- Gao, Y. (2018). TiO₂ Nanoparticles Prepared Using an Aqueous

- Peroxotitanate Solution. *Elsevier*. <https://www.sciencedirect.com/science/article/pii/S0272884204001816> (August 20, 2018).
- Gondim, Brenna Louise Cavalcanti (2018). Effect of Chitosan Nanoparticles on the Inhibition of *Candida* Spp. Biofilm on Denture Base Surface. *Archives of Oral Biology*, **94** : 99–107. <https://doi.org/10.1016/j.archoralbio.2018.07.004>.
- Guisbiers, Grégory (2017). Inhibition of *Candida Albicans* Biofilm by Pure Selenium Nanoparticles Synthesized by Pulsed Laser Ablation in Liquids. *Nanomedicine : Nanotechnology, Biology, and Medicine*, **13(3)** : 1095–1103. <http://dx.doi.org/10.1016/j.nano.2016.10.011>.
- Ha, Jennifer F. (2011). Candidemia and Invasive Candidiasis/ : A Review of the Literature for the Burns Surgeon. *Burns*, **37(2)** : 181–95. <http://dx.doi.org/10.1016/j.burns.2010.01.005>.
- Haghighi, F. (2013). Antifungal Activity of TiO₂ Nanoparticles and EDTA on *Candida Albicans* Biofilms. *Infection Epidemiology & Medicine Original Article Infect. Epidemiol. Med.*, **11(11)** : 33–38. http://journals.modares.ac.ir/article_10035_3ce8159da985eb44ab5cf379f622efb2.pdf.
- Hernández-Sierra, Juan Francisco (2008). The Antimicrobial Sensitivity of *Streptococcus Mutans* to Nanoparticles of Silver, Zinc Oxide and Gold. **4** : 237–240.
- Hollenbach, Eike (2008). To Treat or Not to Treat – Critically Ill Patients with Candiduria. **51** : 12–24.
- Huang, Xiaohua, Prashant K. Jain and Ivan H. El-Sayed (2008). Plasmonic Photothermal Therapy (PPTT) Using Gold Nanoparticles : 217–28.
- Ing, Ling Yien, Noraziah Mohamad Zin, Atif Sarwar and Haliza Katas (2012). Antifungal Activity of Chitosan Nanoparticles and Correlation with Their Physical Properties.
- Jenkinson, H. F. and L. J. Douglas (2002). Interactions between *Candida* Species and Bacteria in Mixed Infections. <https://www.ncbi.nlm.nih.gov/books/NBK2486/?report=reader> (August 20, 2018).
- Jiang, Wei, Hamid Mashayekhi and Baoshan Xing (2009). Bacterial Toxicity Comparison between Nano- and Micro-Scaled Oxide Particles. *Environmental Pollution*, **157(5)** : 1619–25. <http://dx.doi.org/10.1016/j.envpol.2008.12.025>.
- Judith, Paula and Perez Espitia (2012). Zinc Oxide Nanoparticles/ : Synthesis, Antimicrobial Activity and Food Packaging Applications. 1447–64.
- Klasen, H. J. (2000). A Historical Review of the Use of Silver in the Treatment of Burns. II. Renewed Interest for Silver. 26.
- Kobric, Daniel Joel and Daniel Joel Kobric (2012). Antifungal Efficacy of a Citrus Fruit Extract against *Candida Albicans* Cells by Antifungal Efficacy of Citrus Fruit Extracts against *Candida Albicans* Cells.
- Kojic, E. M. and R. O. Darouiche - Clinical microbiology reviews, and undefined (2004). *Candida* Infections of Medical Devices. *Am Soc Microbiol*. <http://cmr.asm.org/content/17/2/255.short> (August 20, 2018).
- Kong, Ming, Xi Guang, Ke Xing and Hyun Jin (2010). International Journal of Food Microbiology Antimicrobial Properties of Chitosan and Mode of Action/ : A State of the Art Review. *International Journal of Food Microbiology*, **144(1)** : 51–63. <http://dx.doi.org/10.1016/j.ijfoodmicro.2010.09.012>.
- Kuhn, D. M., T. George and J. Chandra (2002). Antimicrobial agents, and undefined 2002. “Antifungal Susceptibility of *Candida* Biofilms: Unique Efficacy of Amphotericin B Lipid Formulations and Echinocandins.” *Am Soc Microbiol*. <http://aac.asm.org/content/46/6/1773.short> (August 20, 2018).
- Kulikov, Sergey N. (2014). Antifungal Activity of Oligochitosans (Short Chain Chitosans) against Some *Candida* Species and Clinical Isolates of *Candida Albicans*: Molecular Weight-Activity Relationship. *European Journal of Medicinal Chemistry*, **74** : 169–78. <https://www.sciencedirect.com/science/article/pii/S0223523413008052> (August 21, 2018).
- Lara, Humberto H (2015). Effect of Silver Nanoparticles on *Candida Albicans* Biofilms/ : An Ultrastructural Study. *Journal of Nanobiotechnology* 1–12.
- Lemasters, John J., James DiGuiseppi, Anna-Liisa Nieminen and Brian Herman (1987). Blebbing, Free Ca²⁺ and Mitochondrial Membrane Potential Preceding Cell Death in Hepatocytes. *Nature*, **325(6099)** : 78–81. <http://www.nature.com/articles/325078a0> (August 21, 2018).
- Levin, Mark-david (2007). Hepatotoxicity of Oral and Intravenous Voriconazole in Relation to Cytochrome P450 Polymorphisms. (September): 1104–7.
- Li, Juan (2008). Biased Genotype Distributions of *Candida Albicans* Strains Associated with Vulvovaginal Candidosis and Candidal Balanoposthitis in China : 1119–1125.
- Liao, D. L. and B. Q. Liao (2007). Journal of Photochemistry and Photobiology A, and undefined 2007. Shape, Size and Photocatalytic Activity Control of TiO₂ Nanoparticles with Surfactants. *Elsevier*. <https://www.sciencedirect.com/science/article/pii/S101060300600579X> (August 20, 2018).
- Lima, Enrique, Roberto Guerra, Víctor Lara and Ariel Guzmán (2013). Gold Nanoparticles as Efficient Antimicrobial Agents for *Escherichia coli* and *Salmonella typhi*. 1–7.
- Liu, Wen (2012). Selenium Nanoparticles as a Carrier of 5-Fluorouracil to Achieve Anticancer Synergism. *ACS Nano* **6(8)** : 6578–91. <http://pubs.acs.org/doi/10.1021/nn202452c> (August 17, 2018).
- Lynch, A. S. and G. T. Robertson (2008) Annu. Rev. Med., and undefined 2008. Bacterial and Fungal Biofilm Infections. *annualreviews.org*. <https://www.annualreviews.org/doi/abs/10.1146/annurev.med.59.110106.132000> (August 20, 2018).

- Madeo, Frank (1997). A Yeast Mutant Showing Diagnostic Markers of Early and Late Apoptosis. **139(3)** : 729–734.
- Manuscript, Accepted (2017). Materials Chemistry B.
- Martinez-gutierrez, Fidel, Peggy LOlive and Adriana Banuelos (2010). Synthesis , Characterization , and Evaluation of Antimicrobial and Cytotoxic Effect of Silver and Titanium Nanoparticles. *Nanomedicine: Nanotechnology, Biology and Medicine*, **6(5)**: 681–688. <http://dx.doi.org/10.1016/j.nano.2010.02.001>.
- Mccullough, M. J. and N. W. Savage. Oral Candidosis and the Therapeutic Use of Antifungal Agents in Dentistry : 36–39.
- Melaiye, Abdulkareem (2005). Silver (I) - Imidazole Cyclophane Gem-Diol Complexes Encapsulated by Electrospun Tecophilic Nanofibers/ : Formation of Nanosilver Particles and Antimicrobial Activity. **I** : 125–30.
- Merisko-liversidge, Elaine, Gary G Liversidge and Eugene R Cooper (2003). N Anosizing/ : A Formulation Approach for Poorly-Water-Soluble Compounds. **18**: 113–120.
- Kumamoto, C. A. (2002) Microbiology- Current opinion in, and undefined 2002. Candida Biofilms. *Elsevier*. <https://www.sciencedirect.com/science/article/pii/S1369527402003715> (August 20, 2018).
- Douglas, L. J (2003). Microbiology - Trends in and undefined 2003. Candida Biofilms and Their Role in Infection. *Elsevier*. <https://www.sciencedirect.com/science/article/pii/S0966842X02000021> (August 20, 2018).
- Miranda, I. M. (2013). Anti-Biofilm Activity of Low-Molecular Weight Chitosan Hydrogel against Candida Species.
- Mohanraj, V. J. and Y. Chen (2006). Nanoparticles – A Review. **5(June)** : 561–573.
- Muciformis, Using Hypnea, J. Saraniya Devi and B. Valentin Bhimba (2014). “Antibacterial and Antifungal Activity Of Silver Nanoparticles Synthesized Antibacterial and Antifungal Activity of Silver Nanoparticles Synthesized Using Hypnea Muciformis. (April).
- Nickerson, K. W., A. L. Atkin and J. M. Hornby (2006). Applied and environmental, and undefined 2006. Quorum Sensing in Dimorphic Fungi: Farnesol and Beyond. *Am Soc Microbiol*. <http://aem.asm.org/content/72/6/3805.short> (August 20, 2018).
- Panacek, A. (2009). Antifungal Activity of Silver Nanoparticles against *Candida* Spp. *Biomaterials* **30(31)** : 6333–6340. <https://www.sciencedirect.com/science/article/pii/S0142961209008023> (August 17, 2018).
- Panwar, R. (2018). Efficacy of Ferulic Acid Encapsulated Chitosan Nanoparticles against *Candida Albicans* Biofilm. *Elsevier*. <https://www.sciencedirect.com/science/article/pii/S0882401016300432> (August 21, 2018).
- Peer, Dan (2007). Nanocarriers as an Emerging Platform for Cancer Therapy. 751–60.
- Pişkin, S., P. Arzu and S. Y. Müge (2013). International Conference on, and undefined 2013. Antimicrobial Activity of Synthesized TiO₂ Nanoparticles. pdfs.semanticscholar.org/73af/4a04da315ff18be8fcc504b3f6f59fb6a917.pdf (August 20, 2018).
- Priyadarshini, E., K. Rawat and T. Prasad (2018). Colloids and Surfaces B, and undefined 2018. “Antifungal Efficacy of Au@ Carbon Dots Nanoconjugates against Opportunistic Fungal Pathogen, *Candida Albicans*.” *Elsevier*. <https://www.sciencedirect.com/science/article/pii/S0927776518300067> (August 22, 2018).
- Priyadarshini, Eepsita, Kamla Rawat, Tulika Prasad and H. B. Bohidar (2018). Graphical Abstract. *Colloids and Surfaces B : Biointerfaces*. <http://dx.doi.org/10.1016/j.colsurfb.2018.01.006>.
- Qi, Lifeng (2004). Preparation and Antibacterial Activity of Chitosan Nanoparticles. **339** : 2693–2700.
- Rahi, G. K. and H. A. Ajah (2018). *Pak. J. Biotechnol.* Vol, and undefined 2018. Antagonistic activity of silver nanoparticles synthesis by *Fusarium oxysporum* against *Candida* spp. *pjbt.org*. [http://www.pjbt.org/uploads/2018/Vol-5/PJBT-VOL-15-NO-2-OF-YEAR-2018\(15\).pdf](http://www.pjbt.org/uploads/2018/Vol-5/PJBT-VOL-15-NO-2-OF-YEAR-2018(15).pdf) (August 22, 2018).
- Rai, Mahendra, Alka Yadav and Aniket Gade (2009). Silver Nanoparticles as a New Generation of Antimicrobials. *Biotechnology Advances*, **27(1)** : 76–83. <http://dx.doi.org/10.1016/j.biotechadv.2008.09.002>.
- Ramage, G., S. P. Saville and D. P. Thomas (2005)- Eukaryotic cell and undefined 2005. Candida Biofilms: An Update. *Am Soc Microbiol*. <http://ec.asm.org/content/4/4/633.short> (August 20, 2018).
- Rapid Biosynthesis of Antimicrobial Silver and Gold Nanoparticles by in Vitro Callus and Leaf Extracts from *Lycopersicon Esculentum* Mill - Google. <https://www.google.iq/search?ei=oHp8W-2nFcqSgAbJobaYcQ&q=+Rapid+biosynthesis+of+antimicrobial+silver+and+gold+nano+nanoparticles+by+in+vitro+callus+and+leaf+extracts+from+Lycopersicon+esculentum+Mill+&oq=+Rapid+biosynthesis+of+antimicrobial+silver+and+gold+nano> (August 21, 2018).
- Review A (2007) Pathogenicity and drug resistance in *Candida albicans* and other yeast species. **54(3)**: 201–35.
- Roberto, Douglas (2014). Science Direct Original Article Susceptibility of *Candida Albicans* and *Candida Glabrata* Biofilms to Silver Nanoparticles in Intermediate and Mature Development Phases. *Journal of Prosthodontic Research*, 1–7. <http://dx.doi.org/10.1016/j.jpor.2014.07.004>.
- Roller, S. and N. Covill (1999). The Antifungal Properties of Chitosan in Laboratory Media and Apple Juice. **47**: 67–77.
- Rosa, F. G. De (2018). Invasive Candidiasis and Candidemia: New Guidelines. *researchgate.net*. https://www.researchgate.net/profile/Daniela_Pasero/

- publication/23659759_Invasive_candidiasis_and_candidemia_New_guidelines/links/571e8f6108aed056fa2270cd/Invasive-candidiasis-and-candidemia-New-guidelines.pdf (August 20, 2018).
- Rosa, Francesco Giuseppe De, Daniela Cristina Pasero and Marco Ranieri (2009). Treatment and Prevention of Fungal Infections. (July).
- Sahoo, S. K., S. Parveen and J. J. Panda (2007). The Present and Future of Nanotechnology in Human Health Care, **3** : 20–31.
- Sajid, P. A. (2018). One-Pot Microwave-Assisted in Situ Reduction of Ag⁺ and Au³⁺ Ions by Citrus Limon Extract and Their Carbon-Dots Based Nanohybrids: A Potential Nano-Bioprobe For. *pubs.rsc.org*. <http://pubs.rsc.org/en/content/articlehtml/2016/ra/c6ra24033j> (August 21, 2018).
- Sansonetty, F., A. G. Rodrigues and C. Tavares (2001). “ORIGINAL ARTICLE Cytometric Approach for a Rapid Evaluation of Susceptibility of Candida Strains to Antifungals.” *European Society of Clinical Infectious Diseases*, **7(11)** : 609–18. <http://dx.doi.org/10.1046/j.1198-743x.2001.00307.x>.
- Sc, Haghighi F. M., Roudbar Mohammadi S, Mohammadi D. and M. M. Eskandari (2012). Comparative Evaluation of the Effects of TiO₂ Nanoparticles and Its Photocatalytic Form on the Formation of Fungal Biofilms, **15(60)** : 27–34.
- Seneviratne, C. J., L. Jin and L. P. Samaranayake (2008). Biofilm Lifestyle of Candida : A Mini Review, 582–90.
- Seong, Minju and Dong Gun Lee (2018). Reactive Oxygen Species-Independent Apoptotic Pathway by Gold Nanoparticles in Candida Albicans. *Microbiological Research*, **207**(October 2017): 33–40. <http://dx.doi.org/10.1016/j.micres.2017.11.003>.
- Shi, Jinjun, Alexander R. Votruba, Omid C. Farokhzad and Robert Langer (2010). Nanotechnology in Drug Delivery and Tissue Engineering : From Discovery to Applications. *Nano Letters*, **10(9)** : 3223–3230.
- Silver, Simon (2003). Bacterial Silver Resistance : Molecular Biology and Uses and Misuses of Silver Compounds. 27.
- Singh, Gurpreet and Dhillon Surinder (2014). Facile Fabrication and Characterization of Chitosan-Based Zinc Oxide Nanoparticles and Evaluation of Their Antimicrobial and Antibiofilm Activity.
- Singhi, Sunit and Akash Deep (2009). Invasive Candidiasis in Pediatric Intensive Care Units. 76.
- Slewa, E. K. and J. Azhar (2018). *Pak. J. Biotechnol.* Vol. and undefined 2018. Use nanotechnology in capsulation Omega-3 fatty acid to improve its thermal stability and use it to enrich pasteurized milk. *pjbt.org*. [http://www.pjbt.org/uploads/2018/Vol-5/PJBT-VOL-15-NO-1-OF-YEAR-2018\(6\).pdf](http://www.pjbt.org/uploads/2018/Vol-5/PJBT-VOL-15-NO-1-OF-YEAR-2018(6).pdf) (August 22, 2018).
- Soll, D. R. (2002). Candida and Candidiasis. *ASM Press, Washington*: 123–142.
- Sondi, Ivan and Branka Salopek-sondi (2004). Silver Nanoparticles as Antimicrobial Agent/ : A Case Study on *E. coli* as a Model for Gram-Negative Bacteria, **275** : 177–182.
- Sudbery, Peter E. (2011). Growth of Candida Albicans Hyphae.” *Nature Publishing Group*, **9(10)** : 737–48. <http://dx.doi.org/10.1038/nrmicro2636>.
- Sudbery, Peter, Neil Gow and Judith Berman (2004). The Distinct Morphogenic States of *Candida albicans*. **12(7)**.
- Taguti, Irie and Mary Mayumi (2006). A Simplified Technique for Evaluating the Adherence of Yeasts to Human Vaginal Epithelial Cells. *Journal of Clinical Laboratory Analysis*, **20(5)** : 195–203. <http://doi.wiley.com/10.1002/jcla.20132> (August 20, 2018).
- Tan, Honglue (2013). Quaternized Chitosan as an Antimicrobial Agent/ : Antimicrobial Activity. *Mechanism of Action and Biomedical Applications in Orthopedics* : 1854–69.
- Thein, Z. M., C. J. Seneviratne and Y. H. Samaranayake (2009). Mycoses and undefined 2009. Community Lifestyle of Candida in Mixed Biofilms: A Mini Review. *Wiley Online Library*. <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1439-0507.2009.01719.x> (August 20, 2018).
- Tsang, C. S. P., H. Ng and A. S. McMillan (2007). Antifungal Susceptibility of Candida Albicans Biofilms on Titanium Discs with Different Surface Roughness. *Clinical Oral Investigations*, **11(4)** : 361–68. <http://link.springer.com/10.1007/s00784-007-0122-3> (August 20, 2018).
- Venkatakrishnan, Karthik, Lisa L Von Moltke and David J Greenblatt (2000). Effects of the Antifungal Agents on Oxidative Drug Metabolism Clinical Relevance. **38(2)** : 111–180.
- Vulvovaginitis, Candida (1997). *Candida Albicans*. 10(Table 3).
- Wang, S (2018). Challenge in Understanding Size and Shape Dependent Toxicity of Gold Nanomaterials in Human Skin Keratinocytes. *Elsevier*. <https://www.sciencedirect.com/science/article/pii/S0009261408011329> (August 22, 2018).
- Wani, Irshad A. and Tokeer Ahmad (2013). Colloids and Surfaces B/ : Biointerfaces Size and Shape Dependant Antifungal Activity of Gold Nanoparticles/ : A Case Study of Candida. *Colloids and Surfaces B: Biointerfaces*, **101** : 162–170. <http://dx.doi.org/10.1016/j.colsurfb.2012.06.005>.
- Wetenschappen, Faculteit Farmaceutische (2010). Biofilm Formation By Nosocomial Candida Albicans Isolates and Their Genotypic.
- White, Theodore C. (2002). Resistance Mechanisms in Clinical Isolates of Candida Albicans. **46(6)** : 1704–1713.
- Williams, D. W. (2018). Candida Biofilms and Oral Candidosis: Treatment and Prevention. *Wiley Online Library*. <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-0757.2009.00338.x> (August 20, 2018).
- Wisplinghoff, Hilmar (2004). Nosocomial Bloodstream

- Infections in US Hospitals/ : Analysis of 24 , 179 Cases from a Prospective Nationwide Surveillance Study. **0019**(April2003); 309–17.
- Woo, Keuk-jun Kim Æ (2009). Antifungal Activity and Mode of Action of Silver Nano-Particles on *Candida Albicans*. 235–42.
- Zhang, Haijuan (2014). Solid-Phase Synthesis of Highly Fluorescent Nitrogen-Doped Carbon Dots for Sensitive and Selective Probing Ferric Ions in Living Cells.
- Zhang, Lingling, Yulong Ding, Malcolm Povey and David York (2008). ZnO Nanofluids – A Potential Antibacterial Agent. **18** : 939–44.
- Zhu, Xi (2014). Nanomedicine in the Management of Microbial Infection–Overview and Perspectives. *Nano today* **9(4)**: 478–498. <https://www.sciencedirect.com/science/article/pii/S1748013214000838> (August 17, 2018).