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Review Article

HERBAL REMEDIES USED IN TREATMENT OF BACTERIAL VAGINITIS: A MINI-REVIEW

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Abstract:

Herbal remedies are globally accepted for treatment of several diseases including infections. Certain herbs possess traditional evidence to be used in vaginitis, especially bacterial vaginitis. This paper was designed to gather various data on the possible effectiveness of herbal remedies on different types of vaginitis particularly bacterial vaginitis. By means of major electronic databases, all relevant studies on vaginitis and herbal remedies including research articles, review articles and conference papers published from 1962 to 2016 were used. The terms used in the search were "Herbal remedies", "vaginitis", "bacterial vaginitis", "herbal treatment of vaginitis", "types or varieties of vaginitis", "trichomoniasis", "yeast infections", and "candidiasis". This review exposes that vaginitis is a global problem that affects women mainly in reproductive ages. Bacterial vaginitis occurs more frequently than the other forms of vaginitis, though two types can occur concurrently. Recurrence has been documented for all types of vaginitis. Several studies have been carried out to validate the traditional claim of herbal uses, which most of them have been shown to be effective against the three forms of infectious vaginitis. They have shown efficiency similar to metronidazole on both symptoms and recurrence, with a healthier side effect profile. Tea tree oil, Zataria multiflora, garlic, as well as Persian shallots have proven efficacy in vitro studies against wide the range of organisms implicated in these diseases. Non-infectious vaginitis can also be treated with phytoestrogens from plants such as Ribes nigrum. The use of herbal remedies in infectious vaginitis has been shown to be effective. Therefore, the toxicity profile and therapeutic doses of these plants should be determined to gain better effectiveness.

Keywords: Herbal Remedies, Vaginitis, Bacterial Vaginitis.

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INTRODUCTION:

Herbal medicines (HM) have been and are still in use by developing countries for treatment of several ailments such as cough, cancer, bacterial and fungal infections including vaginitis [1]. Folkloric uses of herbs in the treatment of disease have been practiced since ancient times. Different countries have their specific treatment protocols mainly based on their religious or traditional beliefs and cultures. According to World Health Organization (WHO) over 70% of the world population depend on HM for their primary treatments, since they are readily accessible and available in most cases. Literatures have shown that the use of HM has been in practice as long as 60,000 years ago in Iraq [2]. China also has ancient and current history of traditional medicines [3]. The United States Food and Drug Administration (FDA) has approved about 1200 new drugs from 1950 to date [4]. This has given HM large popularity due to the lack of modern therapy used in the treatment of certain ailments. Currently, modern technologies are utilized by pharmaceutical companies to evaluate the efficacy of certain herbals as potential source of new drug candidates [5, 6]. Some plant species have been reported as potent agents against infections especially culinary herbs as well as several spices such as garlic, ginger, cinnamon, and thyme [7]. Some of these showed a broad activity against several organisms (bacteria, parasites, and viruses), and are usually associated with little side effects but not microbial resistance. Extracts and essential oils of some species such as dill, coriander, cilantro, and eucalyptus, have also been reported to exhibit antimicrobial properties [8]. Vaginitis is an inflammation of the vagina that may be triggered by bacteria, fungi, or parasites characterized by irritation, itching, vaginal discharge with odor, and a burning sensation [9]. Most common types include; bacterial vaginitis, trichomoniasis, and *Vulvovaginal candidiasis*. Bacterial vaginitis is caused by bacteria such as *Gardnerella vaginalis*, *Mycoplasma hominis* and anaerobic bacteria, while *V. candidiasis* and *Trichomonas vaginalis* are caused by fungi and parasites respectively [10]. The *in vitro* potential of some plant species like tea tree oil and garlic has been reported in the treatment of vaginitis especially bacterial and fungal forms [11]. The aim of this article was to profile the evidences and possible effectiveness of a variety of herbal remedies on different types of vaginitis especially bacterial vaginitis.

MATERIALS AND METHODS:

Major electronic databases such as Google scholar, Scopus, PubMed, and EMBASE were used to collect various publications on vaginitis and herbal remedies.

Research and review articles, as well as conference papers published from 1962 to 2016 were studied. The terms used in the search were “Herbal medicines”, “vaginitis”, “bacterial vaginitis”, “*V. candidiasis*”, “herbal treatment of vaginitis”, “herbal treatment of bacterial vaginitis”, “types or varieties of vaginitis”, “trichomoniasis”, “yeast infections”, and “candidiasis”. Data were selected based on the studies conducted *in vitro and in vivo*.

Review Process: Bibliographic search for the current review was conducted on PubMed, Scopus and Google scholar for articles on spontaneous DM in small and wild animals. The term included “DM in canine”, “DM in feline”, “Amyloidosis”, “Pancreatitis”, “Classification of DM in small animals”, “spontaneous diabetes in domestic animals”, “Spontaneous amyloidosis in wild animals”, “Glucose intolerance”, “Hyperinsulinemia in animals” and “Insulin resistance in laboratory animals”.

Vaginitis:

The vagina is usually acidic and contains normal flora of organisms such as bacteria, which are served as a protective cover against overgrowth of normal flora or invasion from external organisms. Certain conditions such as menstrual cycle, pregnancy, use of cosmetic/hygienic agents (shampoos or shaving creams) can interfere with the acidic environment or normal flora and can cause severe inflammation of vagina and also discharge [12]. Vaginitis is an inflammation of the vagina that can be caused by bacterial, fungal, viral infections, or chemical and physical irritation [9]. Women may have recurrent episodes of vaginitis from use of certain contraceptive methods especially tubal ligation, multiple sex partners, as well as improper hygiene [13]. There are three major types of vaginitis; bacterial (most common), candidial, and trichomonal [10].

Bacterial Vaginitis:

Bacterial vaginitis (BV) is an inflammation of the vagina caused by several bacterial species including *G. vaginalis* and *Mobiluncus curtisii* [10]. It is known to affect high number of women, and is usually associated with other complications such as, pelvic inflammatory disease, preterm labor, low birth weight among others [14, 15]. Women with BV may remain asymptomatic except for the vaginal discharge accompanied by foul odor [16]. BV may result from imbalance in the normal vaginal flora, due to the loss of lactobacilli from sexual intercourse with condoms, use of certain antibiotics, or excessive growth of anaerobic bacteria [17]. BV may reoccur in about 60% of women from one to six months [18].

Symptoms and Diagnosis:

Most cases of BV are asymptomatic which majorly affect women of reproductive ages, however itching, burning sensation, and vaginal discharge may occur [9]. Due to the presence of bacterial species indicated in BV in patients not diagnosed with the disease, cultivation of bacteria from vaginal fluid has not been considered an effective way of diagnosis [19]. According to the Nugent score, BV can be diagnosed from Gram staining of vaginal fluid or discharge to differentiate between normal flora and gram negative morphotypes [20]. Another widely used method in BV diagnosis is that by Amsel et al, where a criteria must be fulfilled to ascertain the occurrence of the disease [21]. A slight modification has been made in addition to these criteria by Amsel; where three grades were defined as normal (I), intermediate (II), and consistent with BV (III) [22]. The analysis was carried out qualitatively on Gram stained smears from vaginal fluid. New grades added 0 and IV are epithelial cells with no bacteria and Gram positive cocci only which fell into normal category. Another method made BV diagnosis from urine sample possible by the use of fluorescence in situ hybridization (FISH) based on the analysis of desquamated vaginal epithelial cells found in urine sediment [23]. BV can also be diagnosed using

molecular methods such as real time polymerase chain reaction (RT-PCR) method to detect and quantify target organisms such as lactobacilli and other species [19].

Complications of BV:

BV has been associated with several complications or is known to increase the risk of acquiring certain disease including sexually transmitted diseases (STDs) such as gonorrhea, chlamydial infection, trichomoniasis and human immunodeficiency virus (HIV), as well as reproductive complications [25, 27](Table 1). Different studies have indicated the association between BV and pregnancy complications such as preterm labor and delivery, even miscarriage especially in young women [15, 26]. It has also been related to the reproductive problems such as infertility and pelvic inflammatory diseases, post-operative infection, cervicitis, cervical intraepithelial neoplasia as well as increased risk of STDs [24, 27]. A causative agent of BV (*Mageibacillus indolicus*) found in the endocervix was reported to increase the clinical manifestation of cervicitis [28]. Rather, BV has been strongly allied with female infertility, and may be a reason of unexplained infertility usually underestimated [29].

Table 1: Risks and Complications associated with BV

Risk/Complications	References
Sexually transmitted diseases (Chlamydia, Gonorrhea, HIV)	(25,27)
Miscarriage, preterm labor and delivery	(26,27)
Pelvic inflammatory diseases	(24,27)
Cervicitis	(27,28)
Infertility	(24,29)

Prevention:

Presumptive treatments (metronidazole and miconazole) have been reported to reduce the incidence of vaginal infections including BV and complications of STDs associated with BV [30]. Frequent consumption of probiotics has also been shown to reduce the occurrence and reoccurrence of BV by normalizing the vaginal flora and pH [31]. These products can be taken orally (metronidazole) or administered directly to the vagina (Lactobacilli impregnated vaginal tampons) [32]. Prevention and

reduction in the occurrence of BV will consequently reduce the development of its related complications and risks.

Yeast Infections (Candidiasis):

Candida (C) species (*C. albicans*) are the major cause of yeast infection and are present in the normal vaginal flora though in small numbers. Conditions that can alter their quantities might result in infection [33]. The risk of developing vaginitis due to the C can be increased by the presence of few or combination of the following; disease (diabetes),

condition (pregnancy), agents (antibiotics and intrauterine device), weak body immunity, and use of clothing (underwear) that do not allow free flow of air [34,35]. Symptoms may include vulva swelling and redness, itching and burning sensation; which may also be accompanied with thick, whitish vaginal discharge. Apart from the vagina, C can also be found in human mouth and digestive tract [36]. Yeast infection has been a burden on especially developing countries which mostly affect women within the reproductive ages [35]. Similar to BV, candidiasis can also reoccur in both males and females as a result of masturbation with saliva and in lower ages at first intercourse [37, 38]. Yeast infections can also result from non-candida species such as *C. glabrata*, *C. krusei*, *C. tropicalis* and others, which are mainly associated with therapeutic failure or resistance [38].

Symptoms and Diagnosis:

Common symptoms associated with yeast infection such as painful urination, vulva swelling, itching, and vaginal discharge may also aid in diagnosis [39]. Confirmatory tests for diagnosis are usually conducted in patients with symptoms. This include a wet mount, which is consist of 10% potassium hydroxide (KOH) and saline used to detect the presence of yeast and mycelia; and vaginal cultures to detect different causative organisms [35]. CHROMagar is another method capable of differentiating C and non-candida species [40]. Other advanced molecular methods that are considered to be more sensitive and specific are also available for diagnosis such as polymerase chain reaction (PCR) and random amplification polymorphism DNA (RAPD)[41]. Candidiasis may also increase the risk of preterm birth [42]. Recurrent vaginal candidiasis can be prevented by the use of probiotics, and also clothing (cotton)[43].

Trichomoniasis:

This form of vaginitis is caused by a protozoan *Trichomonas vaginalis*, and the common mode of transmitting the disease is via sexual intercourse. Similar to BV, it is associated with infertility, pregnancy complications, post-operative infections, and increased risk of other STDs [44]. Symptoms are usually vaginal irritation and redness, yellowish vaginal discharge, as well as elevated pH [45]. Certain factors may increase the risk of developing Trichomoniasis such as multiple sex partners, current or previous STDs, as well as unprotected sex with infected partners [46]. This disease has become a public health concern especially in the US where it is said to affect over 5 million women, mostly sexually active [47]. It can also occur in men mostly without symptoms. Infected men may experience painful urination and urethral discharge [48]. The main method for diagnosis of Trichomoniasis is the wet

mount method performed on vaginal discharge [45]. Trichomoniasis can occur concurrently with BV or candidiasis [49].

Symptoms and Diagnosis:

Trichomoniasis may occur with or without symptoms in humans which may vary from vaginal discharge, itching, irritation, swelling, redness, as well as painful urination [45, 50]. Specimens used in diagnosis are obtained from vaginal discharge, urethral secretions or urine samples. Wet mount microscopy is the frequent method used in diagnosing Trichomoniasis; however it cannot be used in infected men due to the poor sensitivity [51]. Culture techniques can last for 3 – 5 days, however limitation may be bacterial contamination [52]. Nucleic acid testing or PCR has been used in diagnosis, but is associated with less sensitivity and false positive results [53]. Antibody based technique has been unable to differentiate between current and previous infection [54]. Others are susceptibility testing, which determine resistant strains of *T. vaginalis*, and pH evaluation to differentiate Trichomoniasis from candidiasis [54].

Non – Infectious Vaginitis:

This is a type of vaginal inflammation caused by agents other than bacteria, fungus, or protozoa. This can happen by utilization of substances that can irritate the cervix such as spermicides, perfumes, soaps, certain antifungal drugs and creams, as well as condoms [55]. However, symptoms are similar to other types of vaginitis, which may include itching, irritation, burning sensation, pain during intercourse, and vaginal discharge. Atrophic vaginitis is caused by very low hormonal (estrogen) levels that may appear due to the exclusion of ovaries, radiation and menopause [56]. Diagnosis of this type of vaginitis can be based on the signs and symptoms. Vaginal pH dictator is used to determine any alteration in the vaginal pH; additionally, a pelvic exam can be carried out to detect the levels of vaginal dryness, redness, and tissue thinning [57].

Herbal Remedies:

Herbs have been used to treat several ailments in different category of people ranging from infants, children, men, and women. These remedies like conventional drugs are also controlled and assessed for safety, quality, and efficacy [58]. Diseases such as diabetes, neurological disorders, fertility, gastro-intestinal system disorders, and several others have documented history of successful therapy with herbal preparations [59-61]. About 53,000 species of herbal medicines are available, but due to their exaggerated use, some are facing the threat of extinction [62]. Some medical practitioners recommend herbal medicines or complementary and alternative medicines for the effective treatment of certain

diseases [63]. As stated in the introduction, several herbal remedies are available for treatment of infections ranging from bacterial, fungal, parasitic, and viral. The efficacy of some plant extracts and essential oils has been evaluated [8]. Sexually transmitted diseases are of public concern due to its contagious nature and high cost of treatment. Researches are going on these herbs to establish scientific evidence and determine the active principle responsible for the antimicrobial effects [64]. The use of *Smilax officinalis* herb in the treatment of STDs in Europe, has dated back to six centuries ago [65], where it was used in the treatment of syphilis. Best remedies available for long term prevention of infections include cranberry, mannose, and probiotics, while berberine and uva ursi can be effective at first sign of infective or prophylaxis [66].

Herbal Remedies in Vaginitis:

The aim of treatment of vaginitis is to restore the vaginal pH below 4.5, as well preserve normal flora such as lactobacillus species. Several plant species have been reported to prevent the risk of transmission and to treat vaginal infections. As mentioned, *G. vaginalis*, *M. hominis*, *C. albicans*, Trichomonads, as well as Herpes simplex virus, *C trichomatis*, and *Neisseria gonorrhoea* are microbial agents responsible for infectious vaginitis [10, 65]. Non-infectious vaginitis has also been shown to be treated with phytoestrogens obtained from plants such as *Ribes nigrum*, *Foeniculum vulgare*, *Panax ginseng*, and others [65]. In a study conducted on indigenous plants from Tanzania, some species possessed antibacterial and antifungal activity against *C. albicans* and *Staphylococcus aureus* [67]. All forms of infectious vaginitis are considered STDs and different herbs have been screened against the causative organisms. The efficacy of the combination of radix of *Saphorae flavescens*, cortex of *fellodendri*, and fructus of *Cnidii* on microbial and fungal isolates has been shown *in vitro* [68].

Herbal remedies for BV:

Culinary herbs and spices also have documented history of use in the prevention and treatment of infections including STDs [10]. The promising activity of lemon grass, tea tree, lavender, and palmarosa oils against both bacteria and fungi isolated from infected vagina has been reported [69]. Most available herbal remedies are effective against the three common types of vaginitis. The use of some herbs such as lemon has been discouraged due to the potential toxicity to vagina based on the concentrations used. Some herbs with established activity against vaginitis have been reported (Table 2).

Tea Tree Oil (TTO):

TTO is known as an essential oil isolated from the leaves of the tea tree, *Melaleuca alternifolia* (Maiden & Betche) Cheel (Myrtaceae). Several studies conducted on TTO have proven its effectiveness on different organisms implicated in vaginitis especially lactobacilli species, *C*, and *T. vaginalis* (Table 2). TTO has been shown to be very effective as an antibacterial, antifungal, especially against *T. vaginalis* [70]. The *in vitro* activity of TTO has been reported against both *C* and non-candida isolates [71]. Evaluation of the products containing tea tree oil revealed minimum inhibitory concentrations and fungicidal concentrations compared to non-tea tree products, which indicated its anti-candida activity. TTO vaginal pessary was reported to cure anaerobic vaginosis in a patient who treated herself for five days with pessary containing 200 mg TTO in a vegetable oil base. Microscopic tests for susceptible pathogens were negative, which indicates the effectiveness of the treatment [72]. The activity of TTO against lactobacilli and a range of organisms implicated in BV were also evaluated. Both anaerobic and aerobic bacteria associated with BV were susceptible to TTO, while lactobacilli tested were resistant [73]. Different components of TTO such as terpinen-4-ol, α -terpineol, linalool, α -pinene, and β -pinene have shown promising antifungal activities [74].

Table 2: Herbs and their active components effective on vaginitis

Herbs and parts Used	Type of Extract	Components	Type of vaginitis	Ref
Tea tree oil (<i>Melaleuca alternifolia</i>)	Oil	Terpinen-4-ol, α -terpineol, linalool, α -pinene, and β -pinene	BV, Candidiasis, and Trichomoniasis	[70,71,74]
Garlic (<i>Allium sativum</i>)	Aqueous	Allicin, alliin, and ajoene	BV and Candidiasis	[77,78]
Persian shallot (<i>Allium hirtifolium</i>)	Alcoholic	Allicin, ajone,	BV, candidiasis, and Trichomoniasis	[82-85]
<i>Zataria multiflora</i>	Oil and cream	Carvacrol, thymol carvacrol, and linalool	BV, Candidiasis, and Trichomoniasis	[80,81]
Goldenseal (<i>Hydrastis canadensis</i>)	-	Hydrastine, berberine	BV, candidiasis, Trichomoniasis	[88]

Garlic (*Allium sativum* L. fam. Alliaceae):

Garlic preparations have been used in treating several diseases including infections [10]. Its antibacterial, antifungal, and antiviral activities have been reported extensively [64]. It has been stated to be either chewed or inserted in the vagina against BV [75]. Garlic tablets have been shown to decrease Amsel criteria with similar efficacy but fewer side effects compared with metronidazole in treating BV [76]. The *in vitro* antibacterial and antifungal activity of *Allium sativum* has been reported [77]. Aqueous garlic extract was also effective against 24 strains of *C. albicans* isolated from vaginal, cervix, and buccal swabs [78].

Shirazi thyme (*Zataria multiflora* (ZM) Boiss. Lamiaceae):

ZM has been shown to be effective as a vaginal cream in BV similar to metronidazole [79]. Both ZM and metronidazole reduced patient's complication and Amsel criteria following five nights of treatment. ZM cream was found to be active against BV and clinical symptoms associated with trichomoniasis [80]. The *in vitro* activity of ZM oil against *T. vaginalis* has been reported [81]. The ZM cream exhibited a better efficacy comparing to clotrimazole cream [82]. The cream reduced all symptoms except vaginal irritation and burning, and its effect on gynecological signs was superior compared to clotrimazole [82].

Persian Shallot (*Allium hirtifolium* Boiss. Alliaceae):

This plant has been used as a spice in Iran for a long time. Its activity against gram negative and positive bacilli, protozoa and yeast has been reported [83]. The hydroalcoholic and dichloromethanic extracts have been shown to decrease oxygen uptake and growth of the organisms (*T. vaginalis*), inhibit lipids, proteins and nucleic acid synthesis, and induce damage to membranes *in vitro*. This effect was comparable to metronidazole [84]. The alcoholic and aqueous extracts were also tested for anti-candidal activity, where displayed activity against 33 species of candida isolated from a patient with chronic candidiasis [85]. Nevertheless, the effect of Persian shallot on bacterial vaginitis have not reported, it has been reported to exhibit activity against bacteria such as, *S. aureus*, methicilin resistance *S. aureus* (MRSA), methicilin sensitive *S. aureus* (MSSA), *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumonia*, and many others [86].

Goldenseal (*Hydrastis Canadensis* L. Ranunculaceae):

The isolated constituents (berberine and hydrastine) of this plant has demonstrated promising antimicrobial activity against wide range of bacteria such as *Streptococcus mutans* and *Fusobacterium*

nucleatum [87]. Berberine sulphate has been shown to inhibit and induce morphological changes in parasites such *T. vaginalis* and the other species [88]. Herbal suppositories containing myrrh, Echinacea, slippery elm, golden seal root, and yarrow have been shown to be effective against BV. Products obtained from dried root of this plant have been traditionally used in treating infections such gonorrhea, eye infections, infectious diarrhea, and vaginitis [89].

Natural remedies rather than herbs: Probiotics:

Probiotics are not considered as herbal remedies, but they are a natural way of treating or preventing vaginitis. In a clinical trial, Falagas *et al.*, has reported the ability of some strains of lactobacilli to prevent the adherence of *Gardnerella vaginalis* to the vaginal epithelium, and also hydrogen peroxide, lactic acid, and bacteriocins which inhibit the growth of bacteria that causes BV. They also described that the intra-vaginal administration of probiotics (*Lactobacillus acidiphillus*, *L. rhamnosus*, and *L. fermentum*) can cure and prevent reappearance of BV, by increasing the vaginal lactobacilli and restoring normal vaginal microbiota [90].

CONCLUSION AND RECOMMENDATION:

Herbal remedies have been mostly considered safe and effective especially in developing countries. HM has been used for centuries to treat various chronic diseases including infections. Vaginitis is the main cause of multiple hospital visits by women, generally in reproductive ages. *In vitro* and *in vivo* investigations on some plants have proven their effectiveness on the different types of vaginitis similar to some conventional therapies such as metronidazole on symptoms and recurrence, with a better side effect profile. Non-infectious vaginitis has also been treated using phytoestrogens from plants. Most of these herbs have been formulated into pessaries or suppositories, which makes them more accessible. Further studies on the mechanisms of their action would be imperative for adequate drug delivery and minimized toxicity. Probiotics are also natural resources that can treat or prevent reappearance of vaginitis.

Conflict of Interest: The authors declare that there is no conflict of interests regarding the publication of this paper.

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