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Short Communication

Preparation of a Topical Product from *Allium sativum* Retrieved from Iranian Traditional Medicine

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Abstract

Background and objectives: Garlic (*Allium sativum* L.) oil has been introduced in Iranian traditional medicine (ITM) as an effective topical agent for urine dribbling. Additionally, the beneficial effects of garlic on prostatic proliferation have been revealed in recent studies. The purpose of this research was formulation of a topical ointment using garlic oil proposed by ITM and quality control of the product. **Methods:** Garlic oil was prepared according to ITM instructions and analysed using GC/MS method. In order to formulate garlic ointment, several experimental formulations were examined. Microbial tests as well as physical assessments including thermal stability evaluation and study of rheological behaviour were performed on the final product. **Results**: GC/MS analysis of garlic oil showed the presence of dialyl trisulfide, one of the major organo-sulfur components of garlic. The herbal ointment containing garlic oil (70%), white petrolatum (23.7%) and white beeswax (6%), showed suitable physical properties as well as plastic tixotropic behaviour and was free of any microbial contamination. **Conclusion:** Regarding the modern evidences about the beneficial effects of garlic and its sulphur compounds on improvement of BPH and prevention of prostate cancer, garlic ointment could be an appropriate candidate for studies in the field of prostate related diseases with respect to its traditional use in ITM.

Keywords: *Allium sativum*; BPH; Iranian traditional medicine; ointment; topical oil

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Introduction

Benign prostatic hyperplasia (BPH) is the most commonly diagnosed disorder considering men's health. [1]. Garlic (*Allium sativum* L.) with warm and dry temperament, has been considered as a desiccative, flatus repulsive and tumefaction resolving agent in Iranian traditional medicine (ITM), also known as Persian medicine [2,3]. Iranian scholars believed that garlic oil "Dohn-ul-thom", obtained by boiling garlic in olive oil, could be effective in urine dribbling [3,4]. Moreover, the beneficial effects of garlic on BPH have been demonstrated in modern researches [5,6].

In ITM, medicinal oils have been traditionally used via topical, oral and even nasal routes to target particular areas of the body for relieving specific disorders [7]. In addition to traditional literature, several modern clinical reports have demonstrated topical effectiveness of the traditional medicinal oils for their anti-inflammatory, analgesic and neuroprotective properties [7-9]. On the other hand, traditional

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formulations should be converted into new dosage forms for better patient acceptance and easier usage [10]. Considering the stability and durability of semi-solids as well as the convenience of using, in this study, a herbal ointment from garlic oil was formulated based on ITM and quality control of the product was carried out to present a qualified formulation for usage.

Materials and Methods

Ethical considerations

This study was approved by the Ethical Committee of Tehran Medical Sciences, Islamic Azad University (ID: 2024, 1395/08/26).

Plant material

Fresh garlic corms were purchased from local market in Tehran and identified at the Herbarium of Traditional Medicine and Materia Medica Research Center (TMRC), Shahid Beheshti University of Medical Sciences, Tehran, Iran. (HMS No. 481). Garlic corms were peeled, sliced, air- dried and stored in a well -closed container.

Preparation of garlic oil

Garlic oil was prepared according to ITM instructions [3,11,12]. Garlic, milk and olive oil (Etka, Iran) (1:4:2) were processed in two stages: first, the crushed parts of the plant were indirectly heated (in water bath) with milk at 80 °C, after softening of garlic, olive oil was added. Heating was continued until the milk was completely evaporated. Subsequent to filtering the whole mixture, the transparent garlic oil was obtained.

Analysis of garlic oil

The methanol fraction of garlic oil was used for analysis by GC/MS (oil: methanol 2:1 v/v). GC/MS analysis was carried out on an Agilent 7890 N gas chromatograph coupled with an Agilent 5975 mass selective detector (Agilent-Technologies, USA). An HP-5MS capillary column (30 m × 0.25 mm, film thickness 0.25 m) was used for GC/MS. The column temperature was programmed from 60 to 280 °C at a rate of 10 °C/min with the lower and upper temperatures being held for 1 and 15 min, respectively. The GC injector and MS transfer line temperatures were set at 280 °C. Helium was used as the carrier gas at a flow rate of 1.0 mL/min. An injection volume of 1 μL was used for methanol fraction of garlic oil. The compounds of garlic oil were identified by their retention times (RT) and mass fragmentation patterns using data of standards at Wiley 7.0 library.

Development of an optimum base for garlic ointment

To obtain a suitable base for garlic topical ointment, white petrolatum, eucerin and white beeswax were selected and several experimental formulations with different compositions were prepared. Olive oil was applied in the experimental formulations instead of the garlic oil. The formulations were prepared by fusion method [13]. The visual properties of the experimental formulations were evaluated and formulations with appropriate appearance, uniform texture and suitable consistency were selected for thermal stability and other tests. Centrifugation at 3750 rpm for 15 min was used to measure the accelerated deterioration of the selected formulations. The most stable formulation which was resistant towards physical changes and centrifugation was selected as the optimal base for preparation of garlic ointment.

Formulation of garlic ointment

Briefly, the oily ingredients were heated in a beaker to about 70 °C using a water bath. After melting of all components, the mixture was slowly cooled and stirred for 30 min until congealed using a stirrer at 500 rpm. Subsequent to evaluation of organoleptic properties and pH of garlic ointment, thermal stability tests and centrifugation, as well as rheological and microbiological evaluations were performed

Rheological properties of garlic ointment

Rheological study was performed using Brookfield viscometer (Brookfield, DV2 RV model, USA) at 25°C.

Microbiological tests

Microbial limit tests including total viable count (TVC) and specified bacteria (*Staphylococcus aureus* and *Pseudomonas aeroginosa*) were conducted on garlic ointment according to WHO guideline [14].

Results and Discussion

Garlic oil was made by boiling the mixture of garlic and milk in olive oil. Milk as a compound containing animal fats, is supposed to be an ameliorator for garlic. Based on ITM references, ameliorator is a compound that modifies the drug either by eliminating and reducing the harm and severity of the components or by maintaining the strength of the compounds and enhancing the

effect. Moreover the ameliorator might be a drug delivery aid to the target organ [2,3].

The prepared garlic oil was analysed using GC/MS method and 29 components were identified. In addition to revealing olive oil constituents such as tritepenoides (squalen) and sesquiterpens (farnesol) as well as fatty acids and their dependent esters, the presence of diallyl trisulfide, one of the major soluble organo-sulfur compounds of garlic, was demonstrated. Diallylsulfide (DAS) exerts antioxidant effects by inhibiting testosterone induced oxidative stress and has been suggested to be helpful in preventing prostate cancer [15].

In this study, a semi-solid product from garlic oil was formulated. In order to achieve the best oleaginous base for the product, eleven experimental formulations were prepared (table 1). Comparison of formulations F_1 to F_4 showed that the raised eucerin content with constant amount of white beeswax resulted in loose consistency of the prepared formulations. So, elimination of eucerin along with increasing of olive oil and white beeswax, led to formation of more consistent formulations (F_5-F_{11}) which contain larger amounts of oil rather than previous formulations. By evaluating the visual properties, formulations F_{10} and F_{11} presented appropriate consistency and uniformity with suitable glossy appearance which were submitted to thermal stability tests and centrifugation. Finally, formulation F_{11} exhibited the most stability towards physical changes, so it was selected as the most suitable formulation for preparation of the final product.

Garlic ointment composed of garlic oil (70%), white petrolatum (23.7%), white beeswax (6%), butylated hydroxy toluene (BHT) (0.04%) as antioxidant and methyl and propyl parabens (0.2 % and 0.06%, respectively) as preservatives. The product was glossy greenish yellow with garlic odour. In addition to its appropriate consistency, uniformity and pH value (5.78± 0.1), garlic ointment was spread easily on the skin. No signs of phase separation and physical changes were observed in the ointment during physical stability tests and centrifugation. Also, no contamination or microbial growth was detected.

Rheological behavior of garlic ointment was evaluated based on the obtained rheogram (figure 1) to show the plastic (Bingham) tixotropic behaviour for the ointment. Viscosity and Bingham yield stress of garlic ointment were 0.948 ± 0.096 Pa.s and 46.7 ± 6.09 Pa, respectively, corresponding to the linear plot of up curve (y = 0.948x+ 46.7). Tixotropy, describes any material that exhibits a reversible time-dependent decrease in apparent viscosity which makes a formulation remain stable following the preparation and packaging [16].

Table 1. Composition of ingredients in the experimental formulations (%w/w)

Formulation	Eucerin	White beeswax	White petrolatum	Olive oil
F_1	23	4	23	50
F_2	46	4	-	50
F_3	-	4	46	50
F_4	18	4	18	60
F_5	-	5	40	55
F_6	-	5	35	60
F_7	-	5	25	70
F_8	-	5	20	75
F_9	-	5	15	80
F_{10}	-	6	14	80
F_{11}	-	6	24	70

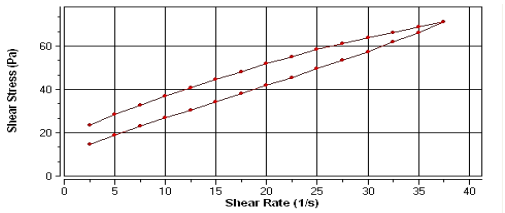

Figure 1. Rheogram of the garlic ointment

Herbal medicines, especially those with antioxidant effects have a special role in the treatment of BPH [6]. *Allium sativum* has shown positive effects on the improvement of BPH [17]. It has also demonstrated chemo-preventive properties due to its organo-sulfur compounds. The formations of tumours has been greatly decreased after administration of fresh garlic in vitro and in vivo [18,19].

Due to the previously reported effects of garlic and its organo-sulfur compounds on improvement of BPH and prevention of prostate cancer in modern researches, the garlic ointment prepared in the present study, could be an appropriate candidate for studies in the field of prostate related diseases with respect to its traditional use in ITM.

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Author contributions

Shirin Fahimi and Maryam Jahandideh designed and supervised the study; Paria Kharazi performed the experiments; Shirin fahimi analyzed the data; Zahra Jafariazar was the pharmaceutical consultant.

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; BPH: benign prostatic hyperplasia; WHO: World Health Organization; DAS: diallyl sulphide; BHT: butylated hydroxy toluene