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Short communication

Formulation and Quality Assessment of *Boswellia* Vaginal Gel

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Abstract

Background and Objectives: Over the centuries, medicinal herbs have been used as major sources of medicine for prevention and treatment of diseases; however, herbal drugs should be converted to new dosage forms for better acceptance and easier usage by patients. The present research has been performed to formulate a herbal gel for vaginitis based on Iranian traditional medicine. **Methods:** The extract of oleogumresin of *Boswellia* was obtained using propylene glycol: water. The gel was prepared using the extract (2% and 5%), carbomer 940 (0.5% and 1%), tri-ethanolamine and distilled water. Further, the prepared gels were evaluated for physicochemical and microbial characteristics. Accelerated stability test was performed on the selected gel for six months. **Results:** The gel with 2% extract of *Boswellia* using propylene glycol: water 80:20 as the solvent and carbomer 1% was selected as the best one. The formulated gel was homogenous, white in color with acceptable physicochemical and microbial characteristics. Hexane soluble content and total acids as boswellic acid in the gel were found 0.25% and 8.7 mg/100 g, respectively. It was stable during centrifugation but it was unstable in temperature cycle test and stability test; therefore, it should be kept in cool place. **Conclusion**: The prepared gel contains volatile compounds with antimicrobial and anti-inflammation activities; therefore, it could be an appropriate candidate for vaginitis.

Keywords: *Boswellia*; formulation, Iranian traditional medicine; vaginal gel; vaginitis

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Introduction

Vaginitis is the most prevalent gynecological complication during reproductive ages. The patients show different symptoms including abnormal vaginal discharge, itching and burning sensation [1,2]. Wide spectrums of microorganisms are involved in the pathogenesis of the disease which cause trichomoniasis, candidiasis and bacterial vaginosis [3,4]. Women may have recurrent episodes of vaginitis due to use of certain contraceptive methods especially tubal ligation, multiple sex partners, as well as improper hygiene [5]. The aim of treatment of vaginitis is keeping the vaginal pH below 4.5 and preserving normal vaginal flora such as lactobacillus species [6]. Nowadays, many people use medicinal plants for various diseases because they have documented history of use in the prevention and treatment of diseases. Several plants have been formulated as vaginal cream, gel or suppositories, which makes them more accessible and increases patients' acceptance as well [7]. *Boswellia* spp. is a member of Burseraceae family. The medicinal part of the species is the oleogumresin that is exuded during incisions in the bark of the trunk [8,9]. Phytochemical investigations of the species have

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indicated that different diterpenoids are the major compositions of the resin. The resin has been utilized to treat rheumatic arthralgia, rheumatoid arthritis, dysmenorrhea, amenorrhea and ulcers. It has also demonstrated sedative, antinociceptive, anti-inflammatory, antihyperlipidemic, antifungal and antibacterial properties [10]. According to Iranian traditional medicine (ITM), *Boswellia* has hot and dry temperament and is used for vaginal discharge and itching as a vaginal form [11]. In the present research, *Boswellia* vaginal gel has been prepared and its quality control tests have been performed.

Material and Methods

Ethical consideration

Ethical Committee of Shahid Beheshti University of Medical Sciences approved this study with the code of IR.SBMU.RETECH.REC.1395.728.

Plant material

Boswellia spp. was purchased from Tehran herbal market. The samples were authenticated by botanists at the Herbarium of Traditional Medicine and Materia Medica Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran (voucher specimen no.: 454HMS).

Extraction of the oleogumresin

In order to prepare the *Boswellia* extract, it was powdered and then mixed with propylene glycol:H_2O in different proportions (100:0, 80:20: 50:50) for 24 h. The ratio of the powder: solvent was 1:10. The best solvent was selected. Then, the mixture was centrifuged and the supernatant was used for gel preparation.

Formulation of the vaginal gel

The vaginal gel was prepared by using carbomer 940 in two different concentrations (0.5, 1%) and triethanolamine was used to make gel plexus and optimum pH. Regarding the vaginal application of the gel, the best formulation was selected according to viscosity and pH parameters. Two concentration of *Boswellia* (2% & 5%) were used for gel preparation.

Quality control tests

Determination of pH

The gel was diluted with distilled water in the proportions of 1:10 and pH was measured at room temperature. Due to vaginal application of this gel, the pH should be 3.5-4.5.

Mechanical stability

In order to assess the mechanical stability of the prepared gel, it was centrifuged at 3750 rpm for 15 min and its stability was evaluated [12].

Termperature cycle test

In this test, for each sample two vials with 5 g gel was used. One group was placed at 4 °C and the other was kept at 40 °C. After two weeks, samples were replaced from 4 °C to 40 °C and vice versa. Finally, after 4 weeks, the samples were evaluated for their appearance and phase separation [12].

Determination of viscosity and rheological behavior of the gel

The viscosity of product was measured through rotational viscometer DV_2 RV model at room temperature. Different shear stresses and shear rates were applied for samples and finally rheogram of the product was obtained to evaluate rheological behavior and determination of viscosity.

Determination of hexane-soluble contents in the gel

Ten grams of gel was dissolved in 40 mL ethanol 96°. Twenty mL hexane was added to the mixture and stirred well. Hexane phase was separated and alcoholic phase was extracted with 20 mL hexane for two more times. Hexane fraction was concentrated using vacuum evaporator at 40 °C. The weight of residue that is hexane-soluble contents was calculated [13].

Determination of total acid content as boswellic acid in the gel

Total acid content of the gel was measured as a marker for quality control of the gel. First, 150 mL chloroform was added to 100 g gel and shaked for 24 h. The liquid phase was separated and dried using a vacuum evaporator. The dried extract was dissolved in 10 mL methanol. The extract was titrated with NaOH 0.005 N using methanol as blank. Phenolphthalein was used as the reagent for determination of the end point [14].

Microbial tests

Microbial tests including total aerobic viable count (TAVC) and tests for specific species

(*Staphylococcus aureus, Pseudomonas aeroginosa* and *Candida albicans*) were performed for the gel based on British Pharmacopoeia guideline [15].

Results and Discussion

Among different solvents containing propylene glycol:H_2O in different ratio (100:0, 50:50, 80:20), ratio of 80:20 was chosen as the best extraction solvent system. By using carbomer 0.5%, more amount of triethanolamin was necessary to produce gel causing higher pH that was not suitable for vaginal use. Carbomer 1% could produce suitable gel with good viscosity, homogenisity and pH (4.0). *Boswellia* gel 5% was skin irritant, therefore, it was omitted and the gel containing *Boswellia* 2%, carbomer 1% with propylene glycol:H_2O 80:20 as the solvent was chosen as the best formulation. The final gel had white color with distinctive *Boswellia* odor. The gel was completely homogenous during centrifuge procedure without any separation or crack. However, in temperature cycle test, it was unstable and the color of the gel turned yellow and the appearance was changed to sticky form. In stability test, the appearance was changed as well which demonstrated that the gel was sensitive to hot condition and it should be kept in a cool place. The hexane soluble content of the gel was found 0.25%, while the total acid content of the gel as boswellic acid was calculated as 8.7 mg/100g. Due to antimicrobial properties of *Boswellia*, no microorganism was grown in the gel. The rheogram of the gel was non-linear due to non Niotonic behavior of the gel. Since this rheogram was not started from zero point and was linear at terminal points, it can be concluded that the gel has plastic behavior [16]. Based on linear part of the chart, viscosity was calculated as 4.39 Pa.s. Yield value of gel with calculation of anti-logarithm of intercept from the origin of linear area equation was obtained 171 Pa.

Boswellia oleogumresin has been used for various medical purposes from ancient times. It demonstrated potent antimicrobial effects during several studies. Antibacterial effect of the resin against *Bacillus subtilis, Staphylococcus aureus, Streptococcus pneumonia, E. coli, Klebsiella pneumonia, Enterobacter aerogenes, Pseudomonas aeroginosa* and *Proteus vulgaris* have been confirmed [17]. In addition, antifungal property of the essential oil has been reported. During an investigation on the antifungal effects of some essential oils, it was found that *Boswellia* essential oil had the best activity and it showed synergistic effects with azoles against azole-resistant strains of *C. albicans* [18]. In another study, anti-candidiasis effects of *Boswellia serrata* essential oil against the isolates of *Candida* which were sensitive and resistant to fluconazole was studied. The results showed that the essential oil displayed an inhibiting effect on all *C. albicans* isolates in-vitro [19]. In addition to antimicrobial properties of *Boswellia*, its anti-inflammatory effect has been exhibited via different models. This effect is ascribed to boswellic acids of the resin which act as anti-inflammatory agent with different mechanisms [20]. Among various anti-inflammatory mechanisms, leukotriene inhibition is the most important one [21].

Conclusion

Regarding the anti-inflammatory and anti-microbial properties of the *Boswellia*, it seems that *Boswellia* gel could be used in vaginitis after complementary examinations such as sensitivity test and clinical trials.

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Author contributions

Homa Hajimehdipoor supervised formulation part; Sahar Dehdari and Leila Ara performed the experimental part; Mojgan Tansaz designed primary idea. All authors read and approved the final manuscript.

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

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Abbreviations

ITM: Iranian traditional medicine