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ORIGINAL RESEARCH

The comparison of the effect of curcumin with nystatin on inhibition level of *Candida albicans*

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Background: Curcumin is a kind of medicinal plant, a member of the ginger family, Zingiberaceae. As the herbal medicine has been globally demanded in recent years and due to the anti-viral, anti-inflammatory, and antifungal properties of curcumin, the present study aimed to compare the inhibitory effect of curcumin with that of nystatin on *Candida albicans* growth.
Methods: In this experimental study, the antifungal effect of curcumin on *Candida albicans* was evaluated. *Candida albicans* is cultivated in Agar Sabuard medium containing chlorophenic, 10-series of curcumin extract, and one 10-series of a disc impregnated with nystatin. Inside of each plate, one disc of herbal extract, one disc of nystatin as a positive control, one disc of methanol and one empty disc as negative control were placed, after 24 hrs, the inhibitory zone diameter of the herbal extract was compared with that of positive control using Mann–Whitney.
Results: The mean of inhibitory zone diameter in nystatin and curcumin was 1.04±20.46 and 1.36±0.89 mm, respectively. Mann–Whitney test shows a significant difference between the inhibitory zone diameter of these materials ($P<0.001$).
Conclusion: The results of this study suggested that curcumin extract did not have any effect on the inhibition of *Candida albicans* in laboratory environment.
Keywords: curcumin extract, nystatin, *Candida albicans*

Introduction

Candidiasis is a rampant fungal infection in many hospitals. The patients with immunity defect, those who underwent translation, cancerous people, HIV infection, or long-term treatment with antibiotic are sensitive to fungal infections.[1] Oral candidiasis is an opportunistic infection in the mouth caused by growing the candidate species called *Candida albicans (C. albicans)*. Its risk factor includes decreasing the activity of the salivary glands, dentures, medications, high carbohydrate diet, smoking, stress, diabetes. These infections may be detrimental if the antifungal treatments are not prescribed.[2–4]

The rampant species of candidiasis include *C. albicans, C. tropicalis*، *C.glabrata*, *C.krusei*, *C. guilliermondii* of which *C. albicans* is the most common; however, *C. glabrata* and *C. krusei* cause hospital infections.[5]

Nystatin is an antifungal drug from the poly N groups created by *Streptomyces noursei, Streptomyces aureus*, and *Streptomycos* species. Nystatin is insoluble in water and soluble in dimethyl formamide. Also, it is soluble in methanol, ethanol, and propylene glycol. For the successful treatment of fungal infections and using the low dose of nystatin, it is necessary to develop the antifungal materials with less toxicity or a kind of material which can be added to a part of nystatin.[6]

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Curcumin is a kind of medicinal plant, a member of the ginger family, Zingiberaceae with a short stalk and brownish yellow. Curcumin is a food additive used widely in Southeast Asia and China. As Indian ancient texts show, curcumin was applied for elimination of inflammation, wound healing, abdominal pain. Indian physicians have recently used curcumin powder for biliary disorders, anorexiementale, cough, diabetic wounds, liver dysfunction, rheumatism, and sinusitis and in China, it was used for abdominal pain. The stained material of curcumin is a fundamental element of this plant and has anti-inflammatory effects.[7,8]

Recent studies showed that curcumin has inhibitory effects on tumor formation in living creatures and antiproliferative effects in the laboratory. Low concentration of curcumin causes anti-inflammatory and antioxidant effects and prevents lipid peroxidation, cleanses superoxide anions, and hydroxyl radicals and dilutes free radicals.[9] Curcumin contains protein (3.6%), fat (5.1%), minerals (3.5%), carbohydrates (69.4%), and moisture content (13.1%).[8] Curcumin is not soluble in water, but it is soluble in acetone, dimethyl sulfoxide, and ethanol. The yellow substance found in turmeric is called curcumin and curcumin (C21H20O6) composed of one diferuloylmethane, 1,7-bis, 1,6-heptadiene, 3,5-dione. In PH3-7 and PH+8, curcumin is the source of hydrogen and electron, respectively, and this mechanism is an explanation for its antioxidant effects.[7] Curcumin has a protective effect in the liver against the toxicity of carbon tetrachloride, D-galactosamine, peroxide, and in the pancreas, it increases the activity of lipase, amylase, trypsin, and Chymotrypsin.[8]

As the herbal medicine has been globally demanded in recent years and due to the anti-viral, anti-inflammatory, and antifungal properties of curcumin, the present study aimed to compare the inhibitory effect of curcumin with that of nystatin on Candida-albicans growth.

Materials and methods

In this experimental study, Timm 2640 standard strain of *Candida albicans* was cultured in the Saburddextor Agar medium containing chloramphenicol. Thirty gram of curcumin powder was dissolved in 100 mL pure methanol, and the solute was placed on the shaker for 48 hrs; then, the extract was passed through the Whatman Filter paper (made in England). The weight of the extracts was measured after filtration and in the next stage, the filtration solution was incubated at 37°C for 48 hrs to get a concentration of 2.5 mg/mL. Then, the empty discs are poured into the beaker, its lid was fastened and sterilized by autoclave. In sterilized condition, all 10 discs were placed in a glassware containing curcumin and covered. After 1 hr, the saturated discs were picked up by means of tongs in sterilized condition and dried up in an incubator at 40ºC for 20 mins.

In this experiment, the method of paper disk diffusion was introduced by Ahmed et al,[10] to evaluate the anticoagulant activity. In this regard, the researcher prepared a suspension of the candidate in sterilized physiology in such a way that the resulting turbidity would be equal to 0.5 MacFarlan. Then, the given suspension was picked from the sterilized swap and covered the whole surface of caplet containing Sabrouraud medium, and in each plate, curcumin extract disc, 100–unit nystatin disc as a positive control, one methanol disc and one empty disc as negative control were used. The discs were arranged at a distance of 15 mm from the edge of the plate and 25 mm from the center of the next disc. All plates were placed in incubator 37°C for 24 hrs and since then the inhibitory and non-inhibitory zone diameters were seen around the discs. Data were analyzed using SPSS 20.

The diameter of inhibitory zones of both nystatin and curcumin groups were compared using Mann–Whitney test.

Results

The mean of inhibitory zones of curcumin extract equals 1.36±0.89. No inhibitory zones around the blank disc and methanol disc as a negative control were seen (Table 1).

Discussion

Turmeric is globally well known for its unique healthy properties as a functional foodstuff. Nowadays, different studies suggest that curcumin has considerable functional properties and according to the studies of some researchers, this plant has

Table 1 The mean of the inhibitory zone of curcumin extract and negative control

	No	Mean ± SD
Curcumin (2.5 mg/mL)	10	1.36±0.89
Methanol	10	0
Blank disc	10	0

The mean of the inhibitory zone of curcumin extract was 1.04 ±20.46. No inhibitory zone around the blank disc and methanol disc as a negative control was seen (Table 2).

Table 2 The mean of the inhibitory zones of nystatin and negative control

	No	Mean ± SD
Nystatin	10	1.04±20.46
Methanol	10	0
Blank disc	10	0

The mean of the inhibitory zone in nystatin and curcumin was 1.04 ±20.46 and 1.36±0.89 mm, respectively (Table 3). Mann–Whitney test shows a significant difference between both substances in terms of the inhibitory zone ($P<0.001$). In other words, the antifungal property of curcumin extract was significantly lower than that of nystatin.

Table 3 The comparison of the inhibitory zone of curcumin with nystatin on *Candida albicans* inhibition level

	No	Mean ± SD
Nystatin	10	1.04±20.46
Curcumin (2.5 mg/mL)	10	1.36±0.89

Notes: *P*-value resulting from Mann–Whitney test.

other properties such as anti-tumor and anti-cancer activity, lowering the cholesterol level of blood and liver, reinforcing the immunity, inhibiting cardiovascular diseases, preventing the membrane damage against peroxidation, anti-inflammatory properties and minimizing rheumatic arthritis, protecting against Alzheimer's disease, and protective effects against aflatoxin B1.[11–13]

The results of this study showed that the curcumin extract (2.5 mg/mL) has a subtle effect on inhibition of *Candida-albicans* growth in the lab environment, so that the inhibitory zone in nystatin equals 1.04±20.46 mm and in curcumin extract 1.36±0.89 mm.

Ataei et al, (2007) found the dramatic effect of antifungal property of turmeric on the standard strain of *Candida-albicans* in their study.[12] Martins et al, (2009) investigated the antifungal activity of curcumin against different species of Candida and found that Brasiliensis is the most sensitive to curcumin.[14]

The results of the mentioned studies were inconsistent with those of the present study, the reason for this inconsistency can be the concentration of given curcumin. According to Ansari et al, antibacterial effect of Nano-curcumin against the infection of methicillin-resistant *Staphylococcus aureus* in pre-clinical conditions, curcumin nanoparticles were able to have antibacterial properties on the *Staphylococcus aureus* at a concentration of 6 µg/mL in vitro setting. This concentration inside the laboratory animal was 10 µg/mL. The results also showed that curcumin nanoparticles had no toxic effects on normal cells, and more than 75% of the cells treated under the highest concentrations were survived by nanoparticles. The results of this study showed that curcumin nanoparticles can be safely used to treat the infections caused by *Staphylococcus aureus*, prophylaxis of bacteremia and endocarditis.[15] In 2016, Babaie and Zamaninejad investigated the inhibitory effect of curcumin on *Candida albicans* compared to nystatin in vitro setting.[16] For this purpose, antifungal activity was used in three methods. A) Counting number of cells: in this method, the amount of *Candida albicans* was measured after required time in different concentrations of curcumin in dimethyl sulfoxide by three methods of cell counting, turbidity, and measurement of the diameter of the inhibitory zone. The results of these three methods showed that curcumin has an antifungal effect and will increase because of high concentration.[16] Another reason for the inconsistency of results is different usages of curcumin. The antimicrobial effects of turmeric and its derivatives such as curcumin, turmeric oil, and turmeric extract on microorganisms. Need to mention that this valuable drug combination, due to poor solubility in aquatic environments, shows a very low bioavailability in the culture medium, especially in vitro.[10] This could cause an error in the laboratory in the determination of the diameter of the inhibitory zone. In the current study, an alcoholic extract of methanol was used to produce this alcoholic plant. According to the Mahasneh, even alcohol has an effect on the antifungal properties, because the solubility of the effective substances of the plant varies in different solvents. Almeida et al (2008) investigated the antimicrobial effects of turmeric powder, commercial curcumin, purified curcuminoid, and turmeric oil on a multifarious growth of bacteria and mucous membranes, and reported that the inhibitory effects of turmeric oil were dramatic.[17] TSAO and YIN (2000) showed that when curcumin is combined with fluconazole, it shows the antifungal effects against systemic fungal infections such as candidiasis.[18] Sharma et al (2010) investigated the simultaneous anti-candida activity of pure polyphenol curcumin against Azole and Poly and they found that using curcumin along with these drugs increases antifungal activity.[19] In a laboratory study entitled the effect of Curcumin using photodynamic therapy on deactivation of *Candida albicans*, Dovigo et al (2013) showed that curcumin-and-LED-treated rats reduced *Candida albicans* significantly.[20] The results of these studies indicated that curcumin was used in combination with other drugs and showed better antifungal properties, indicating that curcumin with other substances represented synergistic properties. Arbabi Kalati et al, (2011) investigated the effect of herbal extracts of thyme, cloves, and cinnamon with nystatin on the inhibition level of *Candida albicans* (laboratory study).

The results showed that inhibition level of Candida in nystatin, cinnamon extract, clove extract, and thyme groups was 32.6 ±0.84, 31.3±0.82, 27.4±0.82, and 13±0.88, respectively. Thyme, Clove, and Cinnamon have antifungal effects on *Candida albicans*.[21] Alalwan et al, showed that Curcumin has the ability to be used in oral health care to amplify current preventative approaches for candidal biofilms on the denture surface.[22] Shinobu-Mesquita et al, reported that the extract of Curcuma zedoaria, had antifungal activity against yeasts of the genus Candida isolated from the oral cavity of the human immunodeficiency virus-infected patients.[23]

Because of the restricted similar studies and their different results, it is difficult to compare it with other ones and it cannot be concluded that there is absolutely no reason for different results. It can be inferred that curcumin does not have the antifungal effect and using essence in further studies is suggested. Due to the large difference in the diameter of the inhibitory zone of curcumin in comparison with nystatin, its antifungal effect was not significant at the laboratory level and apparently, it cannot be used clinically.

Conclusion

The results of this study showed that using curcumin extract with a concentration of 2.5 mg/mL in the laboratory environment does not have an effect on the inhibition of *Candida albicans* growth. To investigate the effects of synergistic curcumin, it is suggested to use its combination with other antifungal substances and determine the inhibitory effect of *Candida albicans* growth by curcumin extract with different concentrations and at different times. The antifungal effect of curcumin on *Candida albicans* should be measured with different methods (turbidity, cell counting, and diameter of the inhibitory zone) and compared.

Disclosure

The authors declare that there are no conflicts of interest in this work.

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