Effect of Topical Application of Black Seed Oil on Imiquimod-Induced Psoriasis-like Lesions in the Thin Skin of Adult Male Albino Rats

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ABSTRACT

Psoriasis is a chronic inflammatory skin disease that affects about 1%–3% of the world's population. Black seed oil, i.e., the oil extracted from black seeds (Nigella sativa seeds), possesses a broad spectrum of pharmacological actions including anti-inflammatory, immunostimulatory, and antioxidant properties. This study aimed to investigate the effect of black seed oil on imiquimod (IMQ) induced psoriasis-like skin lesions. To this end, 30 male albino rats were divided into three groups: group I, control group; group II, psoriasis-induced group receiving daily topical applications of IMQ cream (5%) on the shaved back skin for 10 consecutive days; and group III, black seed oil group receiving a daily topical dose of black seed oil 5 mg/kg body weight for 10 days after induction of psoriasis. Animals of all groups were sacrificed and specimens obtained from the skin of the central part of the back were processed for histological and immunohistochemical staining with proliferating cell nuclear antigen (PCNA). IMQ application led to epidermal inflammation, hyperplasia and alterations in the normal appearance of keratinocytes with degenerative changes observed at both light and electron microscopic levels. Collagenous fibers were abundant in the dermis and PCNA-positive cells were detected in all layers of the epidermis. However, topical use of black seed oil strongly inhibited IMQ-induced psoriasis-like inflammation and alleviated all epidermal and dermal changes observed after IMQ application, allowing us to conclude that black seed oil can be used as an adjuvant topical therapy for treating psoriasis. Anat Rec, 301:166–174, 2018. © 2017 Wiley Periodicals, Inc.

Key words: psoriasis; imiquimod; black seed oil; PCNA

INTRODUCTION

Psoriasis is one of the most common immune-mediated chronic inflammatory skin disorders which affects approximately 1%–3% of the world's population. Active interactions between the immune system and the skin usually occur with systemic manifestation, especially arthritis (Weigle and McBane, 2013). Characteristic features of psoriasis include hyperproliferative keratinocytes, dilated blood vessels in the dermis and massive infiltration of leukocytes. Psoriasis causes cells to build up rapidly on the surface of the skin, forming

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itchy, dry patches, and thick silvery scales. The most common type of psoriasis, psoriasis vulgaris, accounts for 90% of the cases (Griffiths and Barker, 2007). Management of psoriasis involves either topical treatment with immunosuppressants, steroids and several other agents, or systemic treatment such as methotrexate administration, phototherapy, oral retinoids, and biological therapies, with topical treatment remaining the most widely used form of treatment. However, patients treated for psoriasis often present with relapse, adverse drug effects, and other reactions such as development of nonmelanoma skin cancer (Pouplard et al., 2013). Recommended treatment options for psoriasis in traditional medicine are change in lifestyle, preventive measures, as well as herbal therapy (Atyabi et al., 2016). Thus, a novel, more effective therapeutic strategy devoid of side effects is still desirable.

Dysregulation of the immune system is a major hallmark in the development of psoriasis. Regulatory T cells (Tregs) are considered to be inhibitors of autoimmune responses, but their role in the pathogenesis of psoriasis remains unclear. Psoriasis is considered a T-helper 1 (Th1) disease as evidenced by increased levels of cytokines belonging to the Th1 pathway (interferon gamma, interleukin (IL) 2 and 12) in psoriatic plaques (Griffiths and Barker, 2007; Traub and Marshall, 2007). Tregs suppress immune effectors including Th17 cells and maintain immune homeostasis (Sugiyama et al., 2005; Bovenschen et al., 2011). Therefore, to restore the dysregulated immune status in psoriasis, it is necessary to enhance Tregs and/or suppress immune effectors including Th17 cells.

However, other researchers have suggested involvement (Yu et al., 2007) or even a major role for keratinocytes (Kharaeva et al., 2009) in the development of psoriasis. Another feature of psoriatic skin is acanthosis, due to reduced epidermal apoptosis (Boehm, 2006). However, stimulation of apoptosis is associated with retrogression of psoriatic hyperplasia (Heenen and Simonart, 2008). Control of keratinocyte proliferation may constitute a valuable strategy in the management of psoriasis since reestablishment of the homeostatic regulation of keratinocyte proliferation and differentiation is fundamental for restoration of normal epidermis (Tse et al., 2006).

Black seed oil or nigella sativa oil is the oil extracted from black seeds (Nigella sativa), which are tiny, black colored seeds commonly called "black cumin." Multiple in vivo and in vitro studies performed on human and laboratory animals have shown that N. sativa and its ingredients have a wide range of pharmacological actions including antinociceptive (Abdel-Fattah et al., 2000), anti-inflammatory, antihypertensive, antiasthmatic, hypoglycemic, antiparasitic, antimicrobial, antioxidant, and anticancer effects (Padhye et al., 2008; Randhawa and Alghamdi, 2011; Abel-Salam, 2012). In the study of El-Dakhakhny et al. (2002), it was stated that the anti-inflammatory effects of N. sativa oil and its active principle, thymoquinone, may be explained by their action as inhibitors of 5-Lipooxygenase products and the production of 5-hydroxyeicosatetraenoic acid in a concentration-dependent manner, which may be due to its antioxidative action. Moreover, the oil and its active ingredients showed beneficial properties in immunomodulation in that they augmented the immune responses of T cell- and natural killer cells (Salem, 2005).

Hence, the aim of this study was to investigate the effect of black seed oil on an Imiquimod (IMQ)-induced psoriasis-like rat model by light/electron microscopy as well as immunohistochemistry to assess the role of black seed oil in treating psoriasis.

MATERIALS AND METHODS

Study Design

Thirty healthy adult male albino rats weighing about 180–200 g with no apparent skin lesions were used in this study. The animals were kept in adequate ventilation and temperature and were supplied with standard laboratory food and water. They were acclimatized to the laboratory conditions for two weeks prior to initiation of the experiment.

They were divided randomly into three groups:

Group I included 10 rats that served as control group. The skin of this group was exposed to control vehicle cream for IMQ (Vaseline) for the same duration as the corresponding experimental group.

Group II included 10 rats (IMQ-induced psoriasis group).

Group III included 10 rats (IMQ+ black seed oil treated group).

Drugs

- IMQ cream commercially available (5%) (Aldara; 3M Pharmaceuticals), is supplied in single-use packets (12 per box), each of which contains 250 mg of the cream, equivalent to 12.5 mg of imiquimod.
- Pure oil of black seed (El Captain Cap Pharm company) daily topical application after induction of psoriasis.

The central part of the back of all animals (area of 3 cm in diameter) was shaved. Animals of group II received a daily topical dose of 20 mg/cm^2 IMQ cream (5%) in vaseline on the shaved back for ten consecutive days. Based on a previous report (van der Fits et al., 2009), the psoriasis-like skin inflammation rat model was generated by daily topical application of a dose of 20 mg/cm^2 IMQ cream (5%) on the shaved skin for ten consecutive days. Animals of group III received a daily topical dose of 20 mg/cm^2 IMQ cream (5%) in vaseline on the shaved back plus pure black seed oil 5 mg/kg body weight once daily for ten consecutive days (Ahmad et al., 2013).

Scoring Severity of Skin Inflammation

To score the severity of inflammation of the back skin, an objective scoring system was developed. Erythema, scaling, and thickening were recorded on a scale from 0 to 4: 0, none; 1, slight; 2, moderate; 3, marked; 4, severe. The cumulative score (erythema plus scaling plus thickening) was used as a measure of the severity of inflammation (scale 0–12) (van der Fits et al., 2009).

Processing of Specimens

At the appropriate time, the rats were sacrificed by ether anesthesia and specimens were obtained from the skin of the central part of the back.

Light microscopic examination. The specimens were fixed in 10% neutral buffered formalin, embedded in paraffin and cut at 5 um thickness. They were stained by the following histological stains: H&E stain for general histological structure and Mallory's trichrome stain for collagen fiber detection (Bancroft and Layton, 2012).

Immunohistochemistry. The sections were deparaffinized for antigen retrieval, blocked and incubated in 3% hydrogen peroxide for blockage of endogenous peroxidase. The sections were then washed with phosphate buffered saline for blockage of nonspecific sites (reactive sites) and then incubated overnight in a humid chamber at 4°C with monoclonal anti- proliferating cell nuclear antigen (PCNA). Sections were washed with PBS, incubated for 1 hr with peroxidase-labelled IgG followed by di-amino-benzidine for staining the PCNA bound complex. The sections were counterstained with hematoxylin, dehydrated, cleared, and mounted (Elias et al., 1995).

Electron microscopic examination. Thin slices of the skin were divided into small pieces and were fixed in 4% phosphate buffered gluteraldehyde (0.1 M, pH 7.3) for 2 hr, postfixed with 1%phosphate-buffered osmium tetroxide for 30 minutes, then dehydrated in ascending grades of ethanol. After immersion in propylene oxide, the specimens were embedded in epoxy resin mixture. Semithin sections (1 um thick) were stained with 1% toluidine blue and examined by light microscopy for proper orientation (Kuo, 2007). Ultrathin sections (80–90 nm) were double stained with uranyl acetate and lead citrate, and subsequently examined at the Electron Microscopic Unit, Faculty of Medicine Tanta University (JEOL-JEM-100 SX electron microscope, Japan).

Quantitative Morphometric Measurement

Using the image analyzer computer system Leica in the Histology Department, Faculty of Medicine, Tanta University, the following parameters were measured:

a. Epidermal total thickness was measured in H&E-stained sections at a magnification of 400×.
b. The inflammatory cell infiltrate was counted in H&E-stained sections. The cells were counted in several sites including the dermoepidermal junction and the papillary and reticular layers of the dermis.
c. Collagen fiber volume fraction (%): The image analyzer was used to measure the area of collagen fiber content in Mallory's trichrome-stained sections (estimate area%/20 μm^2 frame) at a magnification of 400×.
d. The optic density of PCNA stained sections of different groups was estimated at a magnification of 400×. It was measured using the color detect menu and in relation to a standard measuring frame.

The measurements were performed in ten nonoverlapping fields from each slide of the different rats in each group.

Statistical Analysis

Student's *t*-test was used for statistical evaluation of the data using the statistical package for social sciences (version 11.5; SPSS Inc., Chicago, Illinois, USA) statistical analysis software. All values were expressed as mean ± standard deviation. The level of significance was set at $P \leq 0.05$.

Ethical Approval

All the procedures were performed according to the Guide for Care and Use of Laboratory Animals and were approved (Protocol No. 31310/01l17) by the Local Ethics Committee of Faculty of Medicine, Tanta University, Egypt.

RESULTS

Gross Observations

Topical application of IMQ on the back skin of the rats resulted in erythema, scaling, thickening and signs of inflammation from days 2–3 onward; these symptoms continually increased in severity up to the end of the experiment, while application of control vehicle cream did not result in any signs of skin inflammation. Conversely, the skin of the rats treated with black seed oil showed few scales along with disappearance of signs of inflammation (Fig. 1).

Light Microscopic Results

Examination of slides obtained from control rats revealed normal histology with two main layers of thin

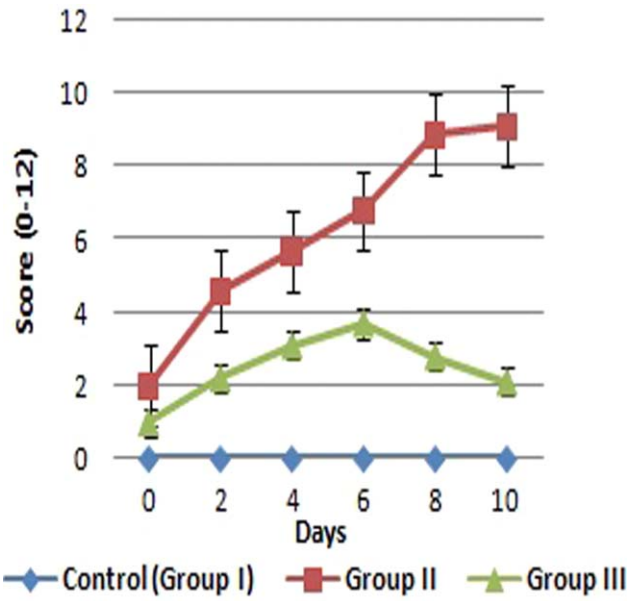

Fig. 1. Cumulative score (erythema plus scaling plus thickness). Symbols indicate mean score ± SD of 10 rat per group.

skin, the epidermis and dermis. The epidermis consisted of the stratum basale, spinosum, granulosum, lucidum, and corneum which represent the acidophilic superficial noncellular horny layer. The thick reticular layer of the dermis contained blood vessels, numerous lymphatics, hair follicles and sebaceous glands, while sweat glands were very seldom seen (Fig. 2a). Examination of back skin sections of group II revealed hyperkeratosis with retention of nuclei in the stratum corneum, epidermal hypergranulosis, hyper-proliferation of keratinocytes with increased epidermal thickening and abundant epidermal rete ridges, as well as abundant inflammatory cellular infiltrates. Some keratinocytes with a vacuolated pale-stained cytoplasm and dark stained nuclei (pyknotic) were also seen (Fig. 2b). In the treated group (group III), the previously observed changes were less pronounced: most of the keratinocytes appeared normal with intact nuclei (Fig. 2c).

Fine collagenous fibers passing parallel to the skin surface were present in the papillary dermis, whereas thick collagenous bundles running in different directions were found in the reticular dermis (Fig. 2d). The collagenous fibers observed in Mallory's trichrome in group II were increased compared to those in the control group (Fig. 2e), while an apparent decrease in collagen fibers was seen in the treated group (group III) (Fig. 2f).

PCNA-positive cells were confined mainly to the basal layer of the epidermis and sebaceous glands and the external root sheath of the hair follicles (Fig. 2g). PCNA-positive cells were no longer confined to the basal layer but also extended to the other layers of the epidermis and also scattered PCNA-positive cells in the dermis were detected (Fig. 2h). In the treated group, however, PCNA-positive cells were mainly detected in the basal layer of the epidermis and external root sheath of the hair follicles (Fig. 2i).

Electron Microscopic Results

Examination of skin sections from control rats revealed that the epidermis was made up of keratinocytes organized as stratum basale, spinosum, granulosum, and corneum. The cells were connected by desmosomal junctions. Normal cell organelles as well as vesicular nuclei with abundant chromatin and prominent nucleoli were observed within the keratinocytes, (Fig. 3a–c).

IMQ application altered the typical aspect of keratinocytes resulting in the following degenerative changes within the cells of the basal layer: marked cytoplasmic vacuolation, multiple large vacuoles with rarefied cytoplasm, shrunken nuclei with some indentation, increase in irregular and peripherally condensed chromatin (Fig. 3d), increased intercellular spaces with desmosome disruption (Fig. 3e,f). The cells of the stratum spinosum equally showed a number of degenerative changes including cytoplasmic vacuolation and rarefaction, shrunken, dark nuclei with peripheral nucleoli, and some degenerated mitochondria with disrupted cristae (Fig. 3g). The granular cell layers were characterized by a marked increase in the kerato-hyaline granule contents (Fig. 3h). Numerous spaces appeared in the stratum corneum, along with loss of the normal regular lamellae (Fig. 3h). Increased thickness and irregularity of collagen fibers under the dermo-epidermal junction was observed (Fig. 3f).

Application of black seed oil for ten days on the skin after induction of psoriatic skin lesion alleviated the epidermal changes observed in the diseased untreated group. The keratinocytes appeared nearly normal with intact nuclei (Fig. 3i), except for a few cells, which had a shrunken, degenerated appearance with dark-stained nuclei, few cytoplasmic vacuoles and some degenerated mitochondria.

Quantitative Morphometric Results

In comparison with the corresponding control group, epidermis thickness, inflammatory cell infiltrate, relative area of collagen fibers and optic density of PCNA were significantly increased in the IMQ-treated group (II) ($P < 0.01$), while the same parameters measured in group III treated with black seed oil after induction of psoriasis showed a slight nonsignificant increase ($P > 0.05$) (Table 1).

DISCUSSION

In this study, the psoriatic rat model was treated with black seed oil (daily topical dose of 5 mg/kg body weight for 10 days after induction of psoriasis). Psoriasis-like skin inflammation was generated by daily topical application of a dose of 20 mg/cm^2 IMQ cream (5%) on the shaved skin for ten consecutive days (group II).

The IMQ-induced psoriasis in rat and mouse serves as a model of human psoriatic lesions since it exhibits similar characteristics including erythema, epidermal thickening, scaling, presence of inflammatory cells (T cells, neutrophils and dendritic cells) and vascular proliferation. Topical treatment with IMQ stimulates the innate immune system followed by induction of adaptive immunity, leading to psoriasis (van der Fits et al., 2009).

Cellular infiltration during the pathogenesis of psoriasis might take the form of epidermal keratinocyte proliferation. The course of psoriasis is influenced by numerous inflammatory pathways, such as IL-12/Th1, IL-23/Th17, and IL-22/Th22 (Kagami et al., 2010). Psoriasis plaques are initiated and maintained via different interactions between cells of the skin and the immune system. T helper cells can be transferred to mutually specialized subtypes depending on the existing cytokine condition. As a result of this cytokine activation, keratinocytes and different cells generate a massive immune response triggering and enhancing inflammatory reactions in the skin (Lowes et al., 2007; Vanaudenaerde et al., 2011).

In this study, both gross anatomical and light/electron microscopic analysis revealed that topical use of black seed oil attenuated the signs of inflammation observed in group II along with normal reappearance of keratinocytes with intact nuclei. These findings are in line with the results of Amin and Hosseinzadeh (2016), who cited various studies showing that the oil of black seeds possesses anti-inflammatory effects, lending further support to the common folk perception of N. Sativa as a potent anti-inflammatory agent. This property may be attributed to its cytoprotective and antioxidant actions in which the oxidant scavenger system is augmented, as well as to its effect on some

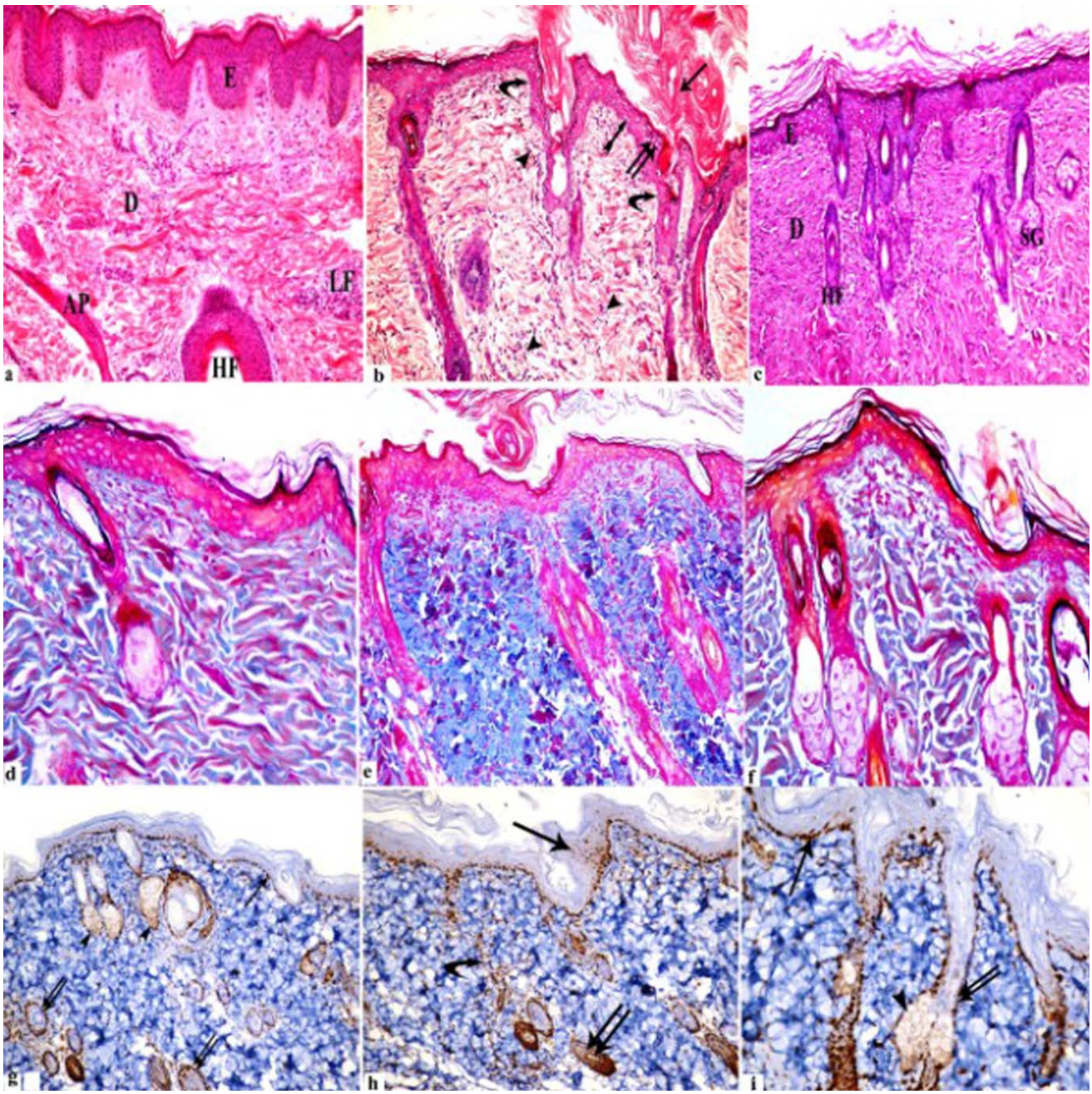

Fig. 2. Photomicrographs of back skin sections of different groups, control group (a) showing the epidermis (E) and the dermis (D) containing lymphatic follicles (LF), hair follicles (HF) and arrector pilli muscle (AP). (b) Sections of group II showing hyperkeratosis with retention of nuclei in the stratum corneum (arrow), hypergranulosis (double arrow), hyperproliferation of keratinocytes with increased epidermal thickening with abundant epidermal rete ridges (waved arrow), abnormally vacuolated keratinocytes with a pale stained cytoplasm and dark stained nuclei (biffed arrow) and abundant inflammatory cellular infiltration (arrow head). (c) Sections of group III showing the epidermal (E) and dermal (D) layers containing multiple hair follicles (HF) and sebaceous glands (SG) appear with a normal structure. Fine collagenous fibers running parallel to the skin surface are present in the papillary dermis and thick collagenous bundles running in different directions are found in the reticular dermis (d). Trichrome stained sections of group II revealing increased numbers of collagen fibers (e) and few collagen fibers present in group III(f). Positive PCNA cells in control group (g) are mainly present in the basal layer of the epidermis (arrow) and sebaceous gland (arrow heads) and the external root sheath of the hair follicles (double arrow). PCNA-positive cells of group II (h) extend to the other layers of the epidermis (arrow), hair follicles (double arrow) and scattered cells in the dermis (curved arrow). In group III (i) PCNA-positive cells are confined mainly to the basal layer of the epidermis (arrow) and sebaceous gland (arrow head) and external root sheath of the hair follicles (double arrow). (a,b,c H&E 200 × - d,e,f Mallory's trichrome 200 × - g, h, i PCNA immunostaining 200 ×).

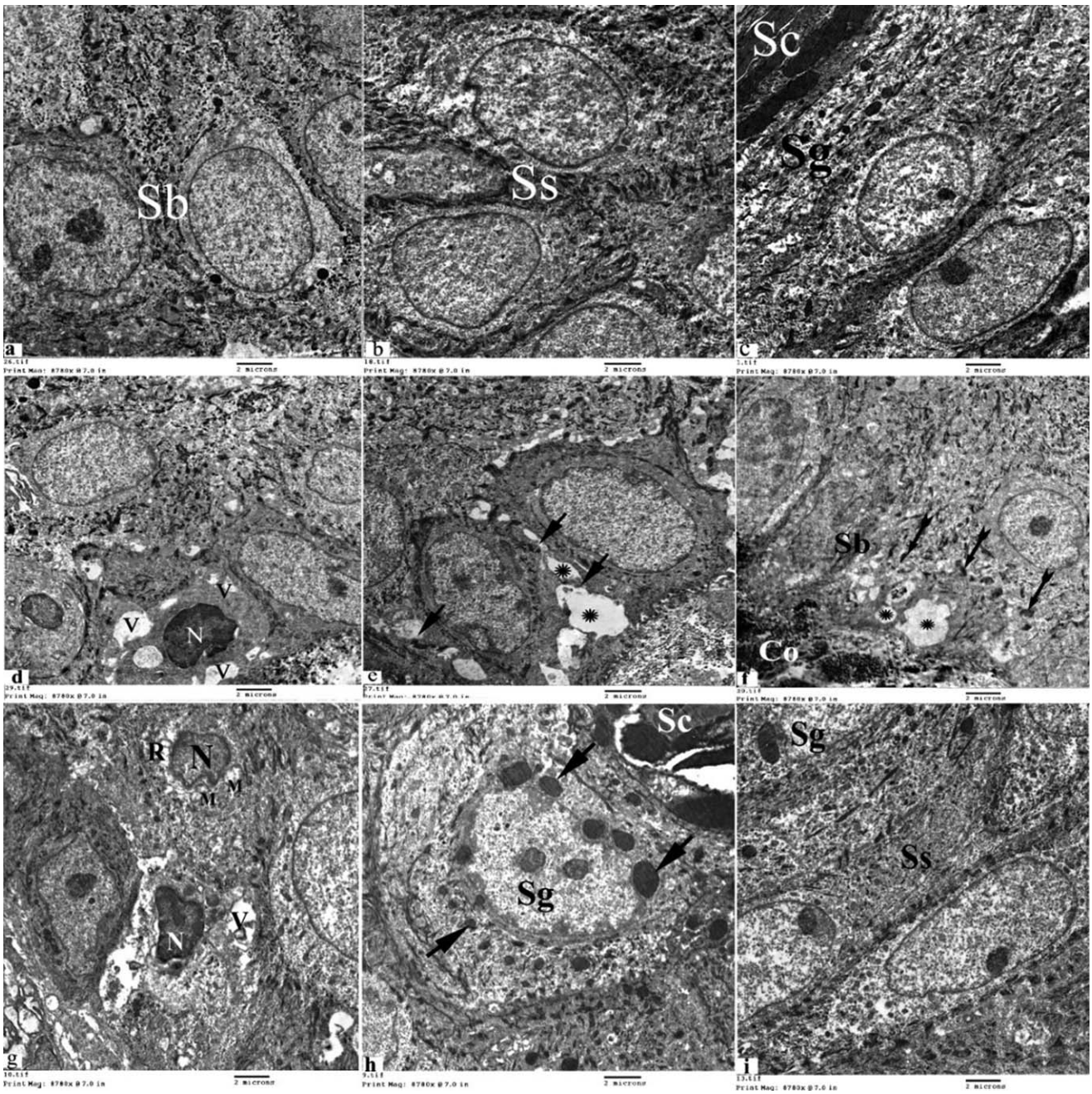

Fig. 3. Electron micrographs of ultrathin skin sections of different groups. Control rats (a-c) showing the different strata of keratinocytes of the epidermis including stratum basale (Sb), spinosum (Ss), granulosum (Sg) and corneum (Sc). The cells are connected with each other by desmosome junctions; the nuclei of keratinocytes appear vesicular with extensive chromatin and prominent nucleoli. Ultrathin skin sections from group II (d-h) demonstrating a basal cell(d-f) with multiple large vacuoles (v), the nuclei (N) of some cells appear small, dark with some indentation and with irregular and increased peripherally condensed chromatin. Increased intercellular spaces (asterisks) and disrupted desmosome junctions (arrow) with disruption of cytoplasmic junctional filaments (biffed arrow). Cells of the stratum spinosum(g) showing cytoplasmic vacuolation (V) and rarefaction (R), nuclei (N) of some cells have an irregular and dark, shrunken appearance. Note some degenerated mitochondria with disrupted cristae (M). Granular cell layers (Sg) showing an apparent increase in the kerato-hyaline granule contents (arrow) (h). The stratum corneum (Sc) has multiple spaces separating the keratin with loss of the normal regular lamellae arrangement (h). Note the increased number and irregularity of collagen fibers (Co) under the dermo-epidermal junction(f). Skin sections from group III, demonstrating different strata of keratinocytes (Ss and Sg) that appear normal with intact nuclei, except for a few cells. Mic. Mag.×1500.

inflammatory mediators including proinflammatory enzymes and cytokines as well as prostaglandins and leukotrienes. We observed an abundant inflammatory cellular infiltrate in the IMQ-treated rats, which was markedly reduced in psoriatic rats treated with black seed oil.

TABLE 1. Morphometeric and quantitative analysis of the effects of IMO with and without black seed oil on skin of rats

Parameters	Control group	IMO-treated group (group II)	IMO + black seed oil treated group (group III)
Epidermal total thickness in μm	20.25 ± 0.83	65.78 ± 2.31 $P < 0.01$	22. 35 ± 0.53 $P > 0.05$
Inflammatory cell infiltrate	5.8 ± 0.43	143.25 ±6.76 $P < 0.01$	7.4 ±1.23 $P > 0.05$
Collagen fiber volume fraction (%)	1.34 ± 0.64	8.34 ± 0.73 $P < 0.01$	1.73 ± 0.91 $P > 0.05$
PCNA immunoexpression (optical density)	15.18 ± 1.74	26.25 ± 3.48 $P < 0.01$	17.23 ± 1.69 $P > 0.05$

Data is expressed as mean ± standard deviation, P value = probability of chance, $P < 0.05$ is significant, tested by using Student "t" test, group II & group III versus group I.

Young et al. (2008) suggested that antioxidant therapy could be made more efficient and specific for the treatment of psoriatic skin disease. The work of Zhou et al. (2009) reinforces the concept that an inadequate antioxidant system participates in the pathogenesis of psoriasis. Keratinocytes and activated leukocytes, mostly neutrophils, generate reactive species in psoriasis (Pelle et al., 2005). The presence of cysteinyl leukotrienes (slow-reacting substances) released from activated leukocytes has been reported in inflammatory diseases including psoriasis (Lewis et al., 1990). Lipid peroxidation is also a characteristic event in psoriatic skin disease (Yildirim et al., 2003). In addition, disturbances in leukotriene homoeostasis may result in inflammatory responses in a wide range of diseases as diverse as psoriasis, rheumatoid arthritis, and inflammatory bowel disease. Black seed oil, which is known to inhibit leukotriene synthesis and histamine release, and act as a superoxide scavenger, might have a soothing effect on inflammation. In addition, it produces valuable immunomodulatory effects by enhancing T cell-mediated and natural killer cell-mediated immune responses (Ali and Blunden, 2003; Salem, 2005; Amin and Hosseinzadeh, 2016). Such a remarkable spectrum of biochemical and cellular actions holds great promise for the prevention and treatment of a variety of human disorders caused by oxidative stress, including psoriasis.

The antioxidative activities of thymoquinone, the most abundant and active compound of N. sativa, have been extensively documented. Pretreatment of female HR-1 hairless mouse skin with thymoquinone attenuated the 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced expression of cyclooxygenase-2 (COX-2). Topical application of thymoquinone induced the expression of glutathione-S-transferase, glutamate cysteine ligase and hemeoxygenase-1 in mouse skin (Kundu et al., 2013). The anti-inflammatory effect of thymoquinone and N. sativa-fixed oil has also been reported earlier by Houghton et al. (1995), who demonstrated a dose-dependent decrease in the formation of thromboxane B2 and leukotriene B4, indicating the inhibition of cyclooxygenase and 5-lipooxygenase pathways of arachidonate metabolism in rat peritoneal leukocytes.

The morphometric results in this study revealed a significantly thicker epidermis in IMQ-treated rats, while rats treated with black seed oil displayed a nonsignificant increase in comparison with control rats. This increased thickness was due to the hyperplasia of basal and suprabasal keratinocytes, as also described by Sun et al. (2013). This was supported by PCNA immunoreactivity revealing a significant increase in PCNA density in IMQ-treated rats as well as a nonsignificant increase in the rats treated with black seed oil as compared to control rats. PCNA is a cofactor of DNA polymerase δ in the process of DNA synthesis of eukaryotic cells. It is a nuclear protein that is correlated with the cell's proliferative state. As such, PCNA immunolocalization can be used as an indicator for the degree of cell proliferation and its expression is indicative of active cell proliferation (Hong et al., 2001). Our results are consistent with those of Dwarampudi et al. (2012), who stated that psoriasis is a disease resulting from the hyperproliferation and abnormal differentiation of keratinocytes and that one of the hallmarks of psoriasis is a greatly reduced or almost absent granular layer in the epidermis (parakeratosis). Administration of a 95% ethanol extract of Nigella sativa seeds resulted in a well-defined granular layer around the epidermis. This may be related to the effect of N. Sativa on restoring normal epidermal differentiation.

According to Zenz et al. (2005), keratinocytes play a noteworthy and essential part in the pathogenesis and advancement of psoriasis. In spite of the fact that psoriasis is thought to be a Th1 disorder, the occurrence of psoriasis does not differ between immunodeficiency virus-infected patients and the general community. Subsequently, epidermal changes may mark the start of skin lesions in psoriasis; as such, prevention of keratinocyte multiplication might be a useful strategy to combat this disease and might be considered as a promising target of anti-psoriatic strategies (Lin et al., 2008).

Our results further revealed a significant increase in the relative area of collagen fibers in IMQ-treated rats, whereas no significant increase in this respect was recorded in rats treated with black seed oil as compared to control rats. An increase in collagen and elastic fibers has been associated with abundant inflammatory infiltrates. Dysfunction and damage of mitochondria caused by reactive oxygen species with lipid peroxidation products together with activation of inflammatory cells resulted in fibrosis and collagen deposition (Shroff et al., 2014). The present work shows that collagen fiber deposition was decreased in group III treated with black seed oil, which might be related to the anti-inflammatory and antioxidative effects of N. Sativa (Kundu et al., 2013; Amin and Hosseinzadeh, 2016). The present results are consistent with the findings of Zhou et al. (2013), who demonstrated inhibition of bleomycin-induced fibrosis as a result of reduced oxidative stress factors upon administration of N-acetylcysteine.

CONCLUSION

The histological results of the present study allow us to conclude that the oil of N. Sativa is capable of suppressing the hyperproliferation and abnormal differentiation of keratinocytes and that black seed oil can be used as an adjuvant topical therapy for the treatment of psoriasis. Further studies are needed to compare its effects with other commonly used drug therapies of psoriasis.

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CONFLICT OF INTEREST

The authors of this manuscript have no conflict of interests to declare.

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