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A Comprehensive Review of Vaginitis Phytotherapy

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Abstract: To overview phytotherapy of vaginitis in order to identify new approaches for new pharmacological treatments. All related literature databases were searched for herbal medicinal treatment in vaginitis. The search terms were plant, herb, herbal therapy, phytotherapy, vaginitis, vaginal, anti-candida, anti-bacterial and anti-trichomonas. All of the human, animal and *in vitro* studies were included. Anti-candida, anti-bacterial and anti-trichomonas effects were the key outcomes. The plants including carvacrol, 1,8-cineole, geranial, germacrene-D, limonene, linalool, menthol, terpinen-4-ol and thymol exhibited anti-candida effects. A very low concentration of geranium oil and geraniol blocked mycelial growth, but not yeast. Tea tree oil including terpinen-4-ol, α-terpinene, γ-terpinene and α-terpineol showed anti-bacterial, anti-fungal and anti-protozoal properties against trichomonas. *Allium hirtifolium* (persian shallot) comparable to metronidazole exhibited anti-trichomonas activity due to its components such as allicin, ajoene and other organosulfides. The plants having beneficial effects on vaginitis encompass essential oils that clear the pathway that future studies should be focused to standardize theses herbs.

Key words: Phytotherapy, plant, bacterial vaginosis, vulvovaginal candidosis, trichomonas vaginitis

INTRODUCTION

Recognized as a prevalent medical problem in women, vulvovaginitis causes substantial discomfort and frequent medical visits. It may occur secondary to infection, allergy, irritation, or systemic disease. The most rampant causes of vaginal discharge in premenopausal women are bacterial vaginosis, vulvovaginal candidiasis and trichomonas vaginitis (Nyirjesy *et al*., 2006).

Bacterial vaginosis: Bacterial Vaginosis (BV), the most common reason of vaginitis in childbearing-age women, happens in up to 30% of the population. It arises when there is a complex change in vaginal flora, involving reduction in the prevalence of hydrogen peroxide-producing lactobacilli and an increase in that of anaerobic micro-organisms such as *Gardnerella vaginalis*, *Prevotella*, *Peptostreptococcus* and *Bacteroides* spp. (Livengood, 2009).

Notwithstanding that about half of the patients with diagnosable BV reveal no vivid symptoms, others may have a malodorous vaginal discharge or local irritation (Srinivasan and Fredricks, 2008). A simple and useful diagnostic criteria was established, requiring the presence of three of four clinical signs for diagnosis of BV. Criteria consists of homogeneous discharge, a positive whiff-amine test, pH >4.5 and the presence of clue cells (Turovskiy *et al*., 2011). Seven days of oral metronidazole (400 mg twice daily) or, vaginal clindamycin (1 g at night) are the first line recommended therapies. Single dose therapy of 2 g metronidazole has been shown to be less effective and is considered in the second line. Side effects of oral metronidazole involve a metallic taste, nausea, peripheral neuropathy and candida infection (Menard, 2011). According to the comparative studies, oral tinidazole, a second generation nitroimidazole has equal efficacy to oral and intra-vaginal metronidazole, tabletes and intra-vaginal clindamycin cream. Besides, tinidazole reveals less side effects. Overall, it conspicuously has better gastrointestinal tolerability and less metallic taste which are often reported in poor conformity to metronidazole therapy (Armstrong and Wilson, 2010).

Vulvovaginal candidosis: Vulvovaginal candidosis (VVC), the second most common reason of vaginitis, is recognized in up to 40% of women with vaginal complaints in the primary care setting (Ilkit and Guzel, 2011). About 70% of women underwent the infection-

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caused by *Candida* spp. at least once through their lives. Moreover, 40-50% of women will experience a reappearance (Corsello *et al*., 2003). The symptoms of vulvovaginal candidiasis encompass pruritus (itching), soreness, irritation, vulvar burning change in vaginal discharge and dyspareunia. Physical investigation often unveils discharge considered as thick, adherent and "cottage cheese-like". In contrast, the discharge can be thin and loose and even resembling to the other types of vaginitis. The vaginal pH is typically 4 to 4. 5 and different in comparison to trichomoniasis or bacterial vaginosis (where the pH is heightened). Clinical diagnosis includes microscopic examination of the vaginal secretions for the purpose of diagnosis and separation of vaginal infections. Butoconazole, clotrimazole, miconazole, econazole, fenticonazole, sertaconazole, ticonazol, terconazole are diverse effective topical azole agents accessible in a variety of formulations for VVC treatment. In general, topical azoles are notably safe and well tolerated notwithstanding that subjects may complain of a burning sense. Besides, cure rates for topical azoles range from 80 to 90% and for oral azole agents, fluconazole, itraconazole and ketoconazole have even higher cure rates. In contrast, oral azoles can cause systemic toxicity dramatically with ketoconazole (Sobel, 2007).

Tricomonas vaginitis: Trichomoniasis is known as the most dominant sexually transmitted disease (Harp and Chowdhury, 2011). Tricomonas vaginalis is the causative agent of trichomonasis accounting for about 4 to 35% of vaginitis diagnosed in symptomatic women (Anderson *et al*., 2004). It varies from an asymptomatic to the critical inflammatory disease. Clinical signs and symptoms encompass vaginal discharge green to brown color, foul odor, edema or erythema and colpitis macularis (Harp and Chowdhury, 2011; Sood and Kapil, 2008). Clinical features of trichomonas vaginitis are not sensitive or specific ample to allow a diagnosis of trichomonal infection based on signs and symptoms alone. Hence, precise, reliable, accessible and economical laboratory diagnostic tests enact a fundamental role in the identification of *T. vaginalis* (Harp and Chowdhury, 2011). Currently metronidazole and the other 5-nitroimidazoles (tinidazole, ornidazole and secnidazole) provide curative therapy of trichomoniasis and remain the basis of therapy (a single oral dose of 2 g of metronidazole or 500 mg twice a day for seven days, or a single dose of 2 g of tinidazole), but metronidazole-resistance (MzR) against *T. vaginalis*, allergic reactions and failure to remedy the infection with two consecutive courses are its critical problems (Lofmark *et al*., 2010; Harp and Chowdhury, 2011).

Herbal medicine: Since long time ago, medicinal plants have been used for the remedy of enormous infectious diseases without any scientific evidence. At present, there is more emphasis on demonstrating the scientific evidence and rationalization of the use of these preparations. Immense research is in progress to identify plants and their active compounds against vaginitis pathogens for the purpose that they may provide an effective approach for treatment of vaginitis (Vermani and Garg, 2002). In the contemporary review, the plants exhibited beneficial effects on the treatment of vaginitis including BV, VVC and trichomonas vaginitis have been discussed.

METHODS

All electronic databases were searched for studies which investigated medicinal plants and their active compounds having effects on vaginitis. The search terms were plant, herb, herbal therapy, phytotherapy, vaginitis, vaginal, anti-candida, anti-bacterial and anti-trichomonas. Besides, the reference lists of articles were reviewed for extra pertinent studies.

Study selection: All of the human, animal and *in vitro* studies with key outcomes of anti-candida, anti-bacterial and anti-trichomonas activities were followed. Data were extracted according to study design, medicinal plant, family name, part of use, active compound and effects (Table 1-3).

RESULTS

Vulvovaginal candidosis: Ethanol extracts of *Acalypha indica* L., *Allium cepa* var. *aggregatum* L., *A. cepa* var. *cepa* L., *A. sativum* L., *A. schoenoprasum* L., *Azadirachta indica* A. Juss, *Camellia sinensis* (L) O. Ktze, *Capsicum annum* L., *Cassia alata* L., *C. stula* L., *C. occidentalis* L., *Coffea arabica* L., *Curcuma longa* L., *Lawsonia inermis* L., *Ocimum sanctum* L., *Piper betle* L. and *Psoralea corylifolia* L. manifested more anti-candida activity than others and it was observed that their active principle is more soluble in a non-polar solvent (Vaijayanthimala *et al*., 2000). Essential oils of *Aloysia triphylla, Anthemis nobilis, Cymbopogon martini, Cymbopogon winterianus, Cyperus articulatus, C. rotundus, Lippia alba, Mentha arvensis, M. piperita, M.* sp., *Mikania glomerata, Stachys byzantina* and *Solidago chilensis* had anti-candida activity. Chemical analyses unfolded the presence of compounds with eminent anti-microbial activity, including 1,8-cineole, geranial, germacrene-D, limonene, linalool and menthol

Table 1: *In vitro* studies considering the plants with beneficial effects on vaginitis

Reference	Effect	Method	Part of plant± active compound	Family	Plant
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Euphorbiaceae	*Acalypha indica* L.
Taran *et al.* (2006)	Anti-trichomonas activity	Serial dilutions and culture medium	Hydroalcoholic and dichlromethanic extract	Alliaceae	*Allium hirtifolium*
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of clove	Liliaceae	*Allium sativum* L.
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of clove	Liliaceae	*Allium schoenoprasum* L.
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of bulb	Liliaceae	*Allium cepa* var. *aggregatum* L.
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of bulb	Liliaceae	*Allium cepa* var. *cepa* L.
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Verbenaceae	*Aloysia triphylla*
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Compositae (Asteraceae)	*Anthemis nobilis*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test (Umbelliferae)	Essential oil	Apiaceae	*Anethum graveolens*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Compositae	*Artemisia sieberi*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Compositae	*Arthemesia dracunculus*
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf and seed	Meliaceae	*Azadirachta indica* A. Juss
Soffar *et al.* (2001)	Anti-trichomonas activity	Media culture	Berberine (quaternary alkaloid)	Berberidaceae	*Berberis aristata*
Samochowiec *et al.* (1979)	Anti-trichomonas activity	Media culture	Alcoholic extract	Asteraceae	*Calendula officinalis*
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Theaceae	*Camellia sinensis* (L) O. Ktze
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of Fruit (dry and green)	Solanaceae	*Capsicum annum* L.
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Caesalpiniaceae	*Cassia alata* L.
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Caesalpiniaceae	*Cassia fistula* L.
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Caesalpiniaceae	*Cassia occidentalis* L.
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of seed	Rubiaceae	*Coffea arabica* L.
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Rutaceae	*Citrus aurantifolia*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil		*Communis hominis*
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of rhizome	Zingiberaceae	*Curcuma longa* L.
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Poaceae	*Cymbopogon martini*
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Poaceae	*Cymbopogon winterianus*
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil		*Cyperus articulates*
Samochowiec *et al.* (1979)	Anti-trichomonas activity	Media culture	Alcoholic extract	Composite	*Echinacea angustifolia*
Mahdi *et al.* (2006)	Anti-trichomonas activity	Media culture	Extract	Myrtaceae	*Eucalyptus comaldensis*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activity	Punched-Whole Test and Paper-Disc Test	Essential oil	Myrtaceae	*Eucalyptus globules*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Apiaceae	*Foeniculum vulgare*
Lee *et al.* (2009)	No inhibitory effect on *C. albicans* strains	Broth susceptibility	Liquiritigenin (LG) and liquiritin (LQ), licorice flavonoid components	Leguminosae	*Glycyrrhiza uralensis*
Cafarchia *et al.* (1999)	Anti-candida activity	Media culture	Extracts of flowers and leaves	Asteraceae	*Inula viscose*
D'Auria *et al.* (2005)	Fungistatic and fungicidal activity against *C. albicans* strains	Media culture	Essential oil	Lamiaceae	*Lavandula angustifolia*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Lavandula estoechas*
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Lythraceae	*Lawsonia inermis* L.
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil		*Lippia alba*
Mondello *et al.* (2006)	Anti-candida activity	Modification of the CLSI (formerly NCCLS) reference M27-A2 broth micro-dilution	Essential oil	Myrtaceae	*Melaleuca alternifolia* Cheel
Hammer *et al.* (1999)	Anti-bacterial activity	Media culture	Essential oil	Myrtaceae	*Melaleuca alternifolia* Cheel
Vila and Canigueral (2006)	Anti-bacterial, anti-fungal and anti-protozoa against trichomonas activities		Essential oil	Myrtaceae	*Melaleuca alternifolia* Cheel
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Lamiaceae	*Mentha arvensis*
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Lamiaceae	*Mentha piperita*
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Lamiaceae	*Mentha* sp.
Bayat *et al.* (2008)	Anti-candida activity and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Mentha spicata*
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Asteraceae	*Mikania glomerata*
Mahdi *et al.* (2006)	Inhibitory effect on *T. vaginalis*	Media culture	Extract	Myrtaceae	*Myrtus communis*
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Labiatae	*Ocimum sanctum* L.
	Anti-candida activity	Media culture	Essential oil (thymol and cavacrol)	Lamiaceae	*Origanum vulgare* L.
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Piperaceae	*Piper betle* L.
Maruyama *et al.* (2008)	Inhibited mycelial growth *C. albicans*	Colorimetric assay	Bourbon Geranium Oil	Geraniaceae	*Pelargonium asperum*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Geraniaceae	*Pelargonium roseum*
Vaijayanthimala *et al.* (2000)	Anti-candida activity	Two-fold serial dilution technique	Water and ethanol extracts of seed	Papilionaceae	*Psoralea corylifolia* L.

Table 1: Continued

Reference	Effect	Method	Part of plant± active compound	Family	Plant
El-Sherbini *et al.* (2009)	Anti-trichomonas activity	Fresh diamond media	Extract	Punicaceae	*Punica granatum*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Rosmarinus officinalis*
Tsuzuki *et al.* (2007)	Anti-candida activity	Broth microdilution assay	Extracts of dried pericarp of fruit and saponin	Sapindaceae	*Sapindus saponaria* L.
Jirovetz *et al.* (2007)	Anti-candida activity	Media culture	Essential oil (thymol and cavacrol)	Lamiaceae	*Satureja montana* L.
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Saturella hortensis*
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Asteraceae	*Solidago chilensis*
Duarte *et al.* (2005)	Anti-candida activity	Media culture	Essential oil	Lamiaceae	*Stachys byzantine*
Zhang *et al.* (2005)	Anti-candida activity	Microbroth dilution assay	Steroid saponins	Zygophyllaceae	*Tribulus terrestris* L.
Hufford *et al.* (1988)	Anti-candida activity	Agar well-diffusion assay	Ethanol extracts of the rhizomes and above ground portion	Liliaceae	*Trillium grandiflorum* (Michx.) salibs
Jirovetz *et al.* (2007)	Anti-candida activity	Media culture	Essential oils (thymol and cavacrol)	Lamiaceae	*Thymus vulgaris*
Bayat *et al.* (2008)	Anti-candida and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Zataria multiflora*
Stevens *et al.* (2002)	Anti-candida activity	Broth microdilution assay	Extract medium	Poaceae	*Zea mays*

Table 2: Animal studies considering the plants with beneficial effects on vaginitis

Reference	Effect	Model	Animal	Part of plant±active compound	Family	Plant
Lee *et al.* (2009)	Anti-candida activity of LG LG protects mice against disseminated candidiasis by the CD4+ T helper 1 immune response	Murine model of disseminated candidiasis Pretreated before injection LG with anti-CD4+ (cluster of differentiation 4) antibody, mice given CD4+ T cells that were pre-treated with LG	Mouse	LG and LQ LG	Leguminosae	*Glycyrrhiza uralensis*
Mondello *et al.* (2006)	Anti-candida activity	Rat vaginal infection	Rat	Essential oil	Myrtaceae	*Melaleuca alternifolia* Cheel
Kassaify *et al.* (2008)	Anti-candida activity		Hamsters	essential oil	Lamiaceae	*Origanum syriacum*
Maruyama *et al.* (2008)	Combined with vaginal washing decreased cell number of C. albicans	Estradiol-treated mice	Mouse	Bourbon Geranium Oil	Geraniaceae	*Pelargonium asperum*
Nogal-Ruiz *et al.* (2003)	Decreased Trichomonas pathogenicity	Infected by the intra-peritoneal route	Mouse	Extract	Polypodiaceae	*Polypodium leukotomas*
Hwang-Huei (1993)	Anti-trichomonas activity	Subcutaneous abscesses	Mouse	Emodin of root and rhizome	Polygonaceae	*Rheum palmatum* L.
Zhang *et al.* (2005)	Anti-candida activity	Oestrogen-dependent rat vaginitis	Rat	Steroid saponins	Zygophyllaceae	*Tribulus terrestris* L.
Stevens *et al.* (2002)	Anti-candida activity	Murine model	Mouse	Zeamatin of corn	Poaceae	*Zea mays*

Table 3: Human studies considering the plants with beneficial effects on vaginitis

Reference	Effect	Duration of treatment	Comparator	No. of patients	Study design	Part of plant± active compound	Family	Plant
El-Sherbini *et al.* (2009)	Anti-trichomonas activity	6 to 8 successive days	Metronidazole and tinidazole	33		Extract	Burseraceae	*Commiphora molmol*
Sharma *et al.* (2009)	Anti-trichomonas, anti-candida and anti-bacterial activites	7 days	Associated symptoms and signs before and treatment	141	Phase II clinical trial	Aqueous alcoholic extract of leaves, aqueous ethanolic extract of the air-dried pericarp of fruits and *M. citrata* oil	Meliaceae, Sapindaceae and Lamiaceae (Labiatae)	Praneem polyherbal tablets (*Azadirachta indica, Sapindus mukoross* and *Mentha citrate*)
Herrera-Arellano *et al.* (2009)	Anti-candida activity	7 days	Conventional treatments	101	A randomized, double-blind and controlled clinical trial	SC-2 (spirostanic saponins) of methanol extract	Solanaceae	*Solanum chrysotrichum*
Giron *et al.* (1988)	Anti-candida activity	15 days	Nystatin	100	Controlled clinical trial	Extract	Solanaceae	*Solanum nigrescens*
Simbar *et al.* (2008)	Anti-bacterial activity	7 days	Conventional treatments	90	Randomized clinical trial	Vaginal cream (Loucorex) including essential oil	Lamiaceae	*Zataria multiflora*

(Duarte *et al.*, 2005). Essential oils of *Pelargonium roseum*, *Rosmarinus officinalis*, *Artemisia sieberi*, *Communis hominis*, *Anethum graveolens*, *Citrus aurantifolia*, *Saturella hortensis*, *Foeniculum vulgare*, *M. spicata*, *Z. multiflora*, *Arthemesia dracunculus*, *Eucalyptus globulus* and *Lavandula estoechas* exhibited inhibitory effect on *C. albicans* and *G. vaginalis*, whereas *Z. multiflora* showed the most activity (Bayat *et al.*, 2008). Liquiritigenin (LG) and liquiritin (LQ), of root of *Glycyrrhiza uralensi* deterred growth of *C. albicans* yeast cells on *in vitro*. Moreover, LG sheltered mice from disseminated candidiasis by the CD4+ (cluster of differentiation 4) Th (helper) 1 immune response (Lee *et al.*, 2009). The flowers extract of *Inula viscosa* uncovered anti-fungal activity against dermatophytes and candida species. These results may be revalent to the diverse flavonoids and different flavonoid concentrations in samples (Cafarchia *et al.*, 1999). Essential oil of *Lavandula angustifolia* showed both fungistatic and fungicidal activity against *C. albicans* strains (D'Auria *et al.*, 2005). *Melaleuca alternifolia* Cheel essential oils i.e., 1,8-cineole and terpinen-4-ol had anti-candida properties. Furthermore, terpinen-4-ol could control *C. albicans* vaginal infections in rat (Mondello *et al.*, 2006). Essential oils of *Origanum vulgare* L., *Satureja montana* L. and *Thymus vulgaris* L.

which are rich in thymol and carvacrol shed in anti-fungal activity against clinical isolates of pathogenic candida species (Jirovetz *et al*., 2007). A very low concentration of geranium oil and geraniol impeded mycelial growth, but not yeast growth on *in vitro*. Hence, that vaginal application of geranium oil or its main component, geraniol, would block candida cell growing in the vagina and its local inflammation since combine with vaginal washing is estimated (Maruyama *et al*., 2008). The extract of *Sapindus saponaria* L. showed anti-candida action against all isolates of yeasts *C. albicans* and *C. non-albicans* and the saponins isolated unveiled vigorous activity against C. parapsilosis (Tsuzuki *et al*., 2007). TTS-12 and TTS-15 (two saponins isolated of *Tribulus terrestris* L.) were very efficient against numerous pathogenic candida species and *Cryptococcus neoformans* on *in vitro*. Moreover, TTS-12 divulged imperative anti-fungal action on *in vitro* and *in vivo*, weakening the virulence of *C. albicans* and killing fungi through destroying the cell membrane (Zhang *et al*., 2005). In provided ethanol extracts of the rhizomes, aboveground portion of *Trillium grandiflorum* composed of the saponin glycosides 1 and 3 as the active components revealed paramount anti-fungal action (Hufford *et al*., 1988). While Zeamatin, a natural plant-derived anti-fungal protein plenteously born in corn, was ineffective alone, it reinforced the efficacy of both nikkomycin Z, a chitin synthase inhibitor and clotrimazole when they were given in combination (Stevens *et al*., 2002). The essential oil of *Origanum syriacum* can surpass the marketable douche materials in elimination and reducing the colonization and adaptability of the *C. albicans* (Kassaify *et al*., 2008). Sc-hmp (spirostanic saponins) had as clinical effectiveness as ketoconazole, but with lower percentages of mycological obliteration (Herrera-Arellano *et al*., 2009). The extract of *Solanum nigrescens* shed in anti-candida activity as the same as nystatin in patients (Giron *et al*., 1988).

Bacterial vaginosis: Lactobacilli and other organisms related to BV were susceptive to trichomonas tree oil, an essential oil from the leaves and twigs of *M. alternifolia,* on *in vitro* (Hammer *et al*., 1999). In another study, tea tree oil including terpinen-4-ol, α-terpinene, γ-terpinene and α-terpineol showed anti-bacterial, anti-fungal and anti-protozoal properties against trichomonas (Vila and Canigueral, 2006). Therapeutic effects of *Zataria multiflora* vaginal cream were parallel to metronidazole vaginal gel on BV in patients (Simbar *et al*., 2008).

Trichomonasis vaginitis: *Allium hirtifolium* (persian shallot) comparable to metronidazole showed anti-trichomonas activity, which it can be because of its components like allicin, ajoene and other organosulfides (Taran *et al*., 2006). Berberine derived from *Berberis aristata* on T. vaginalis *in vitro* showed potency comparable to metronidazole. On the other hand, it has the advantage of being more safe and probable replacement in metronidazole-resistant cases (Soffar *et al*., 2001). The alcoholic extracts of *Calendula officinalis* and *Echinacea angustifolia* revealed activity against *T. vaginalis* on *in vitro* (Samochowiec *et al*., 1979). The extracts of *Myrtus communis* and *Eucalyptus camaldulensis* caused death of *T. vaginalis* (Mahdi *et al*., 2006). The extract of *Punica granatum* (*in vitro*) and *Commiphora molmol* (human study) decreased the pathogenicity of *T. vaginalis* (El-Sherbini *et al*., 2009). Emodin of the root and rhizome of *Rheum palmatum L. manifested* an inhibitory effect on *T. vaginalis* in mice (Hwang-Huei, 1993). Anapsos (*Polypodium leukotomas* extract) was effective against trichomonas pathogenicity as compared to those of the untreated control group (Nogal-Ruiz *et al*., 2003). In a study, the cure rate was 100% for *T. vaginalis*, 77% for *C. albicans* and 68% for BV in patient treated with PPT (Praneem polyherbal tablets) (Sharma *et al*., 2009).

DISCUSSION

In the present paper, we studied the plants having effects on vaginitis owing to three mechanisms encompassing anti-candida, anti-bacterial and anti-trichomonas activities. These plants noticeably involve essential oils showing anti-candida, in some cases anti-bacterial and even anti-trichomonas properties. For instance, carvacrol, 1,8-cineole, geranial, germacrene-D, limonene, linalool, menthol, terpinen-4-ol, thymol had anti-candida action (Duarte *et al*., 2005; Mondello *et al*., 2006; Jirovetz *et al*., 2007). A very low concentration of geranium oil and geraniol obstructed mycelial growth, but not yeast growth on *in vitro* (Maruyama *et al*., 2008). Tea tree oil including terpinen-4-ol, α-terpinene, γ-terpinene and α-terpineol exhibited anti-bacterial, anti-fungal and anti-protozoal properties against trichomonas (Vila and Canigueral, 2006). *A. hirtifolium* (persian shallot) comparable to metronidazole showed anti-trichomonas activity, which can be on account of some anti-trichomonas components encompassing allicin, ajoene and other organosulfides (Taran *et al*., 2006).

Vaginitis is a commonplace medical problem in women (Nyirjesy *et al*., 2006). Hence, there is an essential need to find new agents having more efficacy and safety rather than current ones. To use natural remedies dates back thousands of years. It is also calculated that there

are 250,000-500,000 species of plants on Earth (Borris, 1996) that it can be a great hope to discover new pharmacological agents with more efficiency and less or no undesirable side effects.

To sum up, that essential oils have anti-candida, anti-bacterial and anti-trichomonas activities can be a new approach for the future researches in addition to the screening, standardization and combination therapy of the plants being efficient in treatment of vaginitis.

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