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RESEARCH ARTICLE

Investigation of the Antifungal Activity of Curcumin-Coated Gold Nanoparticles

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ABSTRACT

Objective(s): The COVID-19 pandemic has underscored the global threat posed by opportunistic pathogens, including drug-resistant fungi. Metal nanoparticles are considered general microbicidal agents. These nanoparticles have a broad antimicrobial spectrum.

Methods: The preparation of nanoparticles with curcumin coating was performed through a single-step procedure in which curcumin acted as a reducing and stabilizing agent. The characterizations of the particles were conducted through electron microscopy, dynamic light scattering, and UV-Vis spectroscopy. The cytotoxicity of particles was evaluated with an MTT assay. The antifungal properties of curcumin-coated gold nanoparticles were evaluated up to a concentration of 128 µg/ml against different species of *Candida* and *Aspergillus*, and compared with common antifungal drugs such as fluconazole and itraconazole. TEM was applied to investigate the structural analysis of the particles' interaction.

Results: The particle synthesis was performed using a single-batch green method. Characterized by TEM, UV-Vis, and DLS, the particles exhibited an average diameter of 7.5 ± 4.1 nm and remained stable for over 64 days. Cytotoxicity tests on HepG2 cells showed high biocompatibility. While Cur@AuNPs exhibited antifungal activity against various species of *Candida*, including drug-resistant strains, no significant activity was observed against *Aspergillus* species. These findings suggest potential applications of Cur@AuNPs in treating *Candida*-related infections.

Conclusions: Cur@AuNPs demonstrate inhibitory properties on different species of *Candida* but do not exhibit antifungal activity against either drug-sensitive or drug-resistant *Aspergillus* species.

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INTRODUCTION

Considerable evidence on the expansion of the geographical range and the incidence of dangerous fungal diseases around the world have emerged in recent years. Various reasons have been cited for the increased prevalence of dangerous fungi, including global warming, increased communication, and the expansion of global trade (1). In recent years, the occurrence of invasive and deadly fungal infections has significantly increased among COVID-19 patients (2). Due to the widespread use of antifungal drugs for common fungal infections such as oral and vaginal *Candida* or respiratory fungi such as *Aspergillus*, the risks of more aggressive forms of infections in the general population are always

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increasing. Using substances that inhibit the growth of fungi in different environments is one of the most common ways to prevent infection.

Curcumin is a natural phenol with antimicrobial characteristics against a broad spectrum of pathogens (3). This compound is hydrophobic and is not bioavailable systemically. Curcumin nanoformulations have drawn attention as a solution for this drawback because they can increase curcumin hydrophilicity and boost its bioavailability (4). Recent studies have advanced antifungal nanomaterials, demonstrating the efficacy of metal-ligand complexes in combating drug-resistant fungi through enhanced bioavailability and targeted activity (5, 6). Phytochemical-based formulations, including those inspired by curcumin, offer promising antimicrobial properties but highlight the need for eco-friendly synthesis to improve stability and reduce toxicity (7).

Apart from various medicinal properties, curcumin, as an active phytochemical compound, can be applied for the chemical synthesis of metal nanoparticles. Metal nanoparticles have widely entered in medical research (8), diagnostics (9), cancer treatments (10), health industry (11), and antimicrobial applications (12). Here the aqueous solution of Cur@AuNPs through a one pot green synthesis procedure without any other chemicals or solvent. The antifungal effect of the synthesized nanoparticles has been investigated for the first time against various strains of *Candida* and *Aspergillus* fungus.

MATERIAL AND METHODS

Synthesis of the Cur@AuNPs

Briefly, 20 mM solution of curcumin (diferuloylmethane, $C_{21}H_{20}O_6$ 65%, Sigma-Aldrich, USA) in DMSO (C_2H_6OS, 99.5%, Gibco, Life Technologies GmbH, Karlsruhe, Germany) was prepared. A round bottom flask was filled with 15 mL of deionized water (DIW). The water's pH was adjusted to approximately 9 using a 150 mM potassium carbonate (K_2CO_3) solution sourced from Sigma-Aldrich, USA. Subsequently, 100 µL of curcumin solution was added dropwise into the stirred DIW, causing the initially yellow curcumin solution to shift to a red hue. After a three-minute interval, 2.5 mL of tetrachloroauric (III) acid trihydrate ($HAuCl_4{\cdot}3H_2O$, 2.5 mM, Sigma-Aldrich, Germany) was slowly introduced into the curcumin mixture. The reaction was maintained under continuous stirring for three hours, then the mixture was kept undisturbed in the dark for a period of three days. (13, 14) According to our previous study, the nanoparticles were washed through a series of centrifugation and decantation to remove unreacted reagents (15, 16).

Characterizations of the Cur@AuNPs

Prior to conducting any characterization, the produced Cur@AuNPs were filtered using a 0.2 µm polyvinylidene fluoride (PVDF) membrane. Transmission electron microscopy (Zeiss EM 900, Germany) was employed to examine the size and structural features of the nanoparticles. The nanoparticles' optical characteristics were evaluated via UV-Visible spectroscopy, utilizing a double-beam UV-Vis absorption spectrophotometer (SPEKOL 2000, Analytik Jena, UK) equipped with a quartz cuvette having a 1 cm optical path length. Additionally, dynamic light scattering (DLS) measurements to determine hydrodynamic size were performed using the NANO-flex Particle Sizer (Germany), while the surface charge (zeta potential) was assessed with a Zeta-check instrument (Microtrac, Germany). Finally, the concentration of gold ions within the nanoparticle suspensions was quantified through inductively coupled plasma optical emission spectroscopy (ICP-OES).

In vitro cytotoxicity analysis

HepG2 cells were obtained from the Pasteur Institute of Iran, Tehran. Cells were cultured in DMEM culture medium supplemented with 10% fetal bovine serum (FBS), and 1% penicillin-streptomycin solution. The cells were kept in an atmosphere of 5% CO_2 air at 37°C and the culture medium was changed daily. To investigate the cytotoxicity of Cur@AuNPs, cells were seeded at approximately 100,000 cells per well of a 96-well plate, and after the cells were attached to the plate, the cells were treated with culture containing different concentrations of nanoparticles and incubated for 24 hours. Then the cells were washed with PBS and incubated with 100 µL of MTT solution in buffer or culture medium at a concentration of 0.5 mg/mL for 2-4 hours. Following incubation, the MTT solution was removed and replaced with 100 µL of DMSO. After gently shaking the plate for 2 minutes, absorbance was measured at 570 nm using a microplate reader.

Antifungal activity testing of Cur@AuNPs
Fungal strains

A set of 30 clinically important fungal strains including *Candida albicans* (n=6), *Candida parapsilosis* (n=6), *Candida krusei* (n=6), *Aspergillus fumigatus* (n=6), and *Aspergillus flavus* (n=6) were investigated in the current study. These fungi have previously been identified using sequence analysis of ITS1-5.8S rDNA-ITS2 (for *Candida* species) or beta-tubulin (for *Aspergillus* species) markers.

Broth dilution

The antifungal activity of Cur@AuNPs was determined according to the Clinical and Laboratory Standards Institute (CLSI) protocols for yeasts and filamentous fungi (17). The susceptibility of the isolates to itraconazole (Behvazan Co., Iran) and fluconazole (Amin Pharma. Co., Iran) was also determined using the same method. The tested concentrations for Cur@AuNPs, itraconazle, and fluconazole were 1–512 µg/mL, 0.03–16 µg/mL, and 0.125–64 µg/mL, respectively. *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 5268 were used as quality control. The value of minimum inhibitory concentration (MIC) was considered as the lowest concentration of the nanoparticle that was able to make 50% inhibition (100% for itraconazole against *Aspergillus* species) in comparison to drug-free growth control wells. Minimum fungicidal concentration (MFC) was determined based on a method described previously (18).

Specimen preparation for electron microscopy

For analysis of the Cur@AuNPs interaction with *C. albicans*, cultures were incubated with Cur@AuNPs at 32 µg/mL concentration for 24 hours. After nanoparticle incubation, the treated microorganisms were washed with PBS carefully. For primary fixation a 2-hour incubation with 2.5% glutaraldehyde was applied. Free glutaraldehyde was removed through a series of washing procedures with PBS. Secondary fixation was carried out by 1.5-hour incubation with 1% osmium tetroxide. Dehydration of the fungus was performed in acetone (50, 70, 90, 100%), then infiltrated by resin and finally embedded in pure resin (Epon 812, TAAB, UK). then, the ultra-microtome was applied to obtain thin sections of 50 nm. Finally, the provided slices were stained with uranyl acetate and lead citrate for investigation under TEM (Zeiss EM 900, Germany)

Software and statistics

The data are expressed as means ± SD. Differences between groups were assessed by one-way ANOVA. The diagram was analyzed and presented using Origin 6 software. The size distribution of the particles was obtained from the Gaussian fit of the diameter of 100 nanoparticles that have been analyzed with Digital Micrograph software..

RESULTS AND DISCUSSION

Synthesis and characterizations

This green approach, leveraging curcumin's dual role as reductant and stabilizer, yielded stable, spherical NPs, contrasting with slower kinetics in microbial green syntheses that often yield polydisperse particles (19) or an immunogenic response similar to previous experiences for gene delivery applications (20).

The formation of Cur@AuNPs was verified by the distinct plasmonic red color typical of gold nanoparticles (21). The observation that the plasmonic peak remains at essentially the same wavelength (524 nm vs. 525 nm) over a period of more than two months is a strong and direct indicator of high stability for the Cur@AuNPs. The UV-Vis spectra were applied to investigate the stability of the particles (Figure 1). Similar nanoparticles that have been synthesized by apigenin, which is a natural flavonoid, represent high stability in physiological environments (15). The very high stability of curcumin-coated silver nanoparticles was also investigated in our previous study (22). After making sure that the stable nanoparticles were synthesized, the hydrodynamic diameter of the particles was evaluated, which was 10.88±1.16 nm. TEM analysis revealed the size distribution and morphological characteristics of the synthesized Cur@AuNPs. Cur@AuNPs represent spherical morphology, with an average particle size of 7.5 ± 4.1 nm with all of the nanoparticles were almost spherical (Figure 2).

Studies have shown that nanoparticles produced via green synthesis often exhibit significant variability in both size and morphology (19). This heterogeneity arises because the reduction of metal ions by plant-derived compounds proceeds at a relatively slow rate, resulting in nanoparticles with a broad size distribution (23). In the preparation of Cur@AuNPs, curcumin must first be dissolved in DMSO and can then be further diluted with water, particularly at elevated pH levels. Raising the pH

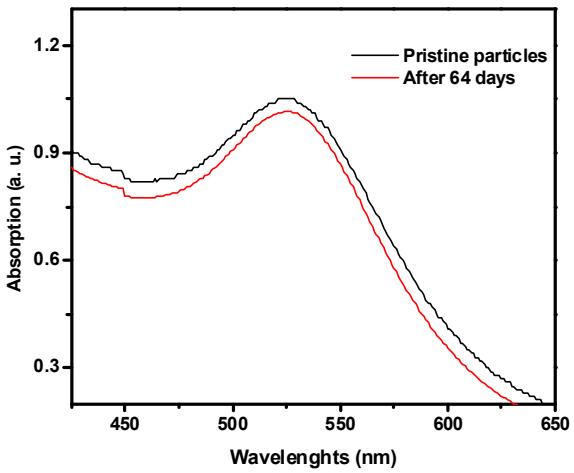

Fig. 1. The stability analysis of Cur@AuNPs over two months with UV-Vis spectroscopy.

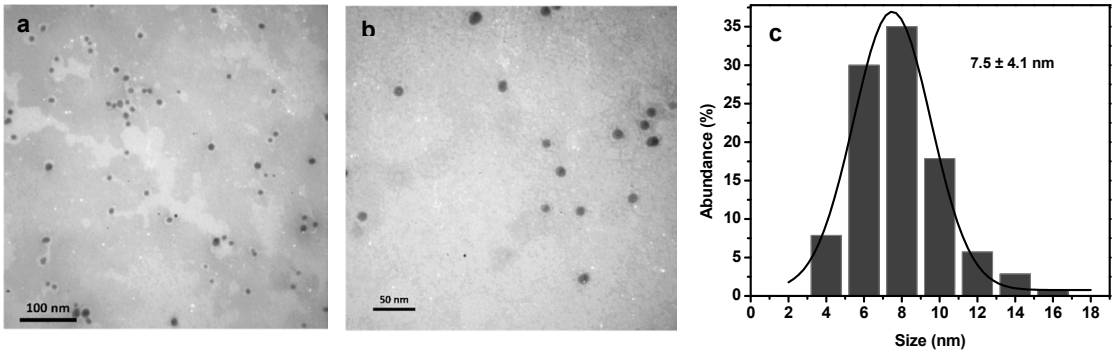

Fig. 2. Transmission electron micrographs of Cur@AuNPs (a, b) and the corresponding size distribution (c).

is crucial to facilitate the release of protons from curcumin's hydroxyl groups, which aids in the reduction of gold ions. It is important to introduce $HAuCl_4$ within 5 minutes, as at pH 9, curcumin degradation intensifies beyond this time frame. By adding $HAuCl_4$, primary gold nuclei are formed with electrons obtained from the degradation of curcumin. It has been demonstrated that small silver particles can have catalytic properties in the destruction of curcumin (24). The catalytic activity of gold was also declared (14). This can provide more electrons for the reduction of gold ions in the growth stage of the nuclei. The slower the growth of the particles, the more homogeneous the shape and size of the nanoparticles will be. That is why the growth of nanoparticles at room temperature without stirring for three days was chosen. To eliminate unbound curcumin, the Cur@AuNPs underwent multiple cycles of centrifugation followed by decantation. Studies have shown that performing this washing process four times effectively clears residual curcumin and gold ions (13, 14). The final nanoparticles had a negative charge of -27.9 ± 0.1 mV, which is actually due to the presence of the polyphenol coating caused by the polymerization of the broken curcuminoids on the surface of the nanoparticles.

Cytotoxicity evaluation

A key challenge in utilizing metal nanoparticles for biomedical applications is their potential toxicity. Since gold is non-biodegradable, its long-term toxicity is a concern, with cytotoxicity depending on parameters such as size, shape, and surface chemistry. For instance, studies show that traditionally synthesized citrate-coated gold nanoparticles with the size of 5 nm are more toxic than 15 or 25 nm ones (25). The use of natural phytochemicals like curcumin for synthesis has produced nanoparticles with reduced toxicity.

Curcumin-coated gold nanoparticles (Cur@AuNPs) have demonstrated high biocompatibility, showing no significant toxicity on human colorectal cancer HT29 (up to 50 µg/mL) (14), human monocytic cell line (THP-1) (26), human prostate cancer cell line (PC-3) VI paper (up to 280 µg/mL) (27), embryonic BD1X rat heart tissue (H9c2) (28), and peripheral blood mononuclear cells (PBMCs) (29). However, cytotoxic effects have been observed in other lines, such as L929 mouse fibroblastic cells (50% cell death at 120 µg/mL) (30), 3T3 Fibroblasts (31), human lung cancer (A549), human breast cancer (MDAMB-231), prostate cancer (DU145) cell lines (32), and MCF-7, as well as HCT-116 (33). In the present study on HepG2 cells, statistically significant effects begin at 4 µg/mL, yet over 90% of cells survive at 16 µg/mL (92.23%), and over 70% survive at 128 µg/mL (75.41%). By reviewing all these reports, it can be concluded that if Cur@AuNPs are washed well to remove ions, free curcumin, and other by-products not attached to the surface, the resulting nanoparticles are very biocompatible toward various cell lines.

Antifungal activity of Cur@AuNPs

MIC values of Cur@AuNPs, fluconazole, and itraconazole against *Aspergillus* and *Candida* isolates used in this study are shown in Table 1. All the *Aspergillus* isolates were unresponsive to fluconazole (geometric mean [GM] MIC: >64 µg/mL), while 5 and 4 isolates were susceptible and intermediate to itraconazole, respectively. Cur@AuNPs, similar to fluconazole, did not show any activity against the *Aspergillus* isolates (GM MIC: >128 µg/mL).

The lack of activity against *Aspergillus's* species may be attributed to several structural and mechanistic factors. Differences in fungal cell wall composition could play a key role, as *Candida* species are primarily composed of β-glucans and mannans, facilitating easier nanoparticle interaction, whereas *Aspergillus* features a higher chitin content and a more rigid structure that may impede Cur@AuNP penetration or adhesion (34). Additionally, variations in curcumin release kinetics or nanoparticle uptake might differ between the genera, with *Aspergillus* filamentous morphology

Table 1. The minimum inhibitory concentration (MIC) values of curcumin-coated gold nanoparticles (Cur@AuNPs) and two comparator antifungal drugs against *Aspergillus* and *Candida* species

No.	Species	Minimum Inhibitory Concentration (MIC) Values (µg/mL) and interpretations				
		Fluconazole	Interpretation	Itraconazole	Interpretation	Cur@AuNPs
1	*Aspergillus fumigatus*	>64	Resistant	16	Resistant	>128
2	*Aspergillus fumigatus*	>64	Resistant	8	Resistant	>128
3	*Aspergillus fumigatus*	>64	Resistant	16	Resistant	>128
4	*Aspergillus fumigatus*	>64	Resistant	2	Intermediate	>128
5	*Aspergillus fumigatus*	>64	Resistant	0.5	Susceptible	>128
6	*Aspergillus fumigatus*	>64	Resistant	2	Intermediate	>128
7	*Aspergillus flavus*	>64	Resistant	0.5	Susceptible	>128
8	*Aspergillus flavus*	>64	Resistant	1	Susceptible	>128
9	*Aspergillus flavus*	>64	Resistant	0.5	Susceptible	>128
10	*Aspergillus flavus*	>64	Resistant	2	Intermediate	>128
11	*Aspergillus flavus*	>64	Resistant	2	Intermediate	>128
12	*Aspergillus flavus*	>64	Resistant	1	Susceptible	>128
13	*Candida albicans*	>64	Resistant	>16	Resistant	64
14	*Candida albicans*	>64	Resistant	>16	Resistant	64
15	*Candida albicans*	>64	Resistant	0.5	Resistant	16
16	*Candida albicans*	>64	Resistant	>16	Resistant	8
17	*Candida albicans*	64	Resistant	0.06	Susceptible	32
18	*Candida albicans*	0.25	Susceptible	0.06	Susceptible	16
19	*Candida parapsilosis*	16	Resistant	0.125	Susceptible	32
20	*Candida parapsilosis*	16	Resistant	0.125	Susceptible	16
21	*Candida parapsilosis*	16	Resistant	0.25	Resistant	64
22	*Candida parapsilosis*	16	Resistant	0.06	Susceptible	128
23	*Candida parapsilosis*	0.5	Susceptible	0.06	Susceptible	64
24	*Candida parapsilosis*	2	Resistant	0.25	Resistant	64
25	*Candida krusei*	>64	Resistant	0.25	Not applicable	64
26	*Candida krusei*	64	Resistant	0.25	Not applicable	32
27	*Candida krusei*	64	Resistant	16	Not applicable	32
28	*Candida krusei*	64	Resistant	0.25	Not applicable	64
29	*Candida krusei*	64	Resistant	0.25	Not applicable	128
30	*Candida krusei*	>64	Resistant	0.25	Not applicable	32

potentially leading to reduced internalization compared to the yeast-like form of *Candida* (22). Furthermore, fungal efflux pumps and inherent drug resistance mechanisms in *Aspergillus*, such as those contributing to azole tolerance, could actively expel curcumin or limit Cur@AuNP efficacy (35). These observations align with studies on curcumin nanoformulations, which often show stronger antifungal effects against *Candida* than *Aspergillus* due to these biological barriers (4). Future experiments, including comparative uptake assays using fluorescently labeled nanoparticles, efflux pump inhibitor co-treatments, or cell wall disruption models, could further elucidate these mechanisms and guide optimizations for broader-spectrum activity.

The fungistatic effect of citrate-capped gold nanoparticles (36), and $NaBH_4$-capped gold nanoparticles (37) was declared for *Candida* strains. Since the nanoparticles made with these chemicals do not have steric stability, they are very unstable in physiological environments. Therefore, they cannot be easily used for biomedical applications. These chemicals themselves have toxic effects on eukaryotic cells and their removal from the surface or solution of nanoparticles cannot be done easily (37). Even the comparative study of nanoparticles has shown that nanoparticles prepared with $NaBH_4$ have more toxicity than the same nanoparticles that have been prepared by $SnCl_2$ against *Candida* strains (37).

Regarding the *Candida* species, all but two (one *C. albicans* [MIC: 0.25 µg/mL] and one *C. parapsilosis* [MIC: 0.5 µg/mL] isolates), were resistant to fluconazole. There were also four isolates with MIC values of ≥16 µg/mL for itraconazole. The activity of Cur@AuNPs was much better against *Candida* species, with the superiority of *C. albicans*, compared to *Aspergillus* species. The GM MICs of Cur@AuNPs against *C. albicans*, *C. parapsilosis*, and *C. krusei* isolates were 25.40 µg/mL, 50.80 µg/mL, and 50.80 µg/mL, respectively. The inhibition activity of the curcumin against the *Candida* strains was attributed to hyphal development suppression by Cur (38). Also, the production of reactive oxygen species (ROS) from Cur (39), and gold nanoparticles has been reported (40). Regarding the MFC values, Cur@AuNPs did not demonstrate any fungicidal activity against *Aspergillus* and *Candida* species. The activity of itraconazole in this regard was much better than the fluconazole and Cur@AuNPs (Table 2).

Antifungal effects of gold nanoparticles with similar biogenic coatings on *Aspergillus* strains have been investigated in some studies. Such coatings for gold nanoparticles prepared by green chemistry method can be from all compounds of an extract of a substance such as a plant or mushroom, or a phytochemical isolated from an extract. Antifungal effects against the *Aspergillus flavus* strain have been observed for gold nanoparticles prepared with *Agaricus bisporus* mushroom extract. However, other strains of *Aspergillus* were resistant to the synthesized nanoparticles (41).

Antifungal effect toward *Aspergillus flavus*, *Aspergillus niger*, and *Candida albicans* for green synthesized gold nanoparticles from *Abelmoschus esculentus* extract was also demonstrated (42). Green-synthesized gold nanoparticles from *Cannabis sativa* represent an inhibitory effect against *Aspergillus* flavus, *Aspergillus fumigatus*, and *Aspergillus niger* (43). Quercetin is a natural flavonoid that could be applied for the synthesis of gold nanoparticles. The inhibitory effect of quercetin against *A. fumigatus* was reported by Milanezi et al (44). Cinnamaldehyde is the main flavonoid from the spice cinnamon and has been applied for the synthesis of gold nanoparticles. The synthesized Cinnamaldehyde-coated gold nanoparticles could inhibit the *C. albicans* at the 75 µg/ml concentration (45).

To evaluate the interaction between nanoparticles and fungal species, transmission electron microscopy imaging of the fungi treated with Cur@AuNPs was performed (Figure 4). The interaction of Cur@AuNPs with the *Candida albicans* samples could be classified into three categories based on the provided micrographs. It was observed that the Cur@AuNPs are accumulated on the surface of the cell wall/membrane (black arrows). This accumulation of nanoparticles on the cell wall can also have a negative effect on the process of cell mitosis. An example of a dividing cell is marked by a white line in the micrograph of Figure 4a. The interaction of metal nanoparticles on microorganisms' membranes could also disturb the membrane potential and create pores. This phenomenon leads to disruption of the microorganism's cell membrane/wall and the exit of ions and cytoplasmic fluid from the microorganism. The cell wall disruptor (orange arrows), and cytoplasmic shedding (green arrows) are observed in the presented TEM micrographs. The entrance of the Cur@AuNPs into the cytoplasm

Table 2. The minimum fungicidal concentration (MFC) values of curcumin-coated gold nanoparticles (Cur@AuNPs) and two comparator antifungal drugs against *Aspergillus* and *Candida* species

No.	Species	Minimum fungicidal concentration (MFC) values vales (µg/mL)		
		Fluconazole	Itraconazole	Cur@AuNPs
1	*Aspergillus fumigatus*	>64	>16	>128
2	*Aspergillus fumigatus*	>64	>16	>128
3	*Aspergillus fumigatus*	>64	>16	>128
4	*Aspergillus fumigatus*	>64	8	>128
5	*Aspergillus fumigatus*	>64	4	>128
6	*Aspergillus fumigatus*	>64	8	>128
7	*Aspergillus flavus*	>64	2	>128
8	*Aspergillus flavus*	>64	4	>128
9	*Aspergillus flavus*	>64	4	>128
10	*Aspergillus flavus*	>64	8	>128
11	*Aspergillus flavus*	>64	16	>128
12	*Aspergillus flavus*	>64	4	>128
13	*Candida albicans*	>64	>16	>128
14	*Candida albicans*	>64	>16	>128
15	*Candida albicans*	>64	8	>128
16	*Candida albicans*	>64	>16	>128
17	*Candida albicans*	>64	2	>128
18	*Candida albicans*	1	1	>128
19	*Candida parapsilosis*	>64	4	>128
20	*Candida parapsilosis*	>64	4	>128
21	*Candida parapsilosis*	>64	4	>128
22	*Candida parapsilosis*	>64	2	>128
23	*Candida parapsilosis*	>64	1	>128
24	*Candida parapsilosis*	2	2	>128
25	*Candida krusei*	>64	4	>128
26	*Candida krusei*	>64	2	>128
27	*Candida krusei*	>64	>16	>128
28	*Candida krusei*	>64	4	>128
29	*Candida krusei*	>64	4	>128
30	*Candida krusei*	>64	2	>128

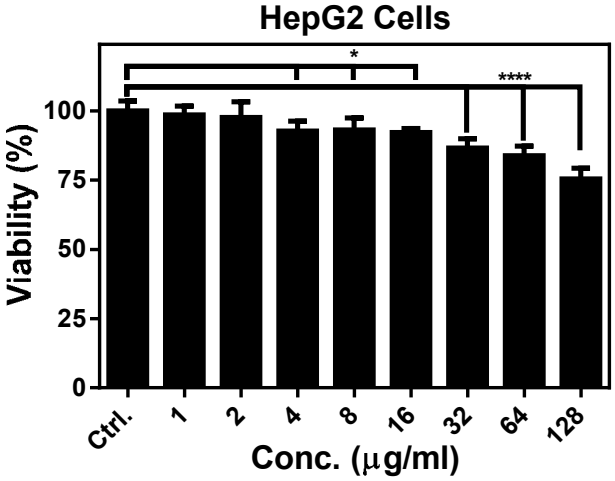

Fig. 3. Cytotoxicity evaluation of Cur@AuNPs on HepG2 cells. 24-hour treatment was applied. (Asterisks point out statistically significant differences: *P < 0.05 and ****P < 0.0001).

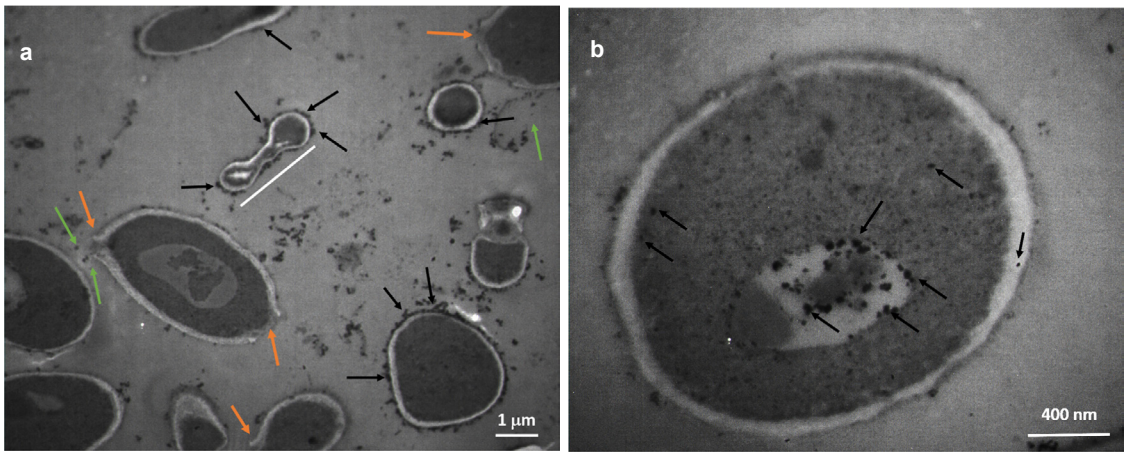

Fig. 4. Transmission electron micrographs of *Candida albicans* that have been treated with Cur@AuNPs at the concentration of 32 mg/ml. TEM images revealed Cur@AuNPs localized on the fungal cell wall (black arrows) (a), with additional particles observed disrupting the membrane and entering the cytoplasm and organelles (b). Orange arrows indicate the cell membrane/wall disruptor (a) and the green arrows indicate the shedding of cytoplasm from the rupture site (a).

of the intact fungal cell is also clear in the TEM micrographs (Figure 4b-c).

CONCLUSION

The synthesis of biocompatible gold nanoparticles with the natural phenolic compound curcumin was performed through a single-step method in which curcumin acts both as a metal ion-reducing agent and as a stabilizing and coating agent. The synthesized Cur@AuNPs demonstrated high biocompatibility, with over 90% HepG2 cell viability observed at concentrations up to 16 µg/mL. Cur@AuNPs exhibited promising antifungal activity against various *Candida* species, including drug-resistant strains, but were ineffective against *Aspergillus* species. These results highlight the potential of Cur@AuNPs as alternative agents for *Candida*-related infections.

ACKNOWLEDGMENTS

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DECLARATION OF INTEREST

None.

ETHICS DECLARATION

This is an *in vitro* study. *The Iran University of Medical Sciences Research Ethics Committee has approved under IR.IUMS.REC.1399.913 code.*

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