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FORMULATION AND CLINICAL TRIAL STUDY OF AJMT CREAM IN TREATMENT OF ECZEMA

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ABSTRACT

Background and Purpose: Topical corticosteroids are first-line treatment for eczema, but the use of these drugs is followed by specific problems such as eczema, atrophy, depigmentation, and so on. In addition, continuous use of these medications leads to the reduced effectiveness of topical corticosteroids. These problems and a tendency to use herbal medicines inspired this study aimed at determining and comparing the effects of an herbal compound in the form of cream AJMT fenugreek (*Trigonella foenum*), chamomile (*Matricaria chamomilla*), walnuts (*Juglans regia* L), and marshmallow (*Althaea officinalis*) with those of Fluocinolone acetonide on hand eczema. The aim of this study was Formulations and preparation of herbal cream to treat eczema with minimal side effects. **Methods:** In this clinical trial, 64 patients with hand eczema that referred to the dermatology clinic of the University of Medical Sciences were randomly divided into two equal groups. One group was treated with AJMT cream, and the other received a two-week treatment with Fluocinolone acetonide. The results were analyzed using the McNemar and Chi square tests. **Findings:** The results indicated that the AJMT cream significantly improved the symptoms of burning, itching, redness, bumps, scaling and fissures, while Fluocinolone improved the symptoms of irritation and redness compared to before treatment ($P < 0.05$). A comparison of the two groups indicated that after intervention, AJMT therapeutic effects on burning, itching, and redness were equal to those of Fluocinolone cream ($P > 0.05$) and were significantly better on the symptoms of bumps, scaling, and cracks ($P < 0.05$). **Conclusion:** Given the better effects of AJMT herbal cream than metal Fluocinolone acetonide on hand eczema symptoms and the long-term effects of topical steroids, use of the herbal cream AJMT is recommended.

INTRODUCTION

Eczema is the most common inflammatory disease of the skin [1], and hand eczema is considered the most abundant type of eczema (15%) [2-3]. About 2-10% of the world's population suffer from hand eczema. Because of contact with water and detergent, two times more women suffer from this disease than men. Eczema is also more prevalent among people under the age of 40 years [1]. It occurs because of discrete factors or a combination of factors, including internal ones, such as eczema naturally, or external factors, such as irritation or allergic eczema. Contact eczema, a simulative dermatitis, contracted through direct contact with foreign materials (such as water, soap, and detergent), leads to direct damage caused by the cell. In the allergic contact type of eczema, IV cell sensitivity is delayed in response to allergens (such as nickel, dyes, plastics, and perfumes) that are in direct contact with the skin [4-5].

Contact eczema comprises 90-95% of all occupational diseases; stimuli-caused eczema makes up 80% of cases, and 68% of skin problems cause career changes [6]. The most common types of hand eczema are by stimuli (35%), natural (22%), and allergies (19%) [1]. Moreover, for the past 50 years, topical corticosteroids have been used to treat skin diseases. Corticosteroid creams and ointments are often prescribed to relieve itching and inflammation caused by skin diseases like eczema. These materials prevent the release of the chemicals that cause inflammation [7-8]. However, long-term use of corticosteroids, especially high-power ones, could lead to systemic or local effects. Children are more prone to these complications. The local effects are greater than the systemic side-effects. The most common side-effects include skin atrophy, a temporary reduction in the use of pigments, and decreased immunity at the site of usage [8].

Due to sensitiveness of a few patients to some of these drugs and many pathogens become resistant to them, scientists turn to natural and herbal remedies. Today, research in the field of herbal medicines, their prescription and use is expanding in countries throughout the world. The search for more effective drugs with less side effects is essential [9-10-11].

The aim of this study was Formulations and preparation of herbal cream to treat eczema with minimal side effects.

MATERIALS AND METHODS

This study is a double blind clinical trial including patients who were referred to the special clinic in Kashani Hospital. After receiving permission from the Ethics Committee and Deputy University of Medical Sciences and the consent of the participants, 64 patients with hand eczema were randomly divided into two groups of 32 patients each. After some patients withdrew from the study, 30 patients remained in each group. The first group was treated with the herbal cream AJMT, and the other group with Fluocinolone acetonide 2%. Patients were examined by a dermatologist before treatment and two weeks after treatment, and symptoms such as burning, itching, erythema level, papules and vesicles bumps, and fissures of the skin were evaluated and recorded in a questionnaire designed for this purpose. To avoid risk factors such as detergent, water, and soil, patients in both groups were provided with chemicals, the continued use of cotton gloves under plastic gloves, and other necessary training.

KEY WORDS

Eczema, Chamomile,
Marshmallow, Fenugreek,
Fluocinolone
Acetonide, Walnut

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The plan was to try to avoid any error, and the time of drug consumption was kept as near the same as possible in both groups. Patients in both groups were advised to apply a sufficient amount of cream twice a day to the affected area and that washing that area must be avoided.

Patients over ten years of age and having no systemic disease or other skin condition (such as infection or fungus) or a history of oral and topical medication use before and during treatment, and non-pregnant women were included in this study.

Extraction Methods and Herbal Cream Preparation: To prepare the cream AJMT, four medicinal herbs, fenugreek seeds, walnut leaves, chamomile and marshmallow root, produced by academic research in order to identify and then dry extract was prepared. Then based on final concentrations of the powder in the formulations, herbal extracts were prepared. Concentrations of these plants were as follows: 5% of fenugreek seeds, 5% of marshmallow, 5% of chamomile, and 5% of walnut leaves.

Cream formulation: An oil-in-water (O/W) emulsion-based cream (semisolid formulation) was formulated. The emulsifier (stearic acid) and other oil soluble components (cetyl alcohol) were dissolved in the oil phase (Part A) and heated to 75°C. The preservatives and other water soluble components (methyl paraban, propyl paraban, triethanolamine, propylene glycol, ethanol extract of *Matricaria chamomilla*, *Trigonella foenum graceum*, *Juglans regia* L., and *Althaea officinalis*) were dissolved in the aqueous phase (Part B) and heated to 75°C. After heating, the aqueous phase was added in portions to the oil phase with continuous stirring until the emulsifier was cooled [Table 1].

Determination of stability of formulation: Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. To assess the drug and formulation stability, stability studies were done according to ICH guidelines. The cream was poured into a bottle and kept in the humidity chamber, maintained at $32 \pm 2^\circ\text{C}/70 \pm 5\% \text{RH}$, and $42 \pm 2^\circ\text{C}/80 \pm 5\% \text{RH}$ for two months. At the end of the experiments, samples were analyzed for their physical properties and viscosity and other physicochemical tests that are shown in [Table 2].

At baseline, this project is divided into two groups of healthy volunteers and, treatment was continued in the usual way. The information collected from the two groups of patients at different stages of treatment using indicators was subjected to McNamara and chi-square analyses.

Characteristics of plants used in this study

1. Marshmallow (*Althaea officinalis*) is an herbaceous plant that grows to a height of 2 m. Its roots, leaves, and flowers are used in herbal medicine. It affects smooth skin irritation, and the marshmallow root has anti-inflammatory properties [12-14]. Marshmallow is one of the most important medicinal plants. Althea mucilage compounds (plant mucilage) include sugars, starch, pectin, and other ingredients. This plant used to treat skin diseases such as eczema.
2. Walnut (*Juglans regia* L.) is a beautiful, base tree whose leaves, bark, and buds are used in herbal medicines. It's most important compounds include Tanen, Zhoglon, naphthoquinone, and vitamin C. Walnut can be used to treat eczema along with the secretion of anti-inflammatory and astringent properties [15]. Cream 2% is used for external treatment [16].
3. Common chamomile (*Matricaria Chamomilla*) is an annual herbaceous plant growing 20 to 80 cm in height. The flower color is greenish-yellow, and the flowers are used in making medicine. Chamomile and its extract are the most widely used plant in herbal treatment in the world [17]. This plant grows in some areas of Lorestan and Khuzestan, Iran. Its flowers have essential oils (Recubizul, Farnesol, and Chamazulene), Taten, glycosides, and flavonoids. Chamomile is used for the treatment of dermatitis, urine burns, pediatric rash, and cracking of the nipple (16). Its antibacterial and antifungal properties are used [18] for external treatment at concentrations of 3-10% [19].
4. Fenugreek (*Trigonella foenum graceum* L.) is an annual plant that grows up to 50 cm tall. Its grain is used and contains mucilage, sapogenin, aromatic materials, and large amounts of iron and phosphorus. It also contains an alkaloid called trigonellin at the index amount. Plant mucilage compounds have healing, softening, and anti-inflammatory properties and can be applied topically, particularly to treat eczema [20].

Given the high prevalence of hand eczema and its complications, common medications (topical steroids) have a relatively small effect; therefore, there is a growing tendency to use natural remedies. This study examined a total of four plants, each having anti-inflammatory, emollient, astringent, and anti-bacteria and fungi properties and being effective against eczema. This study aimed to determine the efficacy and effects of herbal creams AJMT and compare them with those of fluocinolone acetone on hand eczema in patients referring to a dermatology clinic in Shahrekord.

RESULTS

In the group treated with herbal cream AJMT, 60% of participants were females (n=19) and 40% were male (13 persons). Thirteen patients (40%) were housewives, 6 (20%) were construction workers, 3 (10%) were farmers, and 10 (30%) had other jobs. The most frequent age was 30-40 years old. The group treated with Fluocinolone acetonide cream comprised 30 patients with eczema, 21 of whom (70%) were female and 9 (30%) were male; 15 (50%) were housewives, 6 (20%) were farmers, and 10 patients (30%) had other jobs. In terms of demographic characteristics, the two study groups were not significantly different ($P > 0/05$).

Table 1: Composition of cream

Material	% of material in formulation W/W
Dry extract of <i>T. Foenum</i>	5
Dry extract of <i>M. Camomilia</i>	5
Dry extract of <i>J. regia</i>	5
Dry extract of <i>A. officinalis</i>	5
Cetyl alcohol	3
Stearic acid	12
Glycerol	4
Methyl paraben	0.02
Tri ethanolamine	Qs
Water	Qs

Table 2: Physical properties of AJMT cream

pH of the Cream	Viscosity	Acid value	Saponification value	Homogeneity	After feel	Irritancy test	Appearance	Removal
6.35±2	28001±20	6.3±2	29.1±0.7	Good	Emolient	Not reaction	No change in color	Removed by washing with water

Table 3: Comparison of AJMT cream and fluocinolone cream in the treatment of eczema

Clinical signs	AJMT				Fluocinolone Acetonide			
	Before treatment		After treatment		Before treatment		After treatment	
	Percent	Number	Percent	Number	Percent	Number	Percent	Number
Burning and itching	80	25	10	3 *	90	29	0	0 *
Red	80	25	20	6 *	90	29	10	3 *
Ness **	40	13	10	3 *	80	25	60	19
Papules **	10	3	0	0	20	6	0	0
Scaling **	80	25	30	10.	100	32	80	25
Fissure **	60	19	10	3 *	70	22	60	19

* $P > 0.05$ before treatment between the two groups in all variables

** $P < 0.05$ between the two groups after treatment.

-AJMT Cream (combination of extracts of fenugreek, chamomile, walnuts, and marshmallow).
n = 30 in each group.

McNemar's test indicated that in the group treated with AJMT, all symptoms except papules, i.e. burning, itching, redness, bumps, scaling, and fissures, were significantly different before and after treatment ($P < 0.05$), and recovery was achieved. Fluocinolone also resulted in statistically significant differences before and after the intervention for symptoms of skin irritation, itching, and redness ($P < 0/05$).

A comparison of the two groups using the chi-square test indicated that after treatment, the therapeutic effects on burning or itching and redness AJMT and Fluocinolone had no statistically significant difference ($P > 0.05$), while the therapeutic effects in the group treated with AJMT on symptoms of bumps, papules, scaling, and fissures were significantly better than those of the group treated with Fluocinolone ($P < 0.05$) [Table 3].

DISCUSSION

The results indicated that in the group that used AJMT, except for papules signs, other symptoms such as burning, itching, redness, and so on, were significantly different after treatment. In the group using Fluocinolone, the symptoms of irritation and redness had statistically significant differences before and after intervention, but these differences were not significant for other symptoms.

A comparison of the two groups indicated that after intervention with AJMT, burning or itching and redness in the AJMT and Fluocinolone group had no statistically significant difference in symptom relief, while the

therapeutic effects of AJMT on scaling and fissures were significantly better than in the group treated with Fluocinolone.

Several studies have shown the twofold properties of medicinal plants in the treatment of eczema. For example, Paller compared plant Tacrolimus ointment and pimecrolimus cream and found the Tacrolimus ointment to be more effective in the treatment of eczema, but the effects of these two drugs are identical [22]. This study shows that this compound is effective on the treatment of eczema.

In the results of Tai in a study of herbal medicine, Sanfujiu indicated that, in the treatment of eczema, the plant was effective in 6.44% of patients, and 52.1% of them had no effects from treatment [23].

Based on the study findings, it seems that the herbs used in cream AJMT somehow have anti-inflammatory properties. Fenugreek has skin-softening properties. The plant is used as a poultice to treat inflammation of the skin [24]. Moreover, it is used as a skin cleanser and to treat wounds and abscesses [25].

Pereira et al. determined that the walnut has antifungal and antimicrobial effects, and walnut leaves are claimed to have antioxidant properties [26]. Walnut has Zhaglon (a naphthoquinone) that is effective in treating cutaneous and especially fungal diseases of the skin and dermatitis, such as rash and hives [14]. It seems that a walnut is likely to prevent secondary infection; it is effective in patients with eczema and prevents patients from becoming resistant to the usual treatment.

Marshmallow is also effective in relieving irritation and has a softening effect. The root has anti-inflammatory properties that can be used in the treatment of burns. [14]. In general, flowers and plant roots can be used as a skin moisturizer, anti-inflammatory and increase the water used on the skin [25].

The anti-itch effect of combining AJMT cream is probably from the chamomile compounds. Chamazulene, The sesquiterpene compounds, bisabolol, and flavonoids in chamomile extract have anti-inflammatory and anti-allergy effects. Azole compounds in the essential oil of the plant inhibit the release of histamines and possibly play a major role in the treatment of dermatitis and itching. Skin cream Chamomile (MC) is now available and used as the treatment for skin inflammation, dryness, and cracked skin. [17]. This plant has antimicrobial, regenerative, and antioxidant properties that allow its topical use in the treatment of wet eczema, impetigo and open wounds [27-28-29].

One reason for the different therapeutic effects of herbal creams AJMT and topical steroids on the same characteristic may be the chamomile. Unlike corticosteroids, this plant has antibacterial and skin-healing properties while as mentioned earlier topical corticosteroid effects of this plant are the photos.

Gharavi et al. used a combination of cornflower extract, mallow, chamomile, and marigold in the treatment of disorders of skin dryness. They found that this combination was effective in treating skin roughness [29]. Kazemipour et al. combined garlic, chamomile, and marshmallow in healing surface wounds of the common carp. They came to the conclusion that this combination is effective in healing such ulcers [30]. These studies confirm that marshmallow and chamomile may also be effective in combination AJMT on both inflammation and skin dryness.

Evaluating the anti-inflammatory effects of chamomile cream (MC) and steroids and non-steroid drugs in the treatment of dermatitis, Aertgeerts came to the conclusion that chamomile cream (MC) of both non-vegetarian combination was more effective [31]. The findings of this study were met with recent research direction.

In the present study, the efficacy of chamomile, Marshmallow, walnut leaves, and fenugreek was studied in the treatment of dermatitis that does not exist and thus the effectiveness of this combination of properties inflammatory, antimicrobial, healing, antioxidant and emollient is concerned on these plants.

No overall features exist in a single plant and the cream Fluocinolone alone, and the results may be due to the properties of the composition of the herbal cream. Since chronic eczema requires the long-term use of topical medications such as cortisone and steroids and because all symptoms were resolved with no known long-term side effects from these drugs, such as discoloration of the skin, atrophy, striae and secondary infections, and so on, it can be claimed based on the findings that the herbal cream AJMT is one of the most convenient and effective treatments, and very few side effects in the treatment of hand eczema were seen. At the same time, the need for further investigation and follow-up studies regarding long-term use of the drug is acknowledged.

CONCLUSION

The results show that both Fluocinolone acetonide and cream AJMT can instigate the partial recovery of hand eczema lesions, but the long-term use of corticosteroid can cause skin complications. Because the combination of plants in AJMT improved some symptoms of hand eczema to a greater extent than topical Fluocinolone, it is advised that cream AJMT can be used for the treatment of hand eczema.

CONFLICT OF INTEREST

There is no conflict of interest.

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None

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