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Silver Nanoparticles Display Inhibitory Effect against Drug-Resistant Pathogenic *Candida* Isolates from Different Clinical Specimens

Rasha M. Elnagar[(1)#], Mohammed Elshaer[(2)], Mona A. Abd El-Raouf[(1)]
[(1)]Department of Medical Microbiology and Immunology, Faculty of Medicine, Mansoura University, Mansoura, Egypt; [(2)]Department of Clinical Pathology, Faculty of Medicine, Mansoura University, Mansoura, Egypt.

THE RESISTANCE of *Candida* to antifungal agents is an emerging global health problem, especially with the emergence of new species. Therefore, the focus has shifted to alternative agents like silver nanoparticles (AgNPs), received significant attention. The aim of this study was to evaluate the *in vitro* antifungal susceptibility of AgNPs against resistant *Candida* isolates from various clinical specimens. The antifungal effect of AgNPs was assessed by the broth microdilution method using different concentrations (0.062-1µg/mL). The Minimum Inhibitory Concentration (MIC_{50}) and Minimum Fungicidal Concentration (MFC) of AgNPs were determined. As a result, of 109 recovered *Candida* isolates, 65.1%, and 34.9% were *C. albicans* and non-*albicans Candida* (NAC), respectively. Moreover, 35.8% of the *Candida* isolates were non-susceptible to conventional antifungal drugs. The MIC_{50} of AgNPs against resistant isolates was lower (0.125-1µg/mL) than that of fluconazole (1-64µg/mL), itraconazole (0.016-4 µg/mL), voriconazole (0.016-4µg/mL), and amphotericin B (0.016-1µg/mL). The scanning electron micrograph revealed that AgNPs treatment altered the cell morphology of *Candida*. In conclusion, AgNPs exhibited a notable fungicidal effect against resistant *Candida* isolates and may be an adequate substitute for antifungal agents.

Keywords: Antifungal agents, *Candida* spp., Resistance, Silver nanoparticles (AgNPs).

Introduction

Candida species (spp.) typically inhabit the oral cavity, upper respiratory tract, gastrointestinal and urogenital systems. Nevertheless, they are opportunistic pathogens that can cause diverse infections, from superficial to deep-seated candidiasis, particularly in immunodeficient individuals (Seyoum et al., 2020), such as those that are critically ill, undergoing organ transplantation, or infected with the human immunodeficiency virus (HIV) (Sardi et al., 2013). Moreover, patients receiving cancer chemotherapy or long-term broad-spectrum antibiotics, undergoing hemodialysis and parenteral nutrition, or with invasive devices, such as indwelling urinary catheters, and peripheral and central venous catheters, for prolonged durations are more prone to colonization and infection with *Candida* (Mikulska et al., 2012).

Candida albicans (*C. albicans*) is, the most prevalent *Candida* spp. causing human mycosis. However, infections caused by non-*albicans Candida* (NAC) species, such as *C. tropicalis*, *C. krusei*, and *C. auris*, have become increasingly more frequent (Hemaid et al., 2021).

About 7% of *Candida* spp. that cause bloodstream infections is resistant to fluconazole (Toda et al., 2019). Resistance of *Candida* spp., particularly NAC, to antifungal agents like azoles has increased significantly, making treatment challenging.

[#]Corresponding author email: drrasha_m@mans.edu.eg, Tel: +201095129425. ORCID: 0000-0002-5661-850X
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Amphotericin B is the primary therapeutic choice to treat *Candida* infections resistant to azoles and echinocandin; however, it can be detrimental to patients (Van Daele et al., 2019). Therefore, investigating alternative therapeutics has become necessary, especially after the increase in rate of infection with resistant strains (Perlin et al., 2017).

Nano-antibiotics have rapidly emerged as disinfectants and low-cost antimicrobial medications (Elsayed et al., 2022). Silver nanoparticles (AgNPs) exhibit potent antimicrobial properties, inhibiting various pathogens, including numerous bacterial and fungal strains (Perween et al., 2019).

Due to their nanoscale size, AgNPs can penetrate the fungal cell wall and increase the permeability of cell membranes, resulting in cell lysis. In addition, they can interfere with DNA replication by releasing silver ions. Besides, AgNPs disrupt signal transduction and lead to cell apoptosis and termination of cell multiplication (Yin et al., 2020).

The antifungal effect of AgNPs has been studied with a lot of interest thus far. The aim of this study was to evaluate the *in vitro* antifungal efficacy of AgNPs against resistant *Candida* isolates from several types of infections.

Materials and Methods

Sample collection and processing

A total of 574 non-duplicated clinical specimens, including urine, blood, respiratory samples, oral swabs, high vaginal swabs, and skin and nail scrapings were taken from outpatients and inpatients in different departments and medical centers of Mansoura University hospitals, Egypt, who were presented with symptoms and/or signs of infection during 2020 and 2021 (Koneman et al., 1997).

All specimens were processed in the Mycology Lab, Medical Microbiology and Immunology Department, Faculty of Medicine, Mansoura University using basic microbiological methods. Germ tube test and VITEK 2 automated system (*bioMérieux Marcy-l'Étoile*, France) were used to identify *Candida* isolates which were stored at −80°C for further processing (Neppelenbroek et al., 2014).

Antifungal susceptibility testing with conventional antifungals

The following antifungal agents were tested, fluconazole (FLC), itraconazole (ITC), voriconazole (VRC) and amphotericin B (AMB) (*Sigma-Aldrich Corporation, Saint Louis, MO, USA*). The Minimum Inhibitory Concentration (MIC) was evaluated by the broth microdilution method based on the revised Clinical and Laboratory Standard Institute M27-S4 guidelines (CLSI, 2012). The final concentrations tested were 0.125 to 64µg/mL for fluconazole, and 0.016 to 16µg/mL for itraconazole, voriconazole, and amphotericin B. The MIC results were determined visually after incubating at 37°C for 24h and 48h. The MICs for azoles were defined as the lowest concentrations that caused a prominent decrease in turbidity (decrease in growth by 50%) while that for AMB was defined as the lowest concentration that resulted in an optically clear solution (complete inhibition of growth) relative to the positive control (CLSI, 2012). *Candida albicans* (ATCC 24433), *C. krusei* (ATCC6258), and *C. parapsilosis* (ATCC 22019) strains (NAMRU-3 Institute, Naval Medical Research Unit Three, Cairo, Egypt) were used as quality controls.

Antifungal susceptibility testing with silver nanoparticles (AgNPs)

The stock solution of ready-use spherical, water-soluble silver nanoparticles (AgNPs) with an average size of (45 ± 5nm) and concentration (200µg/mL) purchased from (*Nano Tec, Cairo, Egypt*) was used. The size and shape of AgNPs were investigated using a high-resolution transmission electron microscope (TEM) at an accelerating voltage of 200kV (*JEOL-JEM 2100 EX II; JEOL Ltd, Tokyo, Japan*). The AgNPs were dissolved in distilled water, autoclaved at 121°C for 20min, and then cooled to room temperature (Zhou et al., 2021).

The cell inoculum was prepared in 5mL of sterile saline from overnight *Candida* cultures grown at 37°C, and its optical was adjusted to that of a 0.5 McFarland standard measured at 530nm. A final inoculum of ($0.5–2.5\times10^3$ cell/mL) was obtained after dilution in Roswell Park Memorial Institute (RPMI) 1640 medium (with L-glutamine and phenol red, without bicarbonate) (*Sigma-Aldrich Corporation, Saint Louis, MO, USA*) (Artunduaga Bonilla et al., 2015).

The broth microdilution method was used to determine the MIC_{50} of AgNPs based on CLSI guidelines. The MIC_{50} was defined as the lowest concentration of AgNPs that could inhibit *Candida* growth by 50% compared with the AgNPs free control (CLSI, 2012; Perween et al., 2019). A total of 100µL of *Candida* suspension was inoculated into the wells of a sterile 96-well microdilution plates containing 100µL of AgNPs at concentrations ranging from 0.062–1µg/mL. After incubating for 24h and 48h at 37°C, the decrease in turbidity of the wells was inspected visually and using a spectrophotometer at 530nm.

Minimum fungicide concentration (MFC)

The contents of each well were mixed with a micropipette, and the entire volume (200µL) was inoculated onto SDA plates and incubated at 37°C for 24–48h. The Minimum Fungicide Concentration **(**MFC) was defined as the lowest concentration of AgNPs at which no colonies were seen (99.9% fungicidal activity) compared with non-AgNPs-treated microbial control (Artunduaga Bonilla et al., 2015).

Scanning electron microscopy

The morphological changes in the surface structure of resistant Candida spp. Before and after treatment with AgNPs were observed under a scanning electron microscope (SEM) (JEOL-JSM 6510 LV; JEOL Ltd, Tokyo, Japan) at an accelerating voltage of 30kV (Lotfali et al., 2021).

Statistical analysis

The IBM SPSS Statistics 23 software for Microsoft Windows (SPSS Inc., Chicago, IL, USA) was used to analyze data. Qualitative variables were presented as numbers and percentages. Continuous variables were expressed as means ± standard deviation (S.D.). Student's t-test and Pearson's chi-square (χ^2) test were used to compare between groups. P values < 0.05 were considered statistically significant.

Results

A total, of 109 non-duplicate *Candida* strains were recovered from 574 distinct clinical specimens collected from patients treated in Mansoura University hospitals. Among the *Candida*-infected patients, 46 (42.2%) were males, and 63 (57.8%) were females. Their ages ranged from 1-71 years (Mean ± SD, 44.6 ± 19.4). About 56% of the patients had comorbidities, including diabetes mellitus, immunological diseases, chronic pulmonary diseases, end-organ failure, and malignancy. About 88.1% of infected patients had risk factors for developing *Candida* infection. Neutropenia and ICU admission were recorded in 6.4% and 10.1% of the patients, respectively. Thirty (27.5%) patients were on prior antibiotic therapy and 16 (14.7%) were undergoing immunosuppressive and radiotherapy (Table 1).

Candida was distributed differently among the various clinical samples. Most of the isolates were recovered from urine (56, 51.4%), followed by respiratory samples (20, 18.3%), blood (15, 13.8%), oral swabs (10, 9.2%), nail scrapping (5, 4.6%), and high vaginal swabs (3, 2.8%). *C. albicans* accounted for 65.1% of the isolates (71/109) while NAC species constituted 34.9% (38/109). Among the NAC species, *C. tropicalis* was the most common (13, 11.9%), followed by *C. glabrata* (12, 11.0%), *C. parapsilosis* (8, 7.3%), *C. krusei* (4, 3.7%), and *C. famata* (1, 0.9%) (Table 2).

The broth microdilution method revealed that the *Candida* isolates exhibited high azole resistance. Of the 109 isolates, (39, 35.8%) were resistant to one or more antifungal drugs tested: 35 (32.1%) to fluconazole, 32 (29.4%) to itraconazole, 18 (16.5%) to voriconazole, and 7 (6.4%) to amphotericin B (Table 3). The MICs of fluconazole, and itraconazole toward resistant *C. albicans* and NAC species did not differ significantly (*P* value = 0.286 and 0.431), respectively. On the other hand, the MICs of voriconazole and amphotericin B were significantly associated with the type of resistant *Candida* isolates (P= 0.001, and 0.025), respectively (Table 4).

The susceptibility of the 39 resistant *Candida* isolates to AgNPs was assessed by the broth microdilution method. AgNPs showed an MIC_{50} of 0.125–1µg/mL; 23.1% of the tested strains had MIC_{50} of 0.125µg/mL; whereas, 56.4%, 15.4%, and 5.1% of the isolates had MIC_{50} of 0.25µg/mL, 0.5µg/mL, and 1µg/mL, respectively. *C. albicans* and NAC species were similarly susceptible to AgNPs (P= 0.720) (Fig.1, Table 4).

TABLE 1. Demographic and clinical data of *Candida* infected patients

Characteristics	*Candida* positive cases (N= 109)	
	N	%
Gender		
Male	46	42.2
Female	63	57.8
Age (Years)		
Mean ±SD	44.6 ± 19.4	
(Min-Max)	1-71 years	
Presence of comorbidity		
Present	61	56.0
Absent	48	44.0
Risk factors	96	88.1
Prematurity	3	2.8
Urinary catheterization	17	15.6
CVC	5	4.6
TPN	4	3.7
MV	3	2.8
Neutropenia	7	6.4
ICU admission	11	10.1
Prior antibiotic administration	30	27.5
Immunosuppressive[a] and radiotherapy	16	14.7

Notes: [a]Immunosuppressive includes anticancer chemotherapy and corticosteroids.

Abbreviations: SD: standard deviation; CVC: central venous catheter; TPN: total parenteral nutrition; MV: mechanical ventilation; ICU: intensive care unit.

TABLE 2. Distribution of *Candida* spp. among different clinical samples

Candida spp. (N= 109)	Clinical samples													
	Urine		Respiratory samples		Blood		Oral swabs		Nail scrapping		Vaginal swabs		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
C. albicans	34	60.7	13	65.0	9	60.0	8	80.0	4	80.0	3	100.0	**71**	**65.1**
NAC*													**38**	**34.9**
C. tropicalis	9	16.1	2	10.0	-	-	2	20.0	-	-	-	-	13	11.9
C. glabrata	8	14.3	3	15.0	-	-	-	-	1	20.0	-	-	12	11.0
C. parapsilosis	2	3.6	1	5.0	5	33.3	-	-	-	-	-	-	8	7.3
C. krusei	2	3.6	1	5.0	1	6.7	-	-	-	-	-	-	4	3.7
C. famata	1	1.8	-	-	-	-	-	-	-	-	-	-	1	0.9
Total	56	51.4	20	18.3	15	13.8	10	9.2	5	4.6	3	2.8	**109**	**100.0**

*NAC: Non-albicans *Candida*

TABLE 3. Antifungal susceptibility profile of *Candida* spp. by broth microdilution method

Candida spp.	Antifungal agents										
	FLC			ITC			VRC			AMB	
	S	SDD	R	S	SDD	R	S	SDD	R	S	R
C. albicans (71)	46	7	18	53	2	16	63	0	8	68	3
C. tropicalis (13)	1	1	11	1	1	11	7	0	6	11	2
C. glabrata (12)	9	2	1	10	1	1	11	0	1	12	0
C. parapsilosis (8)	7	0	1	7	0	1	7	0	1	8	0
C. krusei (4)	1	0	3	2	0	2	2	0	2	2	2
C. famata (1)	0	0	1	0	0	1	1	0	0	1	0
Total (109) N	64	10	35	73	4	32	91	0	18	102	7
(%)	(58.7)	(9.2)	(32.1)	(66.9)	(3.7)	(29.4)	(83.5)	(0.0)	(16.5)	(93.6)	(6.4)

Abbreviations: S: susceptible; SDD: susceptible dose dependent; R: resistant, FLC: fluconazole, ITC: itraconazole, VRC: voriconazole, AMB: amphotericin B.

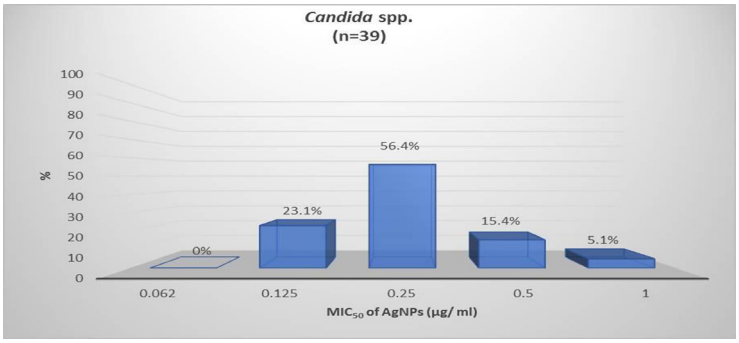

Fig. 1. The minimum inhibitory concentrations (MIC_{50}) of silver nanoparticles (AgNPs) against resistant *Candida* spp.

AgNPs exhibited lower MIC_{50} values (0.125–1µg/mL) than fluconazole (1–64µg/mL), itraconazole (0.016–4µg/mL), voriconazole (0.016–4µg/mL), and amphotericin B (0.016–1µg/mL). The MFC of AgNPs was 0.5 µg/mL and 1µg/mL, and did not differ significantly toward different *Candida* spp. (P= 0.849) (Table 4).

Scanning electron microscopy revealed modifications in *Candida* cell morphology after treatment with AgNPs. The outer surface of the *Candida* cell was disrupted (Fig. 2). Overall, AgNPs exhibited a potent inhibitory effect against *Candida* isolates *in vitro*.

Discussion

Candida can cause life-threatening infections with increased morbidity and mortality rates, especially among immunocompromised patients (Khouri et al., 2016). *Candida* was classified as the fourth worst pathogen causing severe bloodstream infections, with a mortality rate of up to 45% (Alexander et al., 2014).

In the present study, 109 *Candida* isolates were recovered with isolation rate 19.0%, and this was in accordance with the global increase of *Candida* infection due to elevated numbers of patients suffering from immunodeficiency (Öncü et al., 2019). Seyoum et al. (2020) also reported high rate (25%) of *Candida* infection. Consistent with Mohammadi et al. (2013), who reported that 71.1% of their *Candida*-infected patients were females, the proportion of female patients in our study was 57.8%. However, unlike previous studies, 56.0% of the patients in our study suffered from chronic co-morbid diseases and 88.1 % had risk factors for *Candida* infection, such as prior regimens of broad-spectrum antibiotics (27.5%) and immunosuppressants (14.7%) (Kumar et al., 2020; Mashaly & Zeid, 2022).

The prevalence of *Candida* spp. varies across countries. Herein, *C. albicans* was the most abundant isolated *Candida* spp. (65.1%), particularly from urine samples (51.4%), followed by *C. tropicalis* (11.9%), and *C. glabrata* (11.0%). Kaur et al. (2014) also reported the isolation of *C. albicans* at a frequency of 50%, mostly from urine (42.5%), followed by *C. tropicalis* (40%). Perween et al. (2019), and Kumar et al. (2020) recorded higher incidence of *C. albicans* infection (66.02%, and 67.0%) respectively, while, Seyoum et al. (2020) reported the prevalence of *C. albicans* (49.8%), with *C. krusei* being the next most isolated species (15.6%). In contrast, another study showed the abundance of NAC species and *C. krusei* was the most frequently isolated (Mohandas & Ballal, 2011). Moreover, Ghazi et al. (2019) stated the prevalence of *C. tropicalis* and *C. parapsilosis* in Middle East and North Africa countries.

In this study, 35.8% of the *Candida* isolates showed resistance against the four most commonly used antifungal drugs in our locality. High resistance to first-generation azole drugs was observed. Fluconazole and itraconazole showed high MICs against 32.1% and 29.4% of the isolates, respectively. Numerous studies from Egypt have reported similar findings. Mashaly & Zeid (2022) detected fluconazole resistance in 36.4% of their cases, while Hassan et al. (2017) detected it in 61.2%. Besides, results from studies performed in other countries align well with ours in terms of fluconazole resistance (Mohandas & Ballal, 2011; Perween et al., 2019; Dhasarathan et al., 2021; Lee et al., 2021). Silva et al. (2020) reported a high resistance to both fluconazole and itraconazole among their *Candida* isolates. In contrast, a study by Belet et al. (2011) demonstrated high fluconazole susceptibility.

TABLE 4. Sensitivity of silver nanoparticles (AgNPs) against resistant *Candida* isolates compared with conventional antifungal agents

Candida spp. (39)	Antifungal agents (µg/mL)				AgNPs (µg/mL)	
	FLC	ITC	VRC	AMB		
	MIC_{50}	MIC_{50}	MIC_{50}	MIC_{50}	MIC_{50}	MFC
***C. albicans* strain no.**						
1	2	4	0.016	0.512	0.25	0.5
2	64	0.064	0.016	0.256	0.25	0.5
3	64	4	0.256	0.256	1	1
4	64	4	0.016	0.128	0.5	0.5
5	64	4	0.016	0.128	0.25	0.5
6	64	4	0.256	0.256	1	1
7	64	4	0.016	0.256	0.25	0.5
8	64	4	0.016	0.256	0.25	0.5
9	64	4	4	0.128	0.5	0.5
10	64	4	4	0.128	0.25	0.5
11	64	4	4	1	0.25	0.5
12	64	4	4	1	0.5	0.5
13	64	4	4	1	0.5	0.5
14	64	0.064	0.016	0.128	0.125	0.5
15	64	4	4	0.512	0.25	0.5
16	64	4	4	0.128	0.25	0.5
17	16	4	4	0.512	0.25	0.5
18	64	4	0.016	0.128	0.25	0.5
19	64	0.064	0.016	0.128	0.125	0.5
20	64	0.064	0.016	0.128	0.125	0.5
***C. tropicalis* strain no.**						
1	64	0.032	0.016	0.128	0.125	0.5
2	64	4	0.016	0.128	0.125	0.5
3	4	4	0.016	0.016	0.25	0.5
4	64	4	0.016	0.128	0.25	0.5
5	64	4	0.016	0.016	0.125	0.5
6	64	4	0.016	0.016	0.25	0.5
7	64	4	4	0.016	0.5	0.5
8	64	4	4	1	0.5	0.5
9	64	4	4	1	0.25	0.5
10	64	4	4	0.016	0.25	0.5
11	64	4	4	0.016	0.25	0.5
12	64	4	4	0.128	0.25	0.5
***C. glabrata* strain no.**						
1	64	4	4	0.128	0.25	0.5
***C. parapsilosis* strain no.**						
1	64	0.016	0.016	0.016	0.125	0.5
2	1	4	4	0.016	0.125	0.5
***C. krusei* strain no.**						
1	64	0.032	0.128	0.016	0.125	0.5
2	64	4	4	1	0.25	0.5
3	64	4	4	1	0.25	0.5
***C. famata* strain no.**						
1	64	4	0.064	0.256	0.25	0.5
P value	0.286	0.431	0.001*	0.025*	0.720	0.849

Note: The MIC_{50} was defined as the minimum concentration that inhibits 50% of *Candida* growth. The breakpoints for antifungal agents used for *Candida* spp. compared with reference strains according to CLSI guidelines; (FLC) S ≤ 8; SDD 16-32; R ≥ 64), (ITC) S≤ 1; SDD 2; R ≥ 4, (VRC) S≤ 1; SDD 2; R ≥ 4), and (AMB) S≤ 1; R ≥ 1). *$P < 0.05$ (statistically significant).

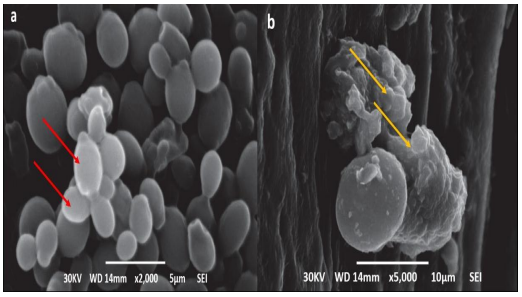

Fig. 2. Scanning electron micrographs of *Candida albicans*: a) Untreated *C. albicans*; the red arrows indicate the smooth surface of untreated *C. albicans*, b) *C. albicans* after treatment with AgNPs; the yellow arrows indicate the rough and damaged outer surface of *C. albicans*

Minimum resistance was observed toward second-generation triazoles: 16.5% of the isolates were resistant to voriconazole while amphotericin B was the most effective antifungal, with only 6.4% of the isolates resistant to it. Similarly, Mirshekar et al. (2021) found in their study that sensitivity to amphotericin B and voriconazole was 100%. The high resistance to fluconazole and itraconazol may be attributed to the widespread use of these agents in our locality. Voriconazole and amphotericin B are used lesser because of their higher cost and adverse side effects. Resistance to azoles was higher in *C. albicans*, and *C. tropicalis* showed the most resistance among NAC species. On other hand, Kumar et al. (2020) reported that 24.0% of the *C. albicans* isolates and none of the NAC isolates in their study were resistant to azoles.

Various new medications used to treat burns and wound infections contain silver due to its antibacterial effect. The potency of AgNPs against resistant bacterial pathogens and plant fungi is now well-recognized. Silver can kill microbes by inhibiting the enzyme responsible for oxygen uptake. Besides, the physical properties of nanoparticles facilitate them to interact with microbes (Perween et al., 2019).

Despite this, very few studies have investigated the role of AgNPs against fungi that cause human infections (Mansoor et al., 2021). We found the MIC_{50} values of AgNPs to be low, ranging from 0.125–1µg/mL. Previously, the MIC of AgNPs has been reported to be about 0.125–0.5µg/mL (Perween et al., 2019), 0.25µg/mL (Panáček et al., 2009), and 0.4–3.3µg/mL (Monteiro et al., 2011). We also observed potent fungicidal effects of AgNPs at low MFCs, consistent with the values of 0.25µg/mL and 0.5µg/mL reported by Zhou et al. (2021). Contrastingly, Meneses et al. (2022) reported that AgNPs had a weaker antifungal effect and higher MICs (26.5–106µg/mL) of AgNPs. These opposite findings are likely due to the lack of a standardized method for determining the antifungal effect of AgNPs.

The MIC_{50} values of AgNPs were remarkably lower than those of azoles, particularly fluconazole. Nasrollahi et al. (2011) also reported a high MIC_{50} of fluconazole compared with AgNPs. The outer surface of AgNPs treated *Candida* isolates appeared altered and rougher than that of the non-treated isolates. Previous studies have reported damage in outer membrane of *Candida* cell and alteration in permeability to allow small sized nanoparticles to enter the cell (Lara et al., 2015; Vazquez-Munoz et al., 2020).

Conclusion

AgNPs may help treat infections caused by resistant *Candida* spp. due to their potent *in vitro* antifungal activity. Although some studies have addressed their safety, more experiments must be conducted to confirm the potential cytotoxicity, in vivo side effects and mode of action of AgNPs. Additionally, the antifungal effect of AgNPs against various fungal pathogens should be investigated.

Conflict of interest: The authors declare no conflicts of interest.

Authors' contributions: Rasha Mokhtar Elnagar designed the study, performed the microbiological laboratory work, analyzed the data, and writing as well as finalizing the manuscript. Mohammed Elshaer collected the clinical isolates and reviewed patients' medical records. Mona Abd El-Hamid Abd El-Raouf performed the microbiological laboratory work and writing the manuscript. All authors revised the manuscript and approved the final version.

Ethical approval: The study protocol and design was approved by the Mansoura Faculty of Medicine Institutional Research Board (R.21.04.1286). Informed written consent was obtained from all participants.

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جزيئات الفضة النانوية تظهر تأثيرًا مثبطًا ضد الكانديدا المقاومة للأدوية من العينات السريرية المختلفة

رشا مختار النجار [1]، محمد الشاعر [2]، منى عبد الحميد عبد الرؤوف

[1] قسم الأحياء الدقيقة الطبية والمناعة- كلية الطب- جامعة المنصورة- المنصورة - مصر، [2] قسم الباثولوجيا الإكلينيكية- كلية الطب- جامعة المنصورة- المنصورة- مصر.

تشكل مقاومة الكانديدا لمضادات الفطريات مشكلة مزعجة للمؤسسات الصحية في جميع أنحاء العالم، خاصة مع ظهور أنواع جديدة. لذلك، حظيت العوامل البديلة الجديدة مثل جزيئات الفضة (AgNPs) باهتمام كبير. وتهدف هذه الدراسة إلى تقييم حساسية مضادات الفطريات في المختبر لـ AgNPs ضد عزلات الكانديدا المقاومة لمضادات الفطريات والتى تم عزلها من عينات سريرية مختلفة من المرضى المترددين على أقسام ومراكز مستشفيات جامعة المنصورة. وذلك عن طريق تقييم التأثير المضاد للفطريات باستخدام تراكيز مختلفة (0.062-1 ميكروغرام/ مل) وقد تم تحديد الحد الأدنى للتركيز المثبط (MIC_{50}) والحد الأدنى لتركيز مبيد الفطريات (MFC) من AgNPs. وتوصلت الدراسة إلى عزل 109 من الكانديدا، كانت 65.1٪ من المبيضات البيضاء و 34.9٪ كانت من المبيضات غير البيضاء (NAC) على التوالي. من بين أنواع المبيضات التي تم تحديدها، كانت 35.8٪ غير حساسة للأدوية التقليدية المضادة للفطريات. كانت قيمة MIC_{50} لـ AgNPs مقابل العزلات المقاومة منخفضة (0.125-1 ميكروغرام/ مل) مقارنة بـ MIC من فلوكونازول (64-1ميكروغرام / مل)، إيتراكونازول (0.016-4 ميكروغرام / مل)، فوريكونازول (0.016-4 ميكروغرام / مل)، والأمفوتيريسين بى (0.016-1 ميكروغرام/ مل) وميكروغرام/ مل). أشارت صورة المجهر الإلكتروني الماسح إلى وجود تباين في مورفولوجيا خلايا المبيضات قبل وبعد العلاج باستخدام AgNPs. الخلاصة: أظهرت جسيمات الفضة النانوية تأثير مبيد للفطريات ضد عزلات الكانديدا المقاومة لمضادات الفطريات وقد تكون بديلاً فعالاً للعوامل المضادة للفطريات.