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Evaluation of the Effect of Topical *Artemisia dracunculus* Administration on Serum Levels of Selected Interleukins and Spleen Index in Imiquimod-Induced Psoriasis in Male Mice Compared to Clobetasol Propionate (Dermovate (R)) Ointment

Thamer A. Mohammed[*], Shihab H. Mutlag[,1] and Bahaa A. Shihab[***]**

[*]'Ministry of Health and Environment, The State Company for Drug and Medical Appliances.
[**]Department of Pharmacology and Toxicology, College of Pharmacy, University of Baghdad, Baghdad. Iraq
[***]Ministry of Health and Environment, Dermatologists in Al-Suwaira General Hospital, Wasit,Iraq.

Abstract

Psoriasis is a long-lasting autoimmune disease that is characterized by swollen skin patches. Normally, these skin patches are dark, swollen, itchy and scaly. The single application of the innate Toll-like receptor7/8 ligand Imiquimod (IMQ) in mice easily induces a dermatitis that closely resemble human psoriasis, critically dependent on the axis of interleukin-23/interleukin-17. The objective of the study is to test *Artemisia dracunculus* possible protective effect on imiquimod-induced psoriasis in mice in its topical dosage form and to compare this effect with dermovate(R) ointment. *Artemisia dracunculus* prepared as an ointment and has been used topically to mice before imiquimod application. The real study results showed that *A. dracunculus* ointment as well as Dermovate (R) ointment can significantly reduce the psoriasis area and severity index in both (*A. dracunculus* ointment + imiquimod 5%) **(Group IV)** and (Dermovate (R) ointment + imiquimod 5%) **(Group V)** as compared with both (Control group) (**Group I):** and (Vehicle ointment + imiquimod 5%) **(Group III)**.
All the results showed that *A. dracunculus* ameliorates psoriasis induced by imiquimod in male mice
Keywords: Psoriasis, Artemisia dracunculus, Imiquimod 5%, IL-23, IL-17.

التأثير الموضعي لنبات الشيح الطرخوني على مستويات الإنترلوكينات المختارة في المصل ومؤشر الطحال في الصدفية

ثامر عبدالله محمد*،١ ، شهاب حطاب مطلك،١ و بهاء احمد شهاب *****

* وزارة الصحة والبيئة ،الشركة العامة لتسويق الادوية والمستلزمات الطبية.
** فرع الادوية والسموم ، جامعة بغداد، بغداد ،العراق.
*** وزارة الصحة والبيئة ، مستشفى الصويرة العام ، واسط ، العراق .

الخلاصة

الصدفية هي مرض مناعي ذاتي طويل الأمد يتميز ببقع جلدية منتفخة. عادة ، تكون بقع الجلد داكنة ومتورمة وتسبب حكة ومتقشرة. إن استخدام الاميكويمود الذي يعمل على مستقبلات Toll 7/8 في الفئران يحث بسهولة على التهاب الجلد الذي يشبه الصدفية البشرية بشكل كبير ، والذي يعتمد بشكل حاسم على محور interleukin-23 / interleukin-17. الهدف من هذه الدراسة هو اختبار التأثير الوقائي المحتمل للاستخدام الموضعي لمستخلص نبات الشيح الطرخوني على الصدفية التي يسببها الاميكويمود في الفئران ومقارنة هذا التأثير مع مرهم الدرموفيت. تم تحضير مستخلص نبات الشيح الطرخوني كمرهم وتم استخدامه موضعياً للفئران قبل وضع الاميكويمود. أظهرت نتائج هذه الدراسة أن مرهم نبات الشيح الطرخوني وكذلك مرهم الدرموفيت يقلل وبشكل كبير مقياس مساحة منطقة الصدفية ومؤشر شدتها في كل من المجموعات (مرهم نبات الشيح الطرخوني + اميكويمود ٥٪)(مجموعة رقم ٤) و (درموفيت مرهم + اميكويمود ٥٪)(مجموعة رقم ٥) بالمقارنة مع كل من (المجموعة الضابطة)(مجموعة رقم ١) ومجموعة (المادة الحاملة + اميكويمود ٥٪)(مجموعة رقم ٣).
جميع النتائج اظهرت أن مرهم نبات الشيح الطرخوني يخفف بشكل كبير من الصدفية الناشئة من استخدام الاميكويمود في الفئران الذكور.
الكلمات المفتاحية: الصدفية ،الشيح الطرخوني، الاميكيمود ٥٪ ، IL-23، IL17

Introduction

Psoriasis is one of the world's most common forms of chronic dermatitis. The latest U.S. epidemiological study showed a prevalence rate of 2.6 percent of the population, which translated into more than 6 million Americans(1) .

Psoriasis is an organ-specific autoimmune disease that is triggered by an activated cellular immune system and is similar to other immune-mediated diseases such as Crohn's disease, rheumatoid arthritis (RA), multiple sclerosis (MS) and juvenile-onset diabetes(2) .

[1]Corresponding author E-mail**:** shihabalhattab@gmail.com
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Because of its high prevalence, psoriasis is considered to be one of the costliest dermatological diseases. Estimates of the costs per patient differ significantly depending on the severity of the disease.[3]

Psoriasis can start at any age, although epidemiological studies suggested that it can most commonly occur for the first time between the ages of 15 and 25.[4] Moreover, its prevalence estimates vary from 0.5% to 4.6%, with rates varying from country to race. In higher latitudes, psoriasis tends to be more common than in lower latitudes and it is more Caucasians than in other races.[5]

At present, the combination of genetic, epigenetic and environmental influences is believed to trigger psoriasis.[6]

Environmental risk factors trigger the body's immune response, where naive T cells in the epidermis, particularly Langerhans cells, are triggered by antigen-presenting cells (APC) which can release cytokines such as interleukin IL-12 and IL-23, encouraging the differentiation of naive T cells into Th1 and Th17 cells. [7]

Psoriasis vulgaris is mediated by T cells and dendritic cells. IL-23 and IL-12 are released by inflammatory myeloid dendritic cells to activate IL-17 producing T cells, Th1 cells, and Th 22 cells to produce abundant psoriatic cytokines IL-17, IFN-γ, TNF, and IL-22.[8]

Significant associations have also been identified in gene regions involving specific inflammatory pathways, namely IL-23 signaling (IL23A, IL12B and IL23R), immune response modulation (IL4, IL13) and nuclear factor kappa-light-chain-enhancer of activated B cells (NFkB) signaling.[9]

Histopathology of various clinical types of psoriasis includes; hyperkeratosis, parakeratosis, acanthosis, elongation of rete ridges, micro-munro abscess, capillary dilatation and dermal infiltration.[10]

It has been reported that the imiquimod (IMQ) 5% cream, which is recommended for the treatment of actinic keratosis and external genital warts; can stimulate the immune system. It was stated that antigen-presenting cells such as monocytes/macrophages and interferon-producing dendritic cells (IFNs) and other cytokines and chemokines can be stimulated by imiquimod.[11] Furthermore, IMQ was reported to stimulate immune cells through the Toll-like signaling pathway 7 (TLR7)-Myeloid differentiation primary response 88 (MyD88).[12]

The single application of the innate TLR7/8 ligand IMQ can easily induce dermatitis that closely resembles human psoriasis, critically dependent on the axis of IL-23/IL-17. This quick and convenient model makes it possible to further elucidate pathogenic mechanisms and test new psoriasis therapies.[13]

Genus Artemisia is principally a temperate northern hemisphere plant group. A few of its 250 species, however, extend to South America and southern Africa.[14]

Artemisia dracunculus L. (Tarragon) is a common seasoning plant used in both its fresh (leaves) and dried (herbs) condition. Tarragon plant is also used for medicinal purposes: it contains 0.05–0.95 percent essential oil, flavonoids, cumarin, phenolic compounds, carotenoids, bitter tastes ,tannins, and mineral compounds.(15) The chemical composition of essential oil (EO) of *A. dracunculus* is estragol (methyl chavicol) in EO reached 84.9%. The other components were trans-beta-ocimen (4.00%), linalool (5.09%), limonene (1.63%), (Z,E)-alloocimene (2.29%), beta-ocimen (0.61%) and 3-caren (0.81%).[16]

Abtahi Froushani SM et al. has been reported that Tarragon decreases the development of IL-17 and IFN-γ pro-inflammatory cytokines, as well as the reduction in splenocyte, ratios of INF-γ to IL-10 and IL-17 to IL-10. In addition, it was observed that the amount of respiratory bursts and nitric oxide production in peritoneal macrophages and the capacity for phagocytosis of macrophages in mice treated with Tarragon were reduced.[17]

Safari H et al (2019) has been reported that *A. dracunculus* extract administration ameliorates the symptoms of experimental autoimmune encephalomyelitis (EAE) in mice. It also caused a decrease in the levels of inflammatory cytokines, including IL-17and IL-23, and caused an increase in the levels of serum antioxidants in the *A. dracunculus* treated mice.[18]

Lee SY et al (2018) have also approved that the extract of some species of *Artemisia* (*Artemisia capillaries*) was effective in the alleviation of psoriatic symptoms in an Imiquimod-Induced Psoriasis Models.[19]

The aim of the study

To test Artemisia dracunculus possible protective effect on imiquimod-induced psoriasis in mice in its topical dosage form and to compare this effect with Dermovate [(R)] ointment.

Materials and Methods

Interleukin 23 and interleukin 17 kits for mice were purchased from CUSABIO Company – China.

Preparation of the ointment

Water in oil emulsion base (w/o) was prepared according to British pharmacopoeia 2019 with the help of the pharmaceutics department /College of Pharmacy /University of Baghdad.

Seventy-five grams of wool fat were melted in a beaker on a water bath to which 25 grams of 75 ºC heated water was added with continuous stirring until congealed. Then 5 gm of the steroid fraction of *Artemisia dracunculus* extract (which is extracted with hexane and ethanol) [20] (with the aid of Pharmacognosy department) was incorporated in the prepared base using a spatula.[21]

Animals

Eight to eleven-week-old BALB/c albino male mice weighing about 20 grams each were supplied from the College of Pharmacy's Animal House, University of Baghdad. The mice were housed in five cages, 8 mice per cage, with sawdust bedding material at 20 ± 1 °C under strict hygienic conventional conditions and subjected to a 12-hour light/12-hour dark cycle at the Animal House. Five cages containing 8 mice per cage were used. The mice were acclimatized for one week, before and during the experiment, and provided with water and *ad libitum* food.

The experiments were carried out in compliance with the International and National Standards for Ethical Conduct in animal care and use and approved by the Faculty of Pharmacy's Animal Ethics Committee.[22]

Induction of psoriasis

Psoriasis was induced by the topical application of a commercially available IMQ 5 percent cream (Aldara; 3 M Pharmaceuticals) on the mice's shaved dorsal skin. For nine consecutive days, a daily topical dose of 62.5 mg (5 percent) of medication was applied, translating into a daily dose of 3.125 mg of the active ingredient.[23]

Experimental protocol

The dorsal skin of forty mice was shaved with an Electric Hair Clipper. All mice were weighed at zero time and the thickness of their right ear was measured with a digital Vernier every two days for 9 consecutive days. The mice were divided into five groups (8 mice each) for topical experiment as the follows:

1. Control group (Group I): Mice in this group received a daily application of 62.5mg/2cm dose of the vehicle of Artemisia dracunculus ointment (wool fat) on their shaved dorsal skin and (5mg) on right ear for 9 consecutive days.

2. Artemisia dracunculus only group (Group II): Mice received daily topical dose of Artemisia dracunculus ointment (62.5mg/2cm) on their shaved dorsal skin and (5mg) on right ear for 9 consecutive days.

3. Vehicle -Imiquimod group (Group III): Mice received daily topical dose of the vehicle of Artemisia dracunculus ointment (wool fat) one hour before imiquimod 5% application (62.5mg/2cm) on their shaved dorsal skin and (5mg) on right ear for 9 consecutive days.

4. Artemisia dracunculus-IMQ-treated group (Group IV): Mice received daily topical dose of Artemisia dracunculus ointment one hour before imiquimod 5% application (62.5mg/2cm) on their shaved dorsal skin and (5mg) on right ear for 9 consecutive days.

5. Clobetasol propionate (dermovate$^{(R)}$)-IMQ-treated group (Group V): Mice were received daily topical dose of 0.05% of clobetasol propionate (dermovate $^{(R)}$) ointment one hour before IMQ 5% application (62.5mg/2cm) on their shaved dorsal skin (62.5mg/2cm) and (5mg) on right ear for 9 consecutive days.

Psoriasis Area and Severity Index (PASI) Calculation

Scoring of skin redness and dorsal skin scaling was done with an objective scoring system on a scale of 0 to 4 (0, none; 1, slight; 2,moderate; 3, marked; 4, very marked). This scoring system is based on the medical Psoriasis Area and Severity Index (PASI), except that the thickness of the skin is measured without taking into account the width of the affected area of the body.[24]

Changes of spleen and calculation of its index

Mice were weighed before being sacrificed, and then, each mouse's spleen was weighed. The spleen index (spleen index =spleen weight/ body weight) was calculated to reflect the changes of body dynamic.[25]

Measurement of ear thickness

The ear thickness (mm) of each mouse was measured with a digital Vernier caliper, at (0, 2,4,6,8 days). The change in ear thickness was used to demonstrate the severity of the inflammation.[26]

Measurements of skin thickness

At the end of the experiment (day 10) the skin thickness of the dorsal area of each mouse was measured (in mm) with an electronic Vernier caliper and the measured thickness was compared with those of the other groups.[27]

Preparation of serum

Blood was collected in an Eppendorf tube by heart puncture, allowed to clot for 15-20 minutes and then centrifuged at 300 rpm for 15 minute. The supernatant, which is the serum, was separated using micropipette and stored at -20 °C until the day of analysis. The serum was utilized for the estimation of serum IL-23 level (pg/ml) and serum IL-17 level (pg/ml).[28]

Statistical analysis

Data were expressed as the mean ± standard deviation (SD). The significance of differences between the mean values was calculated using one way and two ways ANOVA. *P*-value equal to and less than 0.05 were considered significant for all the results data of this study.

Results

Effect of various treatments on the Psoriasis Area and Severity Index (PASI) score in male mice

Table 1 and Figure 1 show that, there was a significant elevation ($P \leq 0.05$) in PASI score in the (vehicle ointment+5% IMQ) group (**Group III**) compared to PASI score of the control group (**Group I**). Furthermore, it can be noticed that in the (*A.dracunculus* ointment +5% IMQ) group (**Group IV**), the topical application of *A.dracunculus* caused significant reduction ($P \leq 0.05$) in PASI score in comparison with the (vehicle ointment + IMQ) group (**Group III**). Also, in the ((clobetasol propionate (dermovate$^{(R)}$) ointment + 5% IMQ)

group (**Group V**), the PASI score was significantly reduced ($P \leq 0.05$) in comparison with the scores of the (vehicle ointment + 5% IMQ) group (**Group III**). In the *A. dracunculus* ointment only group (**Group II**) there was no change in PASI score during the study.

Table 1.The comparison of Psoriasis Area and Severity Index (PASI) score mean among male mice groups

Psoriasis Area and Severity Index (PASI) score				
Control (Group I)	A. dracunculus ointment only (**Group II**)	Vehicle ointment + 5% IMQ (**Group III**)	A. dracunculus ointment + 5% IMQ (**Group IV**)	Clobetasol propionate (Dermovate ®) ointment + 5% IMQ (**Group V**)
Zero	Zero	7.12±0.64*	4.12±1.12*#	2.28±0.48*#

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # $P<0.05$ significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

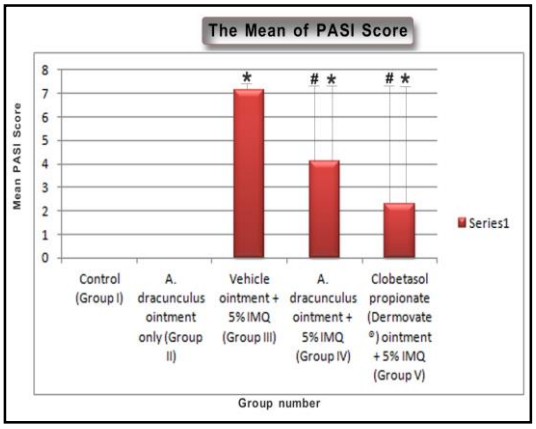

Figure 1. The mean of PASI score of the groups affected by imiquimod

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # $P<0.05$ significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

Effect of various treatments on ear and dorsal skin thickness (mm) in male mice

Tables 2 and 3, and Figures 2 and 3 show that, there was non-significant ($P>0.05$) difference in both ear and dorsal skin thickness (mm) in the (*A. dracunculus* ointment only) group (**Group II**) compared to the corresponding values in the control group (**Group I**). Furthermore, there was a significant increment ($P \leq 0.05$) in both ear and dorsal skin thickness (mm) in the (vehicle ointment + 5% IMQ) group (**Group III**) compared to those thickness in the control group (**Group I**); but in the (*A. dracunculus* ointment + 5% IM Q) group (**Group IV**), the measured ear and dorsal skin thickness (mm) were significantly reduced ($P \leq 0.05$) in comparison with those of the (vehicle ointment + 5% IMQ) group (**Group III**); while in the (clobetasol propionate (dermovate® ointment + 5% IMQ) group (**Group V**), there was a significant reduction ($P \leq 0.05$) in both ear and dorsal skin thickness (mm) in comparison with those of the (vehicle ointment + 5% IMQ) group (**Group III**).

Table 2. Comparisons of ear thickness (in mm) among various groups

Day	Control (Group I)	A. dracunculus ointment only (Group II)	vehicle ointment + IMQ (Group III)	A. dracunculus ointment + IMQ (Group IV)	Clobetasol propionate (Dermovate ®) Ointment + 5% IMQ (Group V)
0	0.22 ± 0.01	0.23 ± 0.02	0.23 ± 0.01	0.20 ± 0.02	0.20 ± 0.01#
2	0.22 ± 0.01	0.23 ± 0.02#	0.26 ± 0.01*	0.21 ± 0.01#	0.21 ± 0.01#
4	0.22 ± 0.01	0.23 ± 0.02#	0.31 ± 0.01*	0.21 ± 0.02#	0.22 ± 0.01#
6	0.22 ± 0.01	0.23 ± 0.02#	0.35 ± 0.01*	0.22 ± 0.01#	0.22 ± 0.009#
8	0.22 ± 0.01	0.23 ± 0.02#	0.40 ± 0.01*	0.22 ± 0.02#	0.22 ± 0.01#

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # $P<0.05$ significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

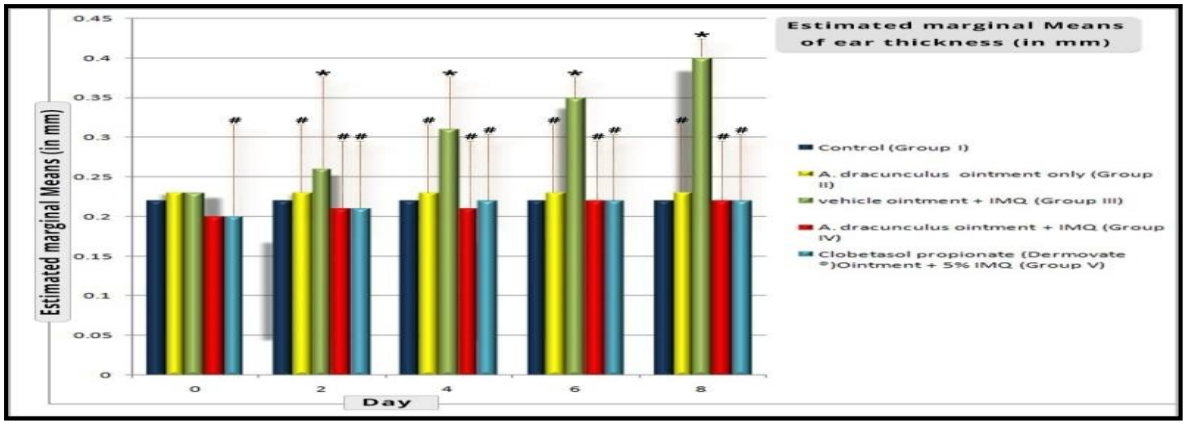

Figure 2. Bar chart showing the comparison of ear thickness (in mm) of various experimental mice groups.

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # *P*<0.05 significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

Table 3. Comparisons of dorsal skin thickness (in mm) among various groups

Dorsal skin thickness (in mm) comparison between the groups					
Groups	Control (**Group I**)	A. dracunculus ointment only (**Group II**)	vehicle ointment + IMQ (**Group III**)	A. dracunculus ointment + 5% IMQ (**Group IV**)	Dermovate ®ointment + 5% IM Q (**Group V**)
	0.50 ± 0.09	0.37 ±0.09#	0.74 ±0.13*	0.50 ±0.12#	0.51 ±0.07#

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # *P*<0.05 significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

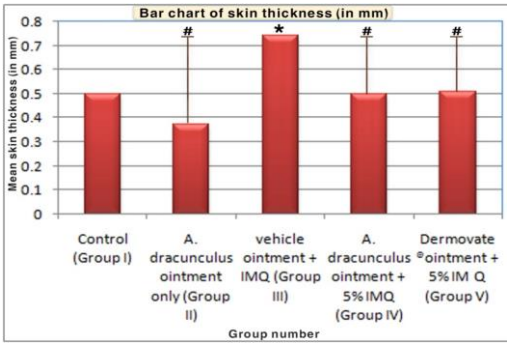

Figure 3. Bar chart showing the comparison of dorsal skin thickness (in mm) of various experimental mice groups.

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # *P*<0.05 significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

Effect of topical administration of Artemisia dracunculus on the spleen index in imiquimod-induced psoriasis in mice

Table 4 and Figure 4 show that, there was a non-significant (*P*>0.05) difference in the measured spleen index in the (*A. dracunculus* ointment only) group (**Group II**) compared to the corresponding measured spleen index in the control group (**Group I**). Furthermore, there was a significant increment (*P*≤0.05) in the measured spleen index in the (vehicle ointment + 5% IMQ) group (**Group III**) compared to those measured spleen index in the control group (**Group I**); but in the (*A. dracunculus* ointment + 5% IMQ)) group (**Group IV**), the measured spleen index was significantly reduced (*P*≤0.05) in comparison with those of the (vehicle ointment + 5% IMQ) group (**Group III**); while in the (clobetasol propionate (dermovate ® ointment) + 5% IMQ) group (**Group V**), there was a significant reduction (*P*≤0.05) in the measured spleen index in comparison with the control group (**Group I**).

Table 4. Comparison of spleen index among various groups (mg/gm)

spleen index comparison between the groups					
Groups	Control (**Group I**)	A. dracunculus ointment only (**Group II**)	Vehicle ointment + 5% IMQ (**Group III**)	A. dracunculus ointment + 5% IMQ (**Group IV**)	Clobetasol propionate (Dermovate ®) ointment + 5% IMQ (**Group V**)
	6.17 ± 1.78	4.81 ± 1.74#	18.67 ± 7.72*	7.44 ± 1.90#	6.12 ± 3.26#

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # $P<0.05$ significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

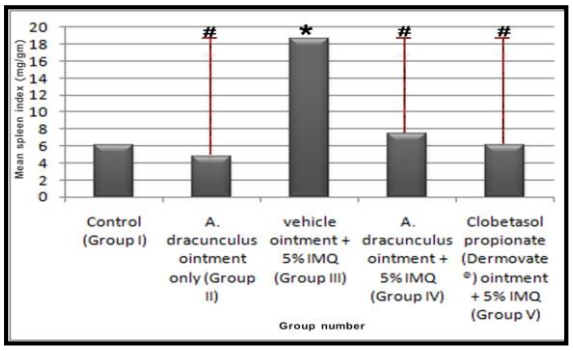

Figure 4. Bar chart showing the comparison of spleen index in (mg/gm) of various experimental mice groups.

- Each value represents mean ± standard deviation (SD).- *= Significantly different with respect to the control group (**Group I**).- # $P<0.05$ significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).- IMQ: Imiquimod.

Effect of various treatments on serum IL-23 and IL-17 level in male mice

Table 5 and Figure 5 show that, there was a significant elevation ($P\leq0.05$) in both serum levels of IL-23 and IL-17 in the (vehicle ointment + 5% IMQ) group (**Group III**) compared to the corresponding levels in the control group (**Group I**) mice; as well as, in the (clobetasol propionate (dermovate ®) ointment + 5% IMQ) group (**Group V**). There was a significant decrease in serum IL-23 and IL-17 levels compared to the (vehicle+ 5% IMQ) group (**Group III**). By comparing the (*A. dracunculus* ointment+5% IMQ) group (**Group IV**) with the (vehicle+ 5% IMQ) group (**Group III**), there was a significant reduction in serum IL-23 and IL-17 levels. Serum IL-23 and IL-17 levels significantly decreased in the (*A. dracunculus* ointment only) group (**Group II**) compared with the (vehicle+ 5% IMQ) group (**Group III**).

Table 5. Comparison of various treatments on serum IL-23 and IL-17 levels.

Groups	Serum IL-23 level (Mean ± SD)pg/ml	Serum IL-17 level (Mean ± SD) pg/ml
Control (Group I)	170.05 ± 55.47	261.56 ± 46.34
A. dracunculus ointment only (Group II)	146.15 ± 36.56#	303.32 ± 53.47#
Vehicle ointment + 5% IMQ (Group III)	638.84 ± 50.75*	692.69 ± 75.81*
A. dracunculus ointment + 5% IMQ (Group IV)	226.53 ± 75.38#	224.41 ± 35.05#
Clobetasol propionate (Dermovate ®) ointment + 5% IMQ (Group V)	211.039 ± 36.43#	197.53 ± 47.04#

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # $P<0.05$ significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

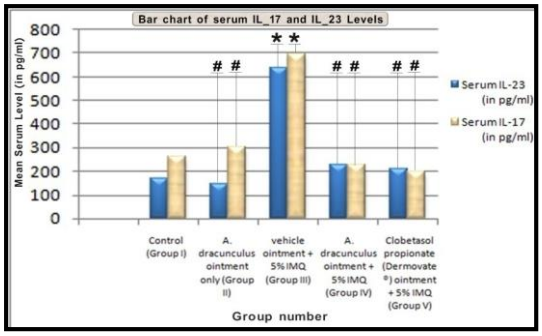

Figure 5. Bar chart showing the comparison of serum IL_23 (pg/ml) and serum IL_17 (pg/ml) levels in the various experimental mice groups.

- Each value represents mean ± standard deviation (SD).
- *= Significantly different with respect to the control group (**Group I**).
- # $P<0.05$ significant in comparison with the (vehicle ointment + 5% IMQ) group (**Group III**).
- IMQ: Imiquimod.

Discussion

Psoriasis is a major public health concern affecting approximately 125 million people worldwide. Most of the statistics on prevalence and incidence of psoriasis was obtained from European countries, the UK. and the United States , there is therefore still a need for a leading, coherent global epidemiological tool on the epidemiology of psoriasis.[29]

Previous data showed that psoriasis incidence varied depending on age and geographic location, being more prevalent in countries more distant from the equator.[30]

The statistical calculation of PASI score indicated that the prepared ointment of A. dracunculus significantly ($P<0.05$) ameliorates the psoriasis-like skin inflammation in Group IV mice received topical A. dracunculus ointment 1hr before 5% IMQ in comparison with the (vehicle ointment + 5% IMQ) (Group III) as shown in table 1 and Figure 1.

Previous studies concerning A. Dracunculus indicate pharmacological properties of this plant, including anti-inflammatory, antibacterial, antidiabetic and antioxidant properties.

Studies have also shown that Tarragon inhibited the production of pro-inflammatory cytokine (interleukin 6) and nitric oxide, indicating its anti-inflammatory property and this consistent with results of the current study [31].

Psoriatic lesions are a result of a complex interplay of dermal infiltrates of activated dendritic cells, T cells, cytokines including but not limited to IFN-γ, tumor necrosis factor α (TNF-α), interleukin (IL)-12, IL-17, and IL-23.[32]

The immunological pathway of IL-23/IL-17 plays a particularly important role in promoting the onset and perpetuation of a disease. Data from in vitro and clinical studies show that IL-17A, a critical cytokine effector in this pathway, is primarily responsible for changes in affected tissues.[33]

Table 5 and Figure 5 showed that there was a significant reduction in serum IL_17 and IL_23 levels in the (*A. dracunculus* ointment+5% IMQ) group (Group IV) as compared with the (vehicle ointment + 5% IMQ) group (Group III). These findings indicated that *A. dracunculus* affects serum IL-17 and IL-23 levels induced by imiquimod.

Innate immune cells such as dendritic cells (DCs) play a critical role in psoriasis pathophysiology by supplying inflammatory / co-stimulative cell differentiation signals for Th17 cells. A recent study (2019) showed the involvement of spleen tyrosine kinase (SYK) in the inflammatory signaling cascade of DC; and the spleen tyrosine kinase (SYK) has also emerged as one of the targets in the cascade of inflammatory signals whose inhibition (by substances such as Tarragon) results in anti-inflammatory effects [34]. Results of the present study (table 4 and Figure 4) are in accordance with those obtained from previous study.

Conclusion

All the results demonstrate that A. *dracunculus* act as a potent anti-psoriatic agent in comparison with the Dermovate® ointment topical administration. It will be a promising intervention in psoriasis in the future. Overall, all the results indicated that *A. dracunculus* suppress serum IL-17, IL-23 level, as indicated by the reduction of (ear and skin thickness and spleen index) which may explain its anti-psoriatic activity.

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