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ORIGINAL ARTICLE/ARTICLE ORIGINAL

Synergistic activity between *Echinophora platyloba* DC ethanolic extract and azole drugs against clinical isolates of *Candida albicans* from women suffering chronic recurrent vaginitis

Activité synergique entre un extrait éthanolique de Echinophora platyloba *DC et des dérivés azolés contre des isolats cliniques de* Candida albicans *de femmes souffrant de vaginite chronique récidivante*

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Azole agents;
Candida albicans;
Echinophora platyloba;
Recurrent vulvo-vaginal candidiasis;
Ethanolic extract;
Traditional Iranian medicine;
Traditional Persian-Iranian medicine

Summary
Objective. — *Candida albicans* is one of the main causes of vaginitis, especially in women with recurrent episodes. The appearance of drug resistant *C. albicans* and adverse effects of chemical agents have raised interest in *Echinophora platyloba* as one of four native species in Traditional Persian-Iranian medicine.
Materials and methods. — This study evaluates the antifungal activity of ethanolic extract from dried aerial parts of *E. platyloba* against 27 clinical isolates of *C. albicans* from women suffering chronic recurrent vaginitis by micro-broth dilution assay. The synergistic effect of azole drugs and *E. platyloba* ethanolic extract were also determined by disc diffusion method after determining the MIC_{90}.
Results. — The results of this study showed a potent synergistic effect of *E. platyloba* ethanolic extract and itraconazole ($P < 0.01$) and fluconazole ($P < 0.001$) but an antagonistic effect

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between *E. platyloba* ethanolic extract and clotrimazole and miconazole against clinical isolates of *C. albicans*.
Conclusion. — These results must be confirmed by clinical application and by further clinical studies.

MOTS CLÉS
Agents azolés ;
Candida albicans ;
Echinophora platyloba ;
Extrait à l'éthanol ;
Vaginite récidivante ;
Médecine traditionnelle iranienne ;
Médecine traditionnelle persane-iranienne

Résumé
Objectif. — *Candida albicans* est l'une des principales causes de vaginite, en particulier dans les formes chroniques et récidivantes. L'apparition des souches résistantes de *C. albicans* et les effets indésirables des traitements chimiques ont suscité un intérêt pour *Echinophora platyloba*, l'une des quatre espèces indigènes utilisées en médecine traditionnelle persane-iranienne.
Matériel et méthodes. — Cette étude évalue l'activité antifongique de l'extrait éthanolique de parties aériennes séchées de *E. platyloba* contre 27 isolats cliniques de *C. albicans* de femmes souffrant de vaginite chronique récurrente par un test de micro-dilution en milieu liquide. L'effet synergique entre les médicaments azolés et l'extrait éthanolique de *E. platyloba* a également été étudié par la méthode de diffusion des disques après détermination de la CMI_{90}.
Résultats. — Les résultats de cette étude ont montré un effet synergique puissant entre l'extrait éthanolique de *E. platyloba* et l'itraconazole ($p < 0{,}01$) et le fluconazole ($p < 0{,}001$), mais un effet antagoniste avec le clotrimazole et le miconazole contre les isolats cliniques de *C. albicans*.
Conclusion. — Ces résultats doivent être confirmés par l'utilisation clinique et par des études cliniques complémentaires.

Introduction

Candida sp. is the most important factor for fungal infections in humans with immune deficiency states or other predisposing factors. These infections can be different in intensity from simple mucosal colonization to lethal form of disease such as septicemia [5].

Candidiasis is one of the most common fungal infections which are made by *Candida* sp. [19] especially by *C. albicans* [7] and recurrent candidiasis causes complication for women referring to clinics [18].

Recurrent vaginitis can cause in common condition without underline disease [7,18,28] and it can lead to difficulty in treatment especially in cases with predisposing factors [7,15,27]. The main treatment for these cases is topical application of azole component such as fluconazole and clotrimazole. Tremendous use of azole drugs bears side effects and has resulted in development of resistant types of *C. albicans*. Considering both drug resistance and side effects, researchers are interested in herbal components with fewer side effects [11,23].

Historically, plants have provided a source of inspiration for novel drugs and have made large contributions to human health and well-being. Natural products have served as a major source of drugs for centuries and about 25—50% of current pharmaceuticals in use are derived from natural products [3,4]. Plants are rich in a wide variety of secondary metabolites, such as tannins, terpenoids, alkaloids and flavonoids, which have been reported to have *in vitro* antimicrobial properties [4,20,29].

Traditional Persian-Iranian Medicine (TPIM) has a major therapeutic role for thousands of years, because traditional healers have used different plants to treat different ailments in patients.

Echinophora platyloba DC is known as ''khosharuz'', ''khusharizeh'', ''tigh turagh'', ''koshandar'' and is one of four native species in TPIM [24,28]. *E. platyloba* is mainly used as flavoring agent in dairy foods and also for preventing tomato paste and pickles from molds especially in Chaharmahal and Bakhteyari Province, Iran [1].

The hypothesis is formed on the basis that *E. platyloba* acts as food preservative against microbial infections especially fungi and yeasts. During the past 10 years, several studies have been conducted on antimicrobial activity of *E. platyloba* ethanolic extract [2,12]. These studies demonstrate the antimicrobial activity of *E. platyloba* ethanolic extract against *Listeria monocytogenes*, *Serratia marscenes*, *Providencia rettgeri* [25], *Trichophyton schoenleinii*, *T. verrucusum*, *T. rubrum*, *Microsporum gypsum*, *T. mentagrophytes*, *M. canis* and *Epidermophyton floccosum* [1], and *C. albicans* [2,12].

Our literature survey shows that study on antifungal activity was performed against *C. albicans* ATCC 10231 by our team [12] and the present study is the first research evaluating the effectiveness of ethanolic extract of *E. platyloba* against clinical isolates of *C. albicans* from women suffering from chronic recurrent vaginitis and also its synergistic effect with azole drugs against these vaginal isolates.

Materials and methods

Plant materials and extraction

E. platyloba DC were collected from the south western parts of Iran (Shahr-e-kord) and were dried in shade condition. A voucher specimen of plant was deposited in the Herbarium at the Faculty of Sciences, Isfahan University, Isfahan, Iran. The aerial parts of the plant were separated, and grinded into powder using pestle. Hundred grams of prepared plant powder were extracted by 500 mL of 75% ethanol for 24 hours at room temperature in percolator. Then, the ethanolic extracts were separated and filtered by Whatman filter paper