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Study the Topical Effect of Six Days Use of Different Lycopene Doses on Imiquimod-Induce Psoriasis-Like Skin Inflammation in Mice

Samer Shukur Mohammed

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Al-Rafidain University College, 10052 Baghdad, Iraq
Email: samer.shukur@ruc.edu.iq

Haitham Mahmood Kadhim

Department of Pharmacology, College of Pharmacy, Al-Nahrain University, Baghdad, Iraq
Email: samerhl2011@gmail.com

Israa Mahdi Al-Sudani

Ibn Sina University of Medical and Pharmaceutical Sciences, Baghdad, Iraq
Email: Israa.Mahdi2022@gmail.com

Wael Waleed Musatafa

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Al-Rafidain University College, 10052 Baghdad, Iraq
Email: wael.walid@ruc.edu.iq

Abstract---Lycopene is a hydrocarbon phytochemical that is present in red vegetables and fruits, several studies reviewed the pharmacological properties of Lycopene across years ago and in different aspects including inflammation, cardiovascular disease, prostatic cancer and different dermatological complaints. Objective: we investigated the potential impact of two different doses of topical Lycopene and as add on therapy to Clobetasol on Psoriasis model that induced by Imiquimod in mice. Methods: This was accomplished by dividing 48 mice into six groups (8 mice per each group). All groups received Imiquimod for induction of Psoriasis (except Group I which is healthy group) across the experiment days. Group II (Induction group) received Petrolatum gel (Vaseline) for six days after 6 days induction period with Imiquimod. The rest groups III, IV,V,VI received Clobetasol propionate 0.05%, 0.125 mg/ml Lycopene, 0.25 mg/ml Lycopene and combination of 0.25 mg/ml Lycopene and 0.05% Clobetasol propionate ointments respectively once daily for six days after 6 days

of induction period with Imiquimod. The results showed that Lycopene had significant anti psoriatic activity through decreasing PASI score and improving histological changes that occurred during Imiquimod application, also It restored the level of serum and tissue inflammatory bio markers (TNF- α , IL-17, IL-23 and NF-K β) significantly especially when using Lycopene as add on therapy to Clobetasol propionate. Conclusion: Lycopene has considerable anti psoriatic activity against Imiquimod induced psoriasis through anti-inflammatory effect, anti-proliferative effect.

Keywords---imiquimod-induce, inflammation, lycopene doses, psoriasis-like skin, topical effect.

Introduction

We can consider Psoriasis as a widespread, chronically persistent illness that is transmitted genetically, most possibly with a dominant mode with variable penetrations, disfiguring, recurring inflammatory and proliferative disease of the skin.(1). Psoriasis has a complicated etiology. In psoriatic lesions, the inflammatory infiltrate is largely composed of activated T cells, according to many studies (2). Approximately (1.3 %-34.7 %) psoriasis individuals experience psoriatic arthritis, contributing to joint deformations and impairment (3). There are five kinds of psoriasis which include guttate, inverse, plaque, erythrodermic and pustular based on clinical appearance. The most prevalent type of plaque is the chronic type, which accounts for between 85% and 90% of all cases. Keratinocyte proliferation and differentiation can be impaired in psoriasis owing to a defect in the acquired and innate immune systems in the layers of the skin. (4). Many immune cells, including dermal dendritic cells, natural killer [NK] T lymphocytes, and neutrophils, play a significant role in recognition of an antigen by the innate system. The mature CD4+ and CD8+ T cells in the skin are the mediating agents for adaptive immunity. The histocompatibility complex (HCC) allows activated myeloid dendritic cells to communicate with T lymphocytes in the lymph nodes (MHC). T lymphocyte CD4+ cell development and proliferation into the Th17 and Th1 cell subsets is aided by the release of pro-inflammatory cytokines by myeloid dendritic cell monocytes. IL-23, IL-12, and TNF- α are cytokines were also involved in pathogenesis of psoriasis. The adaptive immune system must be activated in order to maintain the psoriatic inflammation maintenance phase. Th17 cells secrete cytokines such as IL-17, IL-21, and IL-22, which stimulate the growth of Keratinocytes in the epidermis via activation of the JAK/STAT pathway. As a result of this activation, pro-inflammatory gene transcription is phosphorylated and modulated (5). Additionally, TNF- α , IL-17, and IFN- γ stimulate keratinocyte growth. The TNF--IL-23-Th17 inflammatory pathway is essential in signaling pathways that contribute to the development of plaque-type psoriasis (6). NF-kB is one of proinflammatory gene expression's most powerful regulators. NF-kB mediates cytokine synthesis, for instance the tumor necrosis factor (TNF)- α , Interleukin-6, Interleukin-8 and interleukin (IL)-1 β . During psoriasis, several cytokine transcriptions factors and inflammation mediators released from chronic inflammatory cells that follow the lesions,

modulated and controlled. As NF-kB regulates cytokine gene expression, NF-kB is possibly one of the major factors of disease pathogenesis (7).

Lycopene is a hydrocarbon phytochemical that is present in fruits and vegetables with red color like pink guava, tomato and watermelon, Lycopene appeared to be effective in a different variety of cell lines, including those from oral, prostate cancers (8). Lycopene is also beneficial for patients who suffer from cardiovascular disease (9). Additionally, a study demonstrated that high level of blood lycopene can help lowering oxidative stress and enhancing the function of endothelial cells (10). Furthermore, It showed suppression activity on NF-KB and the production of adhesion molecules in endothelial cells (11). Also, Human keratinocytes can be protected against damage from full spectrum UVR by lycopene according to a prior dermatology study (12). Due to its ability to link between innate and adaptive immunity, Imiquimod can rapidly induces dermatitis similar to human psoriasis, with critical dependency on the IL23/IL17 axis. This rapid and convenient model has an important application in using Imiquimod in inducing Psoriasis like dermatitis and evaluate new treatment strategies and therapies (6). The purpose of this study was to determine the potential therapeutic effect of Lycopene ointment in two different dose (0.125mg and 0.250 mg) and the effect of add on therapy of 0.25mg/ml Lycopene to Clobetasol 0.05% ointment on psoriasiform skin inflammation in mice that provoked by Imiquimod through their effects on index scores of skin (PASI score), serum level of TNF- α , IL-17, IL-23 and NF-KB and tissue level of mentioned markers. In addition, It's effects on histopathological changes would also be studied.

Materials and Methods

Drugs and Reagents

Meda Pharmaceutical Co. (Germany) is the manufacturer of Imiquimod (5%w/w) while Lycopene supplied from Hyperchem (China) for animal studies. Clobetasol 0.05% ointment was purchased from GSK (UK).

Preparation of Lycopene ointment

The composition of Lycopene (0.125mg/ml and 0.25 mg/ml) was grinded in mortar together with equal volume of glycerin (10% w/w) which act as moistening agent, Then add the previous mixture that contain the drug to equal volume of Vaseline and do the dilution, complete the dilution through geometric method until completing the whole volume of Vaseline to get 100ml of preparation (13).

Experimental design and Animals Models

The study was considered as randomized controlled animal design. The work of this study was accomplished Pharmacology department, College of Medicine- AlNahrain University between December 2020 and December 2021. the study was reviewed and accepted by Institutional review board in Medicine College- AlNahrain University. 48 BALB/c Albino mice with 8-11 weeks of age and average body weight 25-40 g obtained from the animal house of Al-Razi scientific center in Ministry of Industry and minerals. Mice were kept in polypropylene

cages and fed a regular pellet meal along with unlimited access to water. Mice were allowed to acclimate for seven days before the study begin, after which they were randomly divided into six groups of eight mice each.

Study design

Shaving the backs of mice prior to daily application of 62.5mg Imiquimod (IMQ) to the back skin of the mouse generated a scaly, inflammatory lesion identical to plaque psoriasis. These lesions exhibit characteristic differentiation and increased epidermal proliferation. The included mice were randomly assigned into the following groups:

- Group I (Control group): apparently mice that are untreated and normal.
- Group II (Induction group): topical dose (62.5mg) of Imiquimod cream (5%) on the shaved dorsal skin for 12 days (6), use of Vaseline petrolatum jell topically for 6 days starting from day 7 .
- Group III (Clobetasol 0.05% ointment group): mice received Imiquimod (as in Group II) and then were treated with clobetasol ointment (0.05%) topically once daily from day 7 for 6 consecutive days (14).
- Group IV (Lycopene 0.125 mg/ml group) : mice received Imiquimod (as illustrated in second group) for 12 days and Lycopene ointment (0.125 mg/ml) topically once daily for six days started from day 7 (15)
- Group V (Lycopene group): mice received IMQ cream (5%) for 12 consecutive days (as mentioned in induction group) and with Lycopene ointment (0.25 mg/ml) topically once daily for six days started from day 7.
- Group VI (combination of Clobetasole 0.05% and Lycopene 0.25 mg/ml): mice received IMQ cream (5%) for 12 days (as mentioned in induction group) and treated with combination ointment of Clobetasole 0.05% and Lycopene 0.25 mg/ml topically once daily for 6 days started from seventh day.

Animal preparation and sampling

After completing the procedure mentioned above, all mice are sedated through using diethyl ether as inhalation (i.e., by a piece of cotton saturated with diethyl ether and put in a glass jar) then, they were sacrificed at day 13 of the test. The blood were collected through cardiac puncture and serum was separated by centrifugation at 2000 rpm for 10 minutes and get the supernatant in Eppendorf tube and stored at -80 C for later ELISA testing (16). The skin samples were mixed with Buffer phosphate saline (1:10 parts), then harvested and prepared for tissue homogenate by electric tissue homogenizer (Staruar, England), centrifuged at 5,000 rpm for 10 minutes to get the supernatant and stored at -80 C for later inflammatory biomarkers examinations (17). In addition to that, the skin tissue samples were kept in 10% formalin and processed for histological study.

Laboratory investigation

Clinical scoring of severity of skin inflammation

PASI is a modified human scoring system based on the Psoriasis Area Severity Index (PASI) that represented a quantitative measure for the severity of inflammation throughout the application procedure, It is composed of erythema,

thickness, and scaling and is rated individually on a scale of 0 to 4, with 0 indicating no signs, 1 indicating faint signs, 2 indicating moderate signs, 3 indicating marked signs, and 4 indicating extremely marked clinical indicators (18,19).

Preparation of skin tissue for histopathological investigation

The skin tissues were rinsed with water and were prepared for transport. The specimen was dehydrated by putting them using different ethanol concentrations (70%, 80 %, 90 %, 95 % and 100 %) for 2hrs each. The specimen was dipped in liquid paraffin at a temperature of 55-60 C, after which xylol was added. Tissue was embedded in paraffin on a cool plate, after which paraffin blocks were formed. Microtome was used to get 5 µm Section thickness. Then, the slice section was placed on the slide in presence of water bath. The technique for staining with hematoxylin and eosin required the tissue to be deparaffinized, rehydrated, placed in hematoxylin, and discolored access stain. Then the sample was dipped in eosin stain, followed by dehydration. Added a few drops of di-N-butyl phthalate (Di-N-BTP) in xylene (Xylene: DPX) to the area, applied a coverslip, and sealed it (20).

The specimen was stained using Hematoxylin solution, which was prepared in the following manner: Aluminum potassium sulfate was dissolved in distilled water using heat. While the hematoxylin solution was dissolved in the alcohol, the resulting combination was detached from the heat after the alcohol had boiled. The addition of a very little amount of mercuric oxide was done carefully and with shaking, which was then directly put into cold water (21). Dissolving 2 g of eosin powder in 25 ml of DW, followed by the addition of 475 ml of 100% alcohol, yielded a 500 ml solution of eosin. The extracellular matrix, including the cytoplasm, takes on a reddish or pink stain (21). Semi-quantitative scoring systems for the assessment of mouse model histopathology include epidermal thickening, parakeratosis, hyperkeratosis, Munro abscess, Acanthosis, Lymphocytic infiltrate and papillary congestion (22). On a scale ranging from 0 to 10, Baker's grading system was employed to assess the pathological changes as in table 1 (23).

Table 1
Histopathological scoring of severity of inflammation (Baker scoring system) (22)

Layers	Feature	Score
Keratin	Munro Abscess	2.0
	Hyperkeratosis	0.5
	Parakeratosis	1.0
Epidermis	Thining over Papillae	0.5
	Rete ridges appearance	1.5
	Acanthosis	0.5
	Lack of granular layer	1.0
Dermis	Lymphocytic infiltrate	
	Mild	0.5
	Moderate	1.0
	Severe	2.0

Measurement of inflammatory markers for TNF- α , IL-17, IL-23 and Nuclear factor Kappa B (NF K-B)

The Sandwich-ELISA practice module is practiced on this ELISA kit to evaluate the level of Tumor necrosis factor- α , Interleukin-17, Interleukin -23 and Nuclear factor Kappa B in both serum and skin tissues according the manufacturer instructions. The optical density (OD) was measured spectrophotometrically at 450 nm wavelength (24,25,26,27).

Statistical analysis

Collected data were analyzed using SPSS version 21 under windows 10. Values were presented as a mean $\pm$ standard error of means (SEM) (SEM). Least significant difference –LSD test (Analysis of Variation-ANOVA) was performed to significant compare between means. Chi-square test was done for significantly compare between % 0.05 and 0.01 likelihood (28).

Results

Clinical evaluation

Upon using Imiquimod for 6 days, the morphological changes began to appear from the first 3 days with complete Psoriatic picture after 6 consecutive days. Signs of Erythema, skin thickness and scaling increased upon comparing to Control group (Group I) as in Figure 1 and PASI score was significantly increased (Table 2). After this period, tested drugs were used topically and significant reduction in PASI scores were noted in all other groups.

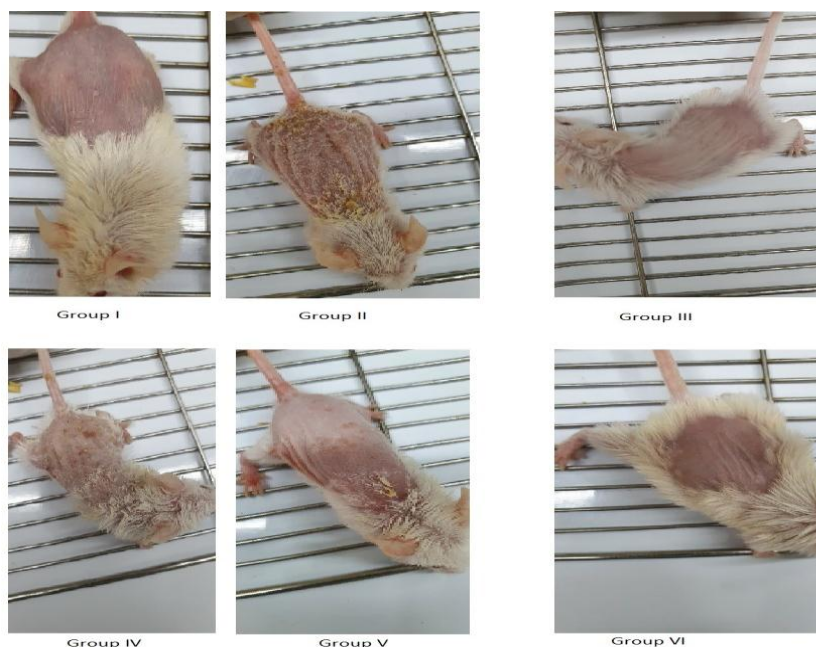


Figure 1. Photographs taken on day 14 of the experiment

Table 2

Effect of tested drug on PASI and Baker scores in Psoriasis induced by Imiquimod

Group No.	Gr.1 (Control)	Gr.2 (Induction) ¹	Gr.3 (Clobetasol)	Gr.4 (Lycopene 0.125 mg/ml)	Gr.5 (Lycopene 0.25 mg/ml)	Gr.6 (Lyco. 0.25mg/ml+ Clob.)
PASI score	0.0±0.0	9.71±0.29	3.29±0.36**	5.33±0.42**	3.67±0.56**	2.0±0.49**
Baker Score	0.00±0.0	7.0±0.39	2.0±0.30**	3.58±0.55**	1.92±0.44**	1.25±0.17**

Histopathological examination

Skin treated with Imiquimod exhibited pathological changes in the epidermis, including significant hyperkeratosis, acanthosis, Munro abscess appearance, an increase in rete-ridges, and perivascular infiltrate of inflammatory cells located in upper dermal layer, feature associated with psoriasis in humans, which were evident in the induction group (group II) and recorded the highest score in Baker scoring system (9.71±0.29). While Clobetasol (Group III), Lycopene (IV, V) and combined groups (VI) significantly decreased overall Baker scores with 3.29±0.36 , 5.33±0.42, 3.67±0.56 and 2.0±0.49 respectively (Table 2) . They reduced epidermal thickness by reducing hyperkeratosis and rete-ridges and reducing inflammatory cell infiltration caused by Imiquimod therapy. While the healthy group (I) demonstrated what seemed to be normal stratified epithelium dermis and epidermis thickness, figure (2) illustrated the histopathological picture for all treated groups.

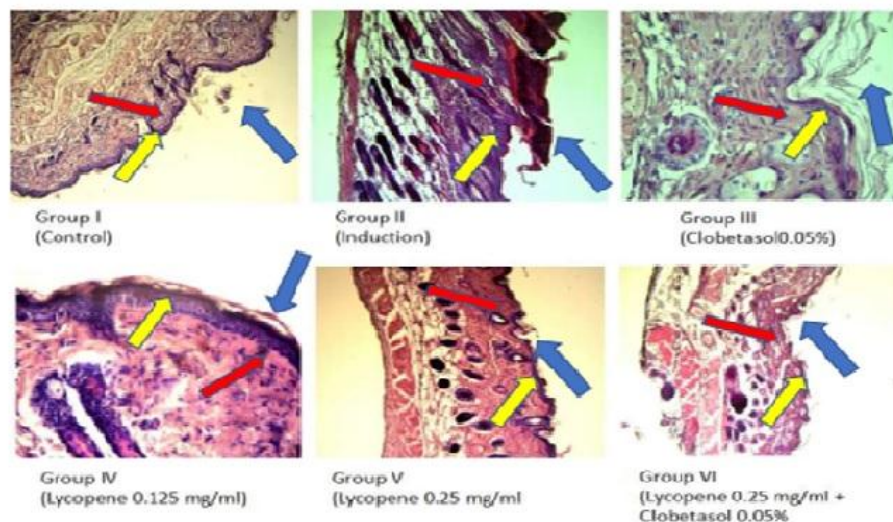


Figure 2. Histopathological representation for all treated group at 10X magnification. Red arrow represent dermis. Epidermis represented by blue arrow while yellow arrow showed Keratinized layer of the skin

Evaluation of serum and tissue biomarkers using ELISA

Table 3 represents the results of statistical analysis of ELISA assays for IL-17, IL-23, TNF- α and NF-K β levels (Mean $\pm$ SEM in Pg/ml) in serum and skin tissue homogenate respectively. When comparing induction group to control group, the levels of IL-17, IL-23, TNF- α and NF-K β were dramatically raised. Clobetasol-treated group had significantly lower levels of both serum and tissue inflammatory biomarkers. While group IV and V treated with 0.125 mg/ml Lycopene and 0.25 mg/ml of same material respectively demonstrated a significant reduction in IL-23, NF-K β and TNF- α with no significant reduction in serum IL-17 upon using low dose of Lycopene. In contrast to that, combined group (Group VI) showed best decreasing effect when comparing with all previous groups with significant reduction in all serum and tissue inflammatory biomarkers.

Table 3
ELISA readings for tested biomarkers in both serum and tissue

Groups	IL-17 (Pg/ml)		Il-23 (pg/ml)		TNF- α (pg/ml)		NF-K β (pg/ml)	
	Serum	Tissue	Serum	Tissue	Serum	Tissue	Serum	Tissue
Group I	7.00 ± 0.87 d	20.14 ± 4.35 f	2.24 ± 0.35 e	7.57 ± 1.90 g	16.42 ± 5.34 e	14.42 ± 3.06 g	54.85 ± 8.22 e	62.85 ± 6.25 h
Group II	27.43 ± 3.61 a	58.00 ± 8.23 i	29.35 ± 5.44 a	40.85 ± 2.59 i	183.14 ± 10.51 a	248.14 ± 18.10 i	242.57 ± 27.27 a	399.85 ± 32.95 i

Group III	12.02 ±3.04 cd	33.57 ±6.05 fjk	9.75 ±1.87 de	15.07 ±1.52 gh	73.85 ±9.62 e	65.28 ±4.26 fh	111.14 ±13.06 cd	131.71 ±12.80 h
Group IV	23.83 ±2.42 a	41.16 ±7.22 jk	20.97 ±2.59 bc	26.00 ±3.23 b	148.33 ±9.99 bc	176.66 ±6.90 b	177.00 ±14.75 b	251.50 ±23.7 bc
Group V	14.28 ±2.12 bcd	33.00 ±4.37 fjk	13.58 ±2.47 cd	17.41 ±2.55 jkh	122.83 ±12.95 cd	138.33 ±4.57 j	113.67 ±11.67 cd	133.33 ±11.33 f
Group VI	9.78 ±2.20 d	25.16 ±2.35 jk	5.65 ±1.27 e	12.33 ±2.59 gh	50.33 ±11.17 e	55.33 ±8.28 h	79.67 ±11.49 de	95.66 ±15.48 fh

Means having different letters in same column differed significantly. P<0.05

IL-17=Interleukin-17, IL-23=Interleukin-23, TNF- α =Tumor Necrosis Factor-alpha and NF-K β =Nuclear Factor- Kappa β ;GI=control ,GII=Induction, GIII=Clobetasol 0.05% , GIV=Lycopene 0.15 mg/ml, GV=Lycopene 0.25 mg/ml while GVI=Lycopene 0.25 mg/ml + Clobetasol ;data represented as mean $\pm$ SEM

Discussion

Studies showed that psoriasis is an autoimmune disease that causes redness, scaling, and thickness of the affected skin as a result of the skin's activated dendritic cells which interact with the surrounding keratinocytes on the surrounding skin surface (29). Psoriasis model is depend on mouse tail model which represent a perfect model for provoking psoriasis due to simplicity in obtaining the psoriasiform skin in these animals with typical phenotype of psoriasis. Mouse model have the same pathophysiological features that seen in human like cutaneous inflammation, hyperkeratosis and dendritic cells CD4 cells manifestation and anti-oxidant system (22).

Imiquimod which is a TLR7/8 agonist specific for toll-like receptors can stimulate innate response through Dendritic cells, monocytes, and macrophages activation and promotes signaling of cytokines cascade through the expression of several inflammatory cytokines in the body. The Th-1 driven immune response is thereby increased, leading to anti-tumor and anti-viral effects (30). Even though IMQ model induces symptoms that are very similar to those of psoriasis, these symptoms resolve spontaneously after six days of treatment. These findings indicated that mice are not genetically damaged and are capable of reverting the inflammatory process in response to IMQ stimulation due to the instability of the adoptive response (14,31). As a result, we administered IMQ to mice's dorsal shaved skin for 12 consecutive days. In The current study, the Imiquimod treatment resulted in significant and greater changes histologically in group II compared to group I, including hyperkeratosis, parakeratosis, acanthosis, appearance of Munro microabcess in epidermal layer, thinning above papillae, lengthening and clubbing over rete ridges, most of samples lost their granular layer and increased inflammatory cell infiltration. The PASI score is significantly higher in the Imiquimod induced group II than that in control group. Imiquimod produces erythema because it may act directly on mast cells via IgE-linked

pathways. Another possibility is that Imiquimod activates mast cells through non-IgE-dependent pathways (32).

ELISA readings for serum and tissue inflammatory biomarkers showed that Imiquimod could highly increase all tested pro inflammatory biomarkers and inflammatory cell signals and it gave a typical picture for plaque psoriasis in mice that resemble to plaque psoriasis occurred in human. These findings were previously discussed by many authors and they showed the effect of Imiquimod on serum and tissue biomarkers (18,33,34,35). Highly potent topical steroids were considered as a gold standard for Psoriasis treatment and their effectiveness due to several mechanism against inflammation and immune suppression (36). Clobetasol's method of action is classified as genomic and non-genomic. The genomic pathway referred to the plasma membrane's Glucocorticoid receptors. Upon binding to its receptors, a steroid molecule migrates into the nucleus and stimulates the development of Glucocorticoids Response Elements, transcription factors with anti-inflammatory capabilities, which are then released into the cytoplasm. (37). The non-genomic route is responsible for the fast action of glucocorticoids. Glucocorticoids have been shown to increase the expression of Annexin A1, a protein that binds to phospholipids and inhibits the synthesis of inflammatory prostanoids. Additionally, it has been found to inhibit the expression and activation of pro-inflammatory cytokines, decrease nitric oxide expression, and affect mast cells function (38). Glucocorticoids promote the transcription of anti-inflammatory genes while inhibiting the transcription of pro-inflammatory genes.

In the current study, Clobetasol exerted a significant inhibitory effect on the inflammatory response generated by Imiquimod. The optimal reduction in PASI score is evident by a decrease in erythema caused by Clobetasol's vasoconstrictor action, which is accomplished by blocking the action of vasodilators such as histamine and bradykinine, and a decrease in thickness and scale caused by Clobetasol's anti-inflammatory and anti-proliferative actions (39). The reduction in clinical severity score is accompanied by an improvement in histological changes associated with inflammatory characteristics, as found in the Clobetasol group (Group III) which appeared through reduction in Hyperkeratosis, Parakeratosis, Munro abscess disappearance, rete ridges, and ameliorating lymphocytic infiltrate. Additionally, when compared to induction group II, the inflammatory cytokines like IL-17, IL-23, TNF- α and NF-K β were considerably reduced when treated with Clobetasol. Despite topical Clobetasol is an effective treatment for psoriasis, it has been found to cause different adverse effects like skin striae, degeneration and telangiectases in addition to their adverse effects which appeared systemically (40). This limitation makes steroidal drugs unsuitable for prolonged usage and the need for new medicine with less adverse effects is increasing.

Lycopene is one of nutraceuticals that can be used to prevent certain disease or to cure some chronic diseases like psoriasis (41). It has many valuable benefits for the skin, it is considered as powerful antioxidant effect and has protective role against harmful effect of UV radiation through initiation of DNA repair pathways (42). In the present study, Both doses of Lycopene showed significant decrease severity score through reduction of erythema, scaling and back skin thickness

with better response with 0.25 mg/ml. these may be attributed to anti-inflammatory effect of lycopene and its ability to inhibit atopic dermatitis in hairless skin in mice that is associated with psoriasis and as previously explained by Hiragun et al. (2016) (43).. These results were supported by ameliorating effect of Lycopene on histological features through decrease hyperkeratosis, Munro abscess, lymphocytic infiltration and papillary congestion with no signs of Acanthosis and Parakeratosis that caused during induction period with Imiquimod. These findings were previously studied and approved that 7 days topical therapy with Lycopene had better effect than 42 days treatment with systemic Lycopene through improving epidermal hyperplasia and proliferation in Imiquimod induced psoriasis in mice (15).

In terms of histochemical analysis by ELISA, there is clear evidence that IL-23/IL-17 play a critical role in Imiquimod induced psoriasis in mice. After dermal dendritic cells are activated, they release IL-23, which promotes the activation and differentiation of T-17 helper cells. These helper cells then secrete pro-inflammatory cytokines which induce the activation and mobilization of other immune cells and keratinocyte proliferation (44). When IL-17 binds to its receptor, it activates the nuclear factor- κ B (NF- κ B) and JUN amino-terminal kinase (JNK) signaling pathways in a TNF- α associated factor. During this study, Lycopene could improve the serum and tissue derived Interleukin 17, Interleukin-23 and NF- κ B especially in high dose of Lycopene (Group V).while TNF- α which is one of the cytokines involved in psoriatic inflammation and considered the master pro-inflammatory marker of the innate immunity due to its multiple origins and targets. It is usually released by T cells, macrophages, monocytes, keratinocytes, natural killer (NK), and antigen-presenting cells. It promotes keratinocyte proliferation, angiogenesis via VEGF and the synthesis of pro-inflammatory cytokines.in this research, Lycopene in two different dose could reduce TNF- α level significantly when compared to that in Imiquimod group(Group II) .these findings complied with other studies that showed reducing effect of Lycopene on IL-17and TNF- α in pregnant mice (45) and Intracellular adhesion molecules that activated through IL-23 cytokines (15), while Yang et al.(2017) suggested that the anti-inflammatory effect of Lycopene through inhibitory effect of Lycopene on NF- κ B in endothelial cells (46).

The combination of several topical medicines for Psoriasis treatment had been widely used through combining steroidal with non steroidal treatment to avoid the adverse effects behind extensive dose of Steriods and to get better result through synergism (47). In the current study, Combination group (Group VI) showed best improvement in clinical severity score and highest ameliorating effect on histological features and Baker scoring system. In addition to that, Combination of Lycopene 0.25 mg/ml with 0.05% Clobetasol showed better inhibition effect on serum and tissue inflammatory biomarkers than Clobetasol alone upon using topically for six consecutive days in Imiquimod induced Psoriasis. These effects may be attributed to synergistic anti-inflammatory effect for both Clobetasol and Lycopene which will be beneficial for halting Psoriasis spread and decreasing its symptoms.

Conclusion

The current study's findings adequately indicated that Lycopene and especially at high dose had anti-psoriasis benefits in Imiquimod induced psoriasis in mice via a molecular pathway involving anti-inflammatory, anti-proliferative effects. Lycopene had the opportunity to be a promising substitutional agent to standard therapies for psoriasis-related local inflammation.

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Conflict of interest

The authors declare that they have no conflict of interest

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Ethics approval

The study was reviewed and accepted by by Institutional review board in College of Medicine- AL-Nahrain University

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