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GC-MS analysis and the effect of topical application of essential oils of *Pinus canariensis* C.Sm., *Cupressus lusitanica* Mill. and *Cupressus arizonica* Greene aerial parts in Imiquimod–Induced Psoriasis in Mice

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ABSTRACT

Ethnopharmacological relevance: Traditionally, Coniferous plants, in particular *Pinus* and *Cupressus* species, have been used in the treatment of burns, skin infections, and immune-mediated inflammatory diseases such as psoriasis.

Aim of the study: A comparative study between essential oils (EOs) extracted from aerial parts of three coniferous plants: *Pinus canariensis* C.Sm. (PC), *Cupressus lusitanica* Mill. (CL) and *Cupressus arizonica* Greene (CA), cultivated in Egypt, was designed to investigate their composition and their anti-psoriasis mechanism.

Materials and methods: The phytochemical profiles were confirmed using Gas Chromatography–Mass Spectrometry (GC-MS) method. *In-vivo* Imiquimod (IMQ)-induced psoriasis model was performed and EOs were applied topically and compared to mometasone cream as a standard subsequently histopathological analysis and inflammatory biomarkers were measured.

Results: In GC-MS analysis, Monoterpene hydrocarbons, sesquiterpene hydrocarbons and oxygenated monoterpenes were the major detected classes in the three plants, except in *Pinus canariensis* essential oil, oxygenated monoterpenes were absent. A significant attenuation of imiquimod-induced psoriasis symptoms after topical application of *P. canariensis* C.Sm., and *C. lusitanica* Mill. essential oils were observed by reducing the psoriasis area severity index (PASI) score, alleviating histopathological alteration, restoring the spleen index, and decreasing serum levels of interleukins 23 and 17A. Indeed, the results of *Pinus canariensis* essential oil is comparable to mometasone and showed no significant difference from standard treatment. On the other hand, the topical application of *C. arizonica* essential oil failed to alleviate imiquimod-induced psoriasis symptoms as observed in the PSAI score, the histopathological investigation, and the spleen index.

Conclusion: The essential oils of *P. canariensis* C.Sm., and *C. lusitanica* Mill aerial parts could be promising candidates for psoriasis treatment and for further studies on inflammation-related skin diseases.

1. Introduction

Psoriasis is a chronic immune-mediated inflammatory disease that affects the skin, joints, or both. It is characterized by erythematous, scaly, and pruritic skin plaques (Griffiths and Barker, 2007; Rachakonda et al., 2014). Psoriasis involves a complex interaction between innate and adaptive immune responses that trigger the release of massive amounts of pro-inflammatory cytokines and chemokines (Fakhir et al., 2016). Although psoriasis is a genetically mediated disorder, some environmental factors such as trauma, infection, and chemicals are implicated in the pathogenesis of this inflammatory disease (Samotij et al., 2020). These stimuli exacerbate the production of interleukin 23 (IL-23) that provokes several cytokines production including IL-17, IL-22, and tumor necrosis factor-alpha (TNF-α) resulting in hyperproliferation and alteration of keratinocytes functions (Ghoreschi et al., 2021). Imiquimod-induced psoriasis was first prescribed by van der Fits

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et al. (van der Fits et al., 2009), and its use was increased over time as it represents an effective psoriasis model. Imiquimod (IMQ), an imidazoquinoline heterocyclic amine, is a ligand for Toll-like receptor (TLR)-7 and 8 and a potent immune activator that is utilized for topical treatment of genital and perianal warts caused by human papilloma virus (Beutner, 1997). IMQ provokes the synthesis of proinflammatory cytokines and causes overexpression and activation of the IL-23/17 axis (Schön, 2019; van der Fits et al., 2009), the latter plays a key role in the pathogenesis of psoriasis (Piskin et al., 2006).

Plants are considered the main source of bioactive compounds (Maruca et al., 2019), and one of these agents is Essential Oils (EOs). They are the main components of aromatic plants with chemical diversity and multiple pharmacological activities *viz* analgesic, anti-inflammatory (Bakkali et al., 2008; Silva et al., 2003) anti-oxidant, anti-cancer, anti-viral, anti-bacterial and anti-diabetic (Edris, 2007; Raut and Karuppayil, 2014).

Coniferous plants are ecologically important woody plants that are characterized by needle-shaped leaves with unique scented resin. The phytochemical characterization of coniferous plants revealed that they are rich in phenolic acids, flavonoids, bioflavonoids, tannins, and lignans (Tanase et al., 2019). The different coniferous extracts and their essential oils were reported to have anti-nociceptive, anti-inflammatory (Fakhri et al., 2022), and antioxidant (Koutsaviti et al., 2021) activities. Their traditional medicinal uses were directed for the treatment of several diseases such as cough, common colds, bronchitis, and wounds in Iran, Turkey, and the Himalayan region (Akaberi et al., 2020; Kizilarslan and Sevg, 2013).

Traditionally, different parts of *Pinus* species (bark, needle, cone, and resin) especially in Egypt, Nordic countries, and Turkey have been used in the treatment of different respiratory infections (Mitić et al., 2018). Internally, they were used to treat peptic ulcers (Yeşilada et al., 1995) and diarrhea (Yesilada and Küpeli, 2007). In the traditional medicine of Turkey, *Pinus nigra* Arn. subsp. pallasiana (Lamb.) Holmboe var. pallasiana stem tar decoction was a popular drink for infection. Additionally, it is used externally in eczema, acne, alopecia, fungus, and psoriasis (Ari et al., 2014; Kozan et al., 2019), ulcers, punctured abscesses, and/or burns (Süntar et al., 2012; Yosita et al., 2022). Moreover, oral intake of the decoction of the resin exudate from the trees of *Pinus masscnlana* showed a remarkable effect in the imiquimod-induced psoriasis-like inflammation mouse model. That effect was mediated through the inhibition of Th1/Th17 cells and epidermal keratinocytes *via* the down-regulation of the relevant inflammatory cytokines such as IL-23, IL-17A, and IL-17F (Li et al., 2019). Even more, *Pinus sylvestris* leaf oil along with 24 other herbs were used traditionally as a medicine formula in the treatment of psoriasis (Yosita et al., 2022).

Different parts of *Cupressus* plants were reported in folk medicine. Plant fruits were used in the treatment of common cold and cough (Yeşilada et al., 1999), female cones and leaves, in rheumatism, gout, diabetes, and as an antiseptic. Furthermore, it was believed that the external application of *C. sempervirens* leaves could heal fresh sores, wounds, and skin burns. In addition, the decoction of its leaves and fruits with *Emblica officinalis* Gaertn. has been used externally to darken and stimulate hair growth (Akaberi et al., 2020). Moreover, *C. arizonica* Greene plant and its preparations/supplements have been used as an immune system stimulant, an astringent, and a tonic for skin and the treatment of broken capillaries and varicose veins (Fakhri et al., 2022). Besides that, the leaves of *C. lusitanica* Mill are used traditionally to cure skin diseases (Teke et al., 2013) and in Kenya, in the treatment of liver, spleen, kidney, bladder, bone, and joint diseases (Isaac and Ogoche, 2014). In Ethiopia, the decoction of the leaves is used to treat toothache (Megersa et al., 2019). In Cameroon, in postpartum pain, and against hair loss (Tsobou et al., 2013).

Recently, the use of essential oils has been documented in the treatment of different inflammatory skin conditions including psoriasis due to its lower adverse reactions (Ashraf et al., 2023). In this context, phototherapy by ultraviolet B exhibits side effects like nausea, dizziness, erythema, and skin cancer. Treatments with methotrexate cause leukopenia, thrombocytopenia, and hepatotoxicity as side effects. In addition to treatment with cyclosporin which causes potent systemic side effects such as nephrotoxicity and hypertension (Hany A. El-Shemy, 2017).

To the best of our knowledge, no reported data has investigated the anti-psoriasis effect of essential oils extracted from *P. canariensis* (PC), *C. lusitanica* (CL), and *C. arizonica* (CA) aerial parts. The present study was designed to investigate their potential in the treatment of psoriasis for the first time. Additionally, the chemical profile of EO of *C. lusitanica* and *C. arizonica*, cultivated in Egypt [There are no indigenous or wild plants grow in Egypt (Amorós, 2018; Saber et al., 2021)], have not been studied to date, despite being previously studied in other countries such as Kenya and Cameroon (Kandgor Bett et al., 2022; Teke et al., 2013). Therefore, the current study compares the EO composition of both plants with *P. canariensis* oil using GC/MS. In addition to investigating the effect of such composition on the anti-psoriasis effect of the three EOs.

2. Material and methods

2.1. Collection of plant material

The aerial parts of *P. canariensis* C.Sm. (family Pinaceae), *C. lusitanica* Mill. and *C. arizonica* Greene (family Cupressaceae) were collected from Orman Botanical Garden at Giza, Egypt in March 2021. Botanical identification was kindly performed and confirmed by Engineer Therese Labib, consultant in Orman Garden and National Gene Bank, Ministry of Agriculture. Voucher specimens were deposited at the herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, Cairo University, Cairo, Egypt (Code (3-10-2021II), (4-10-2021) and (3-10-2021III)) for PC, CL, and CA, respectively.

2.2. Preparation of the EOs

Essential oils of the aerial parts of the three species (~500–1000 g each) were obtained by hydro-distillation using a Clevenger-type apparatus for 3 h. The oils were collected, dried over anhydrous sodium sulphate, and then stored at 4 °C in sealed vials protected from light until further analysis.

2.3. Gas Chromatography–Mass Spectrometry (GC–MS) analysis

The analysis of three oils was established using a Shimadzu GC–MS-QP 2010 (Kyoto, Japan) coupled with a mass spectrometer (SSQ 7000 quadrupole; Thermo-Finnigan, Bremen, Germany). The chromatogram separation was performed using a capillary column (Rtx-5MS, 30 m × 0.25 mm, 0.25 μm film thickness: Rested, Bellefonte, PA, USA). The oven temperature was initially held at 45 °C for 2 min then linearly increased to 300 °C at 5 °C/min for 5 min. The injector temperature was maintained at 230 °C while the detector was set at 280 °C. The carrier gas was helium with a flow rate of 1.41 mL/min. The following conditions were used in the mass spectrometer: ionization voltage of 70 eV, ion source temperature at 200 °C, and the scan range was adjusted from 35 to 500 AMU. The essential oils were diluted in *n*-hexane before analysis (1% v/v). Automated sample injection was applied (1 μL, split ratio of 1:15). The identification of each compound was based on the comparison of its retention index (RI) (calculated relative to a mixture of a series of standard *n*-alkanes between C8 and C28 injected under the same conditions) and its Mass Spectra (MS) with those described in the literature, computer matching and online searching with standard reference databases (NIST11s, Pherobase and PubMed) and by using Automated Mass spectral Deconvolution and Identification (AMDIS) software.

2.4. Animals

A total of fifty-four female BALB/c mice, weighing 18–22 gm, were obtained from National Organization Center, Giza, Egypt. Animals were

allowed to acclimatize for at least one week before the initiation of the experiment in the animal house of the Faculty of Pharmacy, Cairo University under controlled conditions of temperature (23 ± 2 °C) and humidity (65–70%) with a 12/12-h light/dark cycle. Animals were shaved with a sterilized electronic razor and hair removal cream was applied on the back two days before the experiment to remove hair. The study complied with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH Publication No. 85-23, revised 2011) and was approved by the Research Ethics Committee of the Faculty of Pharmacy, Cairo University, Cairo, Egypt (Ethical approval no MP3258). All efforts were exerted to minimize animal suffering during the experiment period.

2.5. Experimental design

All Mice were randomly allocated into nine groups (n = 6); normal control group (60 mg/day Vaseline; group 1), diseased group (62.5 mg/day Imiquimod (IMQ) cream [Aldara® cream 5%]; group 2) (Elgewelly et al., 2022), standard group (62.5 mg/day 5% IMQ cream and 60 mg/day mometasone cream 0.1%; group 3) (Xu et al., 2022). The remaining six groups (groups 4–9) received the same dose of Imiquimod cream as group 3. However, the six groups were treated daily with *Pinus canariensis* essential oil 5% (3μL/60 mg Vaseline; group 4) (Rai et al., 2020), 10% (6μL/60 mg Vaseline; group 5), *Cupressus lusitanica* essential oil 5% (3μL/60 mg Vaseline; group 6), 10% (6μL/60 mg Vaseline; group 7), *Cupressus arizonica* essential oil 5% (3μL/60 mg Vaseline; group 8) and 10% (6μL/60 mg Vaseline; group 9) respectively. Treatments were applied 4 h after IMQ cream application on the shaved back skin (2.5 cm × 2 cm) (Sakai et al., 2016), and the experiment lasted for 7 days. All groups were assessed for erythema, scaling, and skin thickness during the study. On the eighth day, animals were anesthetized with a ketamine/xylazine mixture [(ketamine 100 mg/kg) and xylazine (10 mg/kg)] (Ko and van Rijn, 2019), and blood samples were obtained from the retro-orbital sinus of all mice then animals were euthanized. The weight of the spleen was assessed to calculate the spleen index. The dorsal skin on the back (n = 3/group) was shaved and fixed in 10% formalin for histopathological examination. The remaining lesioned skin was flash frozen in liquid nitrogen and stored at −80 °C.

2.6. Severity scoring of skin inflammation

The severity of psoriatic lesions was assessed according to the modified clinical psoriasis area and severity index (PASI) (Zhou et al., 2020). Erythema, scaling, and skin thickness were observed and assessed independently on a scale from 0 to 4; 0, none; 1, mild; 2, moderate; 3, marked; 4, very marked. The total score of the three parameters (from 0 to 12) was used as an indicator for inflammation severity.

2.7. Spleen index calculation

The body weights and the spleens of all mice were measured, and the spleen index was calculated using the following formula.

$$\text{Spleen index} = \frac{spleen\ weight\ (g)}{Body\ weight\ (g)} \times 10$$

2.8. Enzyme-linked immunosorbent assay (ELISA)

Blood samples obtained from retro-orbital sinus were centrifuged at 1000×*g* for 20 min to separate clear sera that were used for Elisa assay. MyBioSource ELISA kits (CA, USA) were used for a quantitative determination of serum IL-23 (cat#: MBS2023294), and IL-17 (cat#: MBS2887165). All the steps were done according to the manufacturers' procedures. IL-23 and IL-17 were expressed as pg/mL.

2.9. Histopathological examination

Dissected skin wound tissue samples were fixed in 10% neutral buffered formalin for 72 h. Samples were processed in serial grades of ethanol, cleared in xylene then infiltrated with synthetic paraplast tissue embedding medium. Tissue sections (5 μm) were cut by rotatory microtome for the demonstration of different skin layers. Then, fixed onto glass slides and stained by hematoxylin and eosin as a general microscopic examination staining method, then examined by an experienced histologist in a blinded manner for microscopical evaluation of recorded lesions according to Abdelkader et al. (2021) and the scoring system is summarized in Table 1. Microscopic analysis was done using the Full HD microscopic imaging system operated using the Leica application module for histological analysis. Six random non-overlapping fields from each sample per group were scanned and analyzed for obtaining the mean epidermal thickness in H&E staining sections (Abbas et al., 2022).

2.10. Statistical analysis

Data were expressed as mean ± SD. For parametric data, a One-way analysis of variance (one-way ANOVA) was used, followed by the Tukey post hoc test. In the case of analysis of more than one variable, a two-way ANOVA, followed by a Tukey post hoc test, was used to assess both factors (i.e., time and treatment). Noteworthy, statistical analysis was analyzed using Prism (version 8; GraphPad Software, Inc., CA, USA). For all comparisons, the level of significance was fixed at $p < 0.05$.

3. Results

3.1. Phytochemical composition

The oil yield of *C. lusitanica* Mill. (CL), *P. canariensis* C.Sm. (PC), and *C. arizonica* Greene (CA) aerial parts were calculated based on fresh weight and found to be (0.17, 0.15, and 0.11% v/w, respectively). Fig. 1. illustrates the GC chromatograms of PC, CL, and CA oils. The three distilled oil samples had a characteristic aromatic odor. CA and CL oils were yellow, while PC was colorless. Results of GC-MS analysis of the essential oils along with their Retention times (Rt) and Kovats indexes are listed in Table 2. The distribution of detected volatile compounds by chemical classes is shown in Fig. 2. A total of 53 and 65 compounds were identified in CL and CA oils, respectively while only seventeen compounds were identified in PC oil, constituting relative area percentages of 99.97, 93.43, and 99.08 of PC, CL, and CA oil composition, respectively.

Monoterpenes are a class of 10-carbon constituents that consists of two isoprene units that are produced by a wide range of flowering plants (most commonly in the Myrtaceae, Asteraceae, and Lamiaceae) and nearly all conifers (Lerdau et al., 1995). Monoterpenes hydrocarbons (MH) were the most abundant chemical compounds in parsley, lovage, and thyme EOs (Semeniuc et al., 2018). They were reported to have anti-inflammatory and antioxidant properties (Zielińska-Błajet and Feder-Kubis, 2020). In Cupressaceae and Pinaceae families MH were found to be one of the major identified classes. In the current study, PC had the highest concentration of MH followed by CA and finally CL (88.61, 62.35, and 38.76%, respectively). α-pinene, is a bicyclic double-bond terpenoid hydrocarbon that is abundant in coniferous trees

Table 1
The scoring system of lesions detected by microscopical examination of tissue sections.

-	Nil (no lesions were demonstrated).
+	Mild lesion recorded in less than 15% of examined tissue sections.
++	Moderate lesion recorded in 16–35% of examined tissue sections.
+++	Severe lesion recorded in more than 35% of examined tissue sections

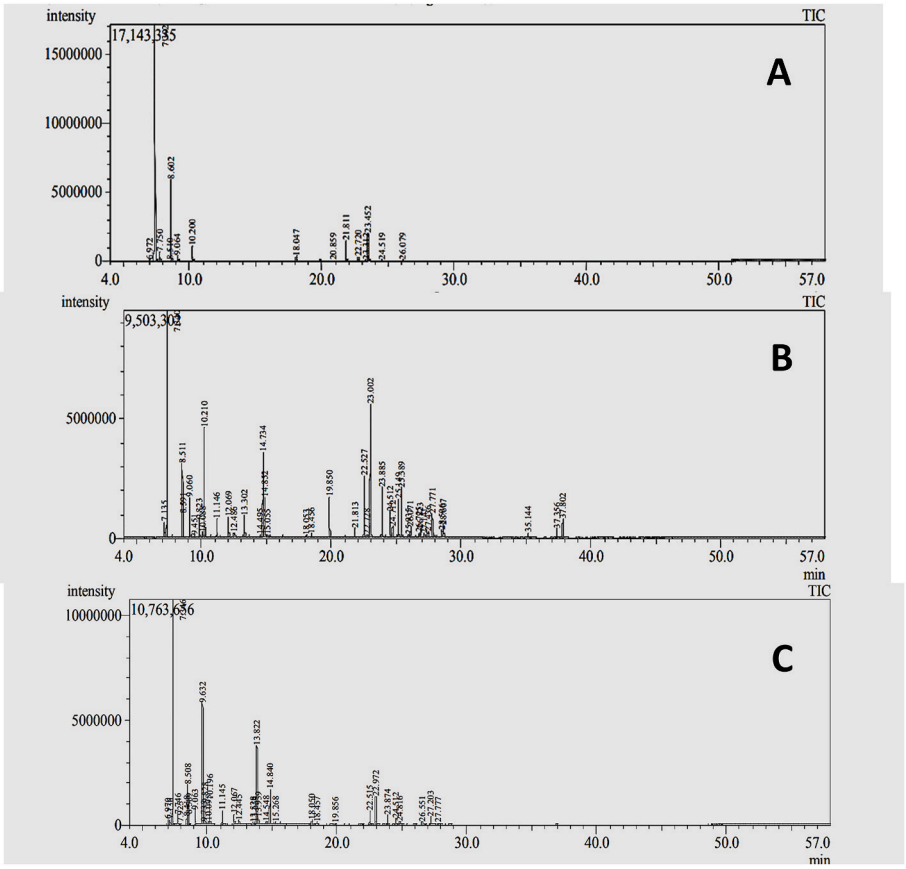

Fig. 1. Chromatogram of GC-MS analysis of A: Pinus canariensis C.Sm., B: Cupressus lusitanica Mill. and C: Cupressus arizonica Greene aerial part's oil.

(Türkez and Aydın, 2016) and has a sharp, piney aroma (Mariotti et al., 2022). It was the major detected compound in the three oils accounting for (70.93, 28.82, and 15.30%) in PC, CA, and CL, respectively. Moreover, *β*-pinene, a structural isomer to *α*-pinene, was detected in concentrations of 12.72, 1.41, and 1.13% for PC, CL, and CA, respectively. *δ*-3-Carene, a bicyclic monoterpene formed after the fusion of cyclohexene and cyclopropane rings, was present in an appreciable amount in CA oil (14.15%) but was minor in CL (0.03%) and absent in PC. Interestingly, D-limonene, the unique cyclic monoterpene found in citrus with a lemon-like odor accounted for 8.44 and 3.08% in CL and CA, respectively, and was absent in PC.

Oxygenated monoterpenes were found in CA and CL (19.82 and 11.00, respectively), while were absent in PC. Noticeably, cyclic monoterpene ketones such as camphor (in CA) and umbellulone (in CL) were detected in an appreciable amount (10.05 and 7.26%, respectively).

Sesquiterpene hydrocarbons, a class of terpenes that consist of two isoprene units, were observed in CL, PC, and CA oils (22.83, 10.28, and 8.42%, respectively). Two carbobicyclic compounds were detected in noticeable amounts in two *Cupressus* species, *cis*-muurola-4(14),5-diene (4.17–11.67%), and *cis*-Muurola-3,5-diene (1.76–4.72%). Besides that, germacrene D (5.60%) one of the commonly found sesquiterpenes in *Pinus* species (Cool and Zavarin, 1992; Gad et al., 2021) was detected in PC (5.60%).

Oxygenated sesquiterpenes were detected in CL, CA, and PC oils (12.26, 2.71 and 0.17%, respectively) in which *epi*-Cubenol (3.07%) and *epi*-Cubebol (2.93%) were the major ones. Besides that, minor diterpenes were detected in CA and CL oils only. The chemical structures of the major identified compounds in the EOs of the studied plants are illustrated in Fig. 3.

3.2. Anti-psoriasis activity

3.2.1. Histopathological examination

Histopathological examination of the control group demonstrated normal organized histological features of skin layers with the thin epidermal layer showing apparent intact keratinocytes (black arrow), intact dermal layer with well-organized collagen fibers and hair follicles (black star) without abnormal inflammatory cells infiltrates (Fig. 4A). On the other hand, topical application of IMQ cream showed a significant massive increase of epidermal thickness (Acanthosis) by 3.2 folds across skin sections (black arrow) with mild hyperkeratosis accompanied with mild clubbing of rete ridges, congested, and dilated subepidermal blood vessels were observed (arrowhead). In addition, moderate inflammatory cells infiltrate throughout the dermal layer was observed (red arrow) (Fig. 4B). Meanwhile, mometasone treatment presented almost intact well-organized histological features of different skin layers including minimal epidermal thickening (black arrow), and apparent intact dermal (star) and subcutaneous layers, with minimal inflammatory cells infiltrates (red arrow) (Fig. 4C). Topical applications of PC, CL and CA essential oils were examined against IMQ-induced psoriasis model in BALB/c mice at two different concentrations: low concentration (5%) and high concentration (10%). The photomicrographs of topical treatment with PC essential oil (5%) demonstrated a significant decrease of epidermal thickening by 57% (black arrow) with focal vacuolization of epidermal keratinocytes (yellow arrow) and mild dermal inflammatory cells infiltrates (red arrow) (Fig. 4D). Moreover, increasing the conc. of PC essential oil to 10% showed the best protective efficacy among the tested formulations with more organized morphological features of skin layers resembling the normal control samples with mild sub-epidermal inflammatory cells infiltrates detected (Fig. 4E). Meanwhile, the photomicrograph of high concentration of CL essential oil (10%) topical treatment displayed mild protective efficacy

Table 2
Identification of volatile compounds detected in GC-MS analysis of essential oils obtained from *Pinus canariensis* C.Sm., *Cupressus lusitanica* Mill. and *Cupressus arizonica* Greene aerial parts.

no	Name	Molecular Formula	Kovats index[a]	*Pinus canariensis* C.Sm. **	*Cupressus lusitanica* Mill. **	*Cupressus arizonica* Greene**
Monoterpene hydrocarbons						
1	Tricyclene	$C_{10}H_{16}$	902	0.06	0.05	0.55
2	*α*-Thujene	$C_{10}H_{16}$	908	–	1.00	0.58
3	*α*-Pinene	$C_{10}H_{16}$	916	**70.93**	**15.30**	**28.82**
4	*α*-Fenchene	$C_{10}H_{16}$	929	–	–	1.00
5	Camphene	$C_{10}H_{16}$	931	1.18	0.10	0.74
6	2,4(10)-Thujadiene	$C_{10}H_{14}$	937	–	–	0.19
7	3,7,7-trimethyl-1,3,5-cycloheptatriene	$C_{10}H_{14}$	955	–	–	0.89
8	Sabinene	$C_{10}H_{16}$	958	0.05	4.53	4.48
9	*β*-Pinene	$C_{10}H_{16}$	961	**12.72**	1.41	1.13
10	*β*-Myrcene	$C_{10}H_{16}$	978	0.94	2.77	2.10
11	*α*-Phellandrene	$C_{10}H_{16}$	993	–	0.15	0.11
12	*δ*-3-Carene	$C_{10}H_{16}$	999	–	0.03	**14.15**
13	*α*-Terpinene	$C_{10}H_{16}$	1006	–	1.34	–
14	*m*-Cymene	$C_{10}H_{14}$	1012	–	–	0.13
15	1,3,8-*p*-Menthatriene	$C_{10}H_{14}$	1014	–	–	0.50
16	*o*-Cymene	$C_{10}H_{14}$	1014	–	0.38	–
17	D-limonene	$C_{10}H_{16}$	1017	–	**8.44**	3.08
18	Sylvestrene	$C_{10}H_{16}$	1018	2.73	–	–
19	*γ*-terpinene	$C_{10}H_{16}$	1048	–	1.54	2.12
20	*p*-Mentha-2,4(8)-diene	$C_{10}H_{16}$	1076	–	–	0.06
21	*α*-terpinolene	$C_{10}H_{16}$	1078	–	1.72	1.71
Total Monoterpene hydrocarbons				88.61	38.76	62.35
Oxygenated monoterpenes						
22	Sabinene hydrate	$C_{10}H_{18}O$	1057	–	0.13	–
23	*β*-linalool	$C_{10}H_{18}O$	1090	–	0.20	0.60
24	2-Methylbutyl 2-methylbutanoate	$C_{10}H_{20}O_2$	1093	–	–	0.18
25	*α*-Thujone	$C_{10}H_{16}O$	1106	–	–	0.10
26	*Cis*-p-Menth-2-en-1-ol	$C_{10}H_{18}O$	1111	–	0.16	0.11
27	*α*-Campholenal	$C_{10}H_{16}O$	1125	–	–	0.18
28	*Cis*-(−)-1,2-Epoxy-p-menth-8-ene	$C_{10}H_{16}O$	1125	–	–	0.28
29	*trans*-Pinocarveol	$C_{10}H_{16}O$	1129	–	–	0.33
30	Camphor	$C_{10}H_{16}O$	1134	–	–	**10.05**
31	Verbenol	$C_{10}H_{16}O$	1136	–	–	0.32
32	Camphene hydrate	$C_{10}H_{18}O$	1138	–	0.02	1.01
33	Isoborneol	$C_{10}H_{18}O$	1147	–	–	0.08
34	Endo-borneol	$C_{10}H_{18}O$	1156	–	–	0.11
35	*α*-phellandren-8-ol (*p*-Mentha-1,5-dien-8-ol)	$C_{10}H_{16}O$	1158	–	–	0.48
36	Pinocamphone	$C_{10}H_{16}O$	1164	–	–	0.06
37	Umbellulone	$C_{10}H_{14}O$	1164	–	7.26	–
38	(−)-Terpinen-4-ol	$C_{10}H_{18}O$	1167	–	3.17	4.73
39	*α*-Citral	$C_{10}H_{16}O$	1173	–	0.14	–
40	*α*-Terpineol	$C_{10}H_{18}O$	1181	–	0.02	0.46
41	Myrtenol	$C_{10}H_{16}O$	1186	–	–	0.23
42	Eucarvone	$C_{10}H_{14}O$	1198	–	–	0.20
43	*β*-Citronellol	$C_{10}H_{20}O$	1219	–	–	0.31
Total Oxygenated monoterpenes				–	11.1	19.82
Sesquiterpene hydrocarbons						
44	*β*-Bourbonene	$C_{15}H_{24}$	1374	0.06	–	–
45	*β*-Elemene	$C_{15}H_{24}$	1380	–	0.11	–
46	*α*-Cedrene	$C_{15}H_{24}$	1402	–	–	0.10
47	*β*-Caryophyllene	$C_{15}H_{24}$	1409	3.68	–	–
48	*β*-Cedrene	$C_{15}H_{24}$	1411	–	–	0.06
49	*cis*-Muurola-3,5-diene	$C_{15}H_{24}$	1436	–	4.72	1.76
50	*α*-Humulene	$C_{15}H_{24}$	1445	0.66	0.23	–
51	*cis*-Muurola-4(14),5-diene	$C_{15}H_{24}$	1455	–	**11.67**	4.17
52	*γ*-Muurolene	$C_{15}H_{24}$	1467	0.08	–	–
53	Germacrene D	$C_{15}H_{24}$	1473	**5.60**	0.06	–
54	*β*-Curcumene	$C_{15}H_{24}$	1486	–	0.15	–
55	*epi*-Zonarene	$C_{15}H_{24}$	1489	–	3.81	1.34
56	*α*-Muurolene	$C_{15}H_{24}$	1491	0.04	–	–
57	*cis*-calamenene	$C_{15}H_{22}$	1514	–	2.08	–
58	*trans*-Calamenene	$C_{15}H_{22}$	1514			0.95
59	*δ*-Cadinene	$C_{15}H_{24}$	1514	0.16	–	–
60	*α*-Calacorene	$C_{15}H_{20}$	1535	–	–	0.04
Total sesquiterpene hydrocarbons				10.28	22.83	8.42
Oxygenated sesquiterpenes						
61	Spathulenol	$C_{15}H_{24}O$	1526	–	0.25	0.36
62	Cubebol	$C_{15}H_{26}O$	1539	–	0.99	0.10
63	*epi*-Cubebol	$C_{15}H_{26}O$	1548	–	2.93	0.14
64	Caryophyllene oxide	$C_{15}H_{24}O$	1575	0.17	0.83	0.10

(*continued on next page*)

Table 2 (*continued*)

no	Name	Molecular Formula	Kovats index[a]	*Pinus canariensis* C.Sm. **	*Cupressus lusitanica* Mill. **	*Cupressus arizonica* Greene**
65	Cedrol	$C_{15}H_{26}O$	1594	–	–	0.35
66	7-*epi*-*cis*-sesquisabinene hydrate	$C_{15}H_{26}O$	1601	–	0.40	–
67	*epi*-Cubenol	$C_{15}H_{26}O$	1605	–	3.07	0.12
68	*Cis*-sesquisabinene hydrate	$C_{15}H_{26}O$	1619	–	0.27	–
69	*β*-Acorenol	$C_{15}H_{26}O$	1622	–	0.11	1.32
70	*τ*-Cadinol	$C_{15}H_{26}O$	1632	–	0.59	–
71	*α*-Cadinol	$C_{15}H_{26}O$	1646	–	1.97	0.22
72	7-*epi*-*trans*-sesquisabinene hydrate	$C_{15}H_{26}O$	1678	–	0.85	–
Total Oxygenated sesquiterpenes				0.17	13.74	2.71
Diterpene hydrocarbons						
74	Isopimara-9(11),15-diene	$C_{20}H_{32}$	1894	–	0.04	–
75	Abieta-7,13-diene	$C_{20}H_{32}$	2080	–	–	0.11
Total Diterpenes hydrocarbons				–	0.04	0.11
Oxygenated Diterpenes						
76	Manool oxide	$C_{20}H_{34}O$	1984	–	0.59	–
77	Copalol	$C_{20}H_{34}O$	2127	–	1.70	–
Total Oxygenated Diterpenes				–	2.29	–
Miscellaneous						
78	Isobutyl isobutyrate	$C_8H_{16}O_2$	897	–	–	0.07
79	Isopentyl isobutyrate	$C_9H_{18}O_2$	1003	–	–	0.37
80	2-Methylbutyl isobutyrate	$C_9H_{18}O_2$	1006	–	–	2.89
81	Nonanol	$C_9H_{20}O$	1091	–	0.57	–
82	3-Acetoxy-*p*-menthan-1-ol	$C_{12}H_{22}O_3$	1129	–	0.13	–
83	5-Methyl-2-hexanol, 2-methylpropionate	$C_{11}H_{22}O_2$	1156	–	0.21	–
84	Bornyl formate	$C_{11}H_{18}O_2$	1192	–	–	0.36
85	*α*-Fenchyl acetate	$C_{12}H_{20}O_2$	1208	–	0.02	–
86	1-Methylheptyl propionate	$C_{11}H_{22}O_2$	1213	–	0.20	–
87	Thymol methyl ether	$C_{11}H_{16}O$	1224	–	–	0.16
88	Carvacrol methyl ether	$C_{11}H_{16}O$	1234	–	–	0.08
89	Epoxy-*α*-terpenyl acetate	$C_{12}H_{20}O_3$	1257	–	–	0.06
90	Bornyl acetate	$C_{12}H_{20}O_2$	1276	0.76	0.18	0.60
91	4-Terpinenyl acetate	$C_{12}H_{20}O_2$	1290	–	0.30	0.30
92	*trans*-Carveyl acetate	$C_{12}H_{18}O_2$	1328	–	–	0.24
93	*α*-Terpinyl acetate	$C_{12}H_{20}O_2$	1339	0.15	3.23	0.24
94	*cis*-14-nor-Muurol-5-en-4-one	$C_{14}H_{22}O$	1682	–	1.31	0.30
Total Miscellaneous				0.91	6.15	5.67
Total identified components						
Total monoterpene hydrocarbons (%)				88.61	38.76	62.35
Total oxygenated monoterpenes (%)				–	11.1	19.82
Total sesquiterpene hydrocarbons (%)				10.28	22.83	8.42
Total oxygenated sesquiterpenes				0.17	12.26	2.71
Diterpene hydrocarbons				–	0.04	0.11
Oxygenated Diterpenes				–	2.29	–
Miscellaneous				0.91	6.15	5.67
Total identified				99.97	93.43	99.08

[a] Kovats index determined experimentally on Rtx-5MS column relative to C8-C28 n-alkanes, ** Relative peak area percent, –, compound not detected in the essential oil, numbers in bold represent highest peak area %.

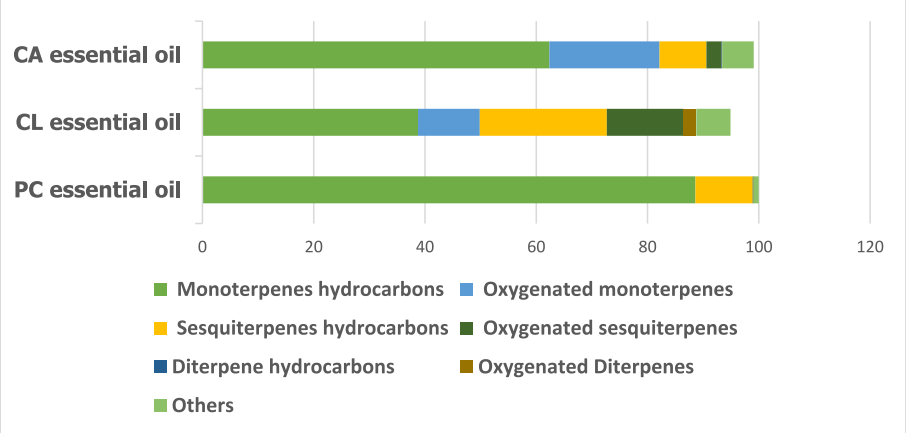

Fig. 2. Distribution of volatile compounds according to their chemical classes in the studied plants, CA: *Cupressus arizaonica* Greene, CL: *Cupressus lusitanica* Mill., PC: *Pinus canariensis* C.Sm.

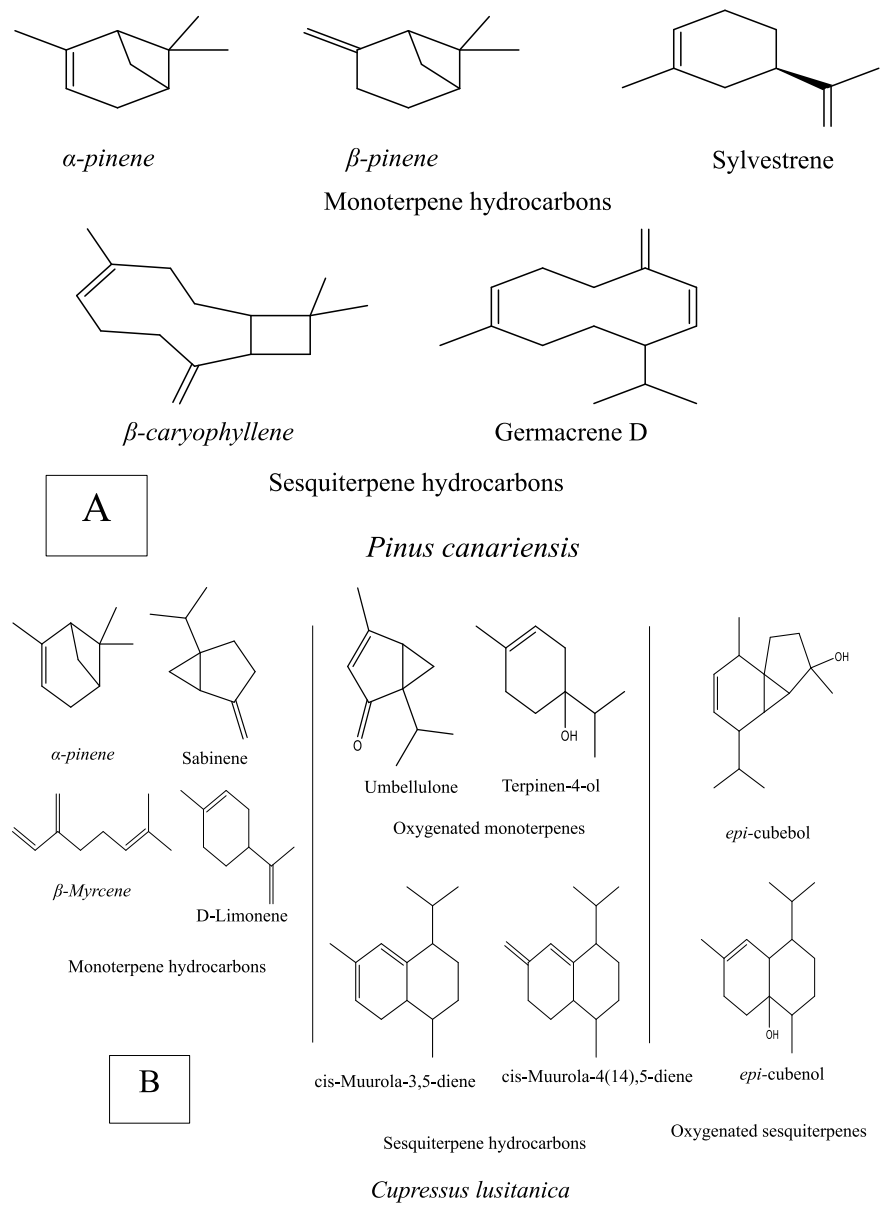

Fig. 3. Chemical structures of the major identified compounds in the EO of the studied plants. A: *Pinus canariensis*, B: *Cupressus lusitanica*, C: *Cupressus arizonica.*

with a decrease of epidermal thickening by 42% (black arrow) as well as dermal inflammatory cells infiltrates (red arrow) (Fig. 4G). On the contradictory, the other three topical treatments of CL essential oil (5%; Fig. 4F), and CA essential oil (5 & 10%; Fig. 4H-I) exhibited diffuse thickening of epidermal layers (black arrow) and hyperkeratotic figures, along with persistent dermal inflammatory cells infiltrates (red arrow) that were showed across the section. Severity scores of histopathological alterations of skin photomicrographs were presented in Table 3.

3.2.2. *Alleviation of IMQ-induced psoriasis-like symptoms*

Topical application of IMQ cream for seven consecutive days provokes significant epidermal erythema (score 3.84; Fig. 5A), scaling (score 3.84; Fig. 5B), and thickening (score 3.67; Fig. 5C) according to PASI score as compared to normal control (score 0). On the other hand, topical treatment with PC essential oil (5 and 10%), as well as CL essential oil (10%), significantly attenuated these psoriasis-like pathological changes. As depicted in Fig. 5, these three topical treatments showed significant improvement in dorsal skin erythema and reduction in scaling and epidermal thickness as compared to the insult group. Moreover, the effect of PC essential oil (5 and 10%) is comparable to the standard treatment and showed no significant difference when compared to mometasone, this could be attributed to the high content of α-pinene that exerts an anti-inflammatory action (De Cássia Da Silveira E Sá et al., 2013). As presented in the cumulative PASI score (Fig. 5D), the overall treatment effect of essential oils was ranked in ascending order as CL (10%), PC (5%, and 10%). These results pointed out the effectiveness of these treatments in relieving IMQ-induced psoriasis-like symptoms. Meanwhile, treatment with CL essential oil (5%), and CA essential oil (5 & 10%) failed to reverse the increment in the previously mentioned parameters, referring to the lower effectiveness of CL and CA essential oils when compared to PC essential oil, furthermore, they showed a significant difference when compared to mometasone.

The spleen index (Fig. 6) is linked to the immune system as it reveals the degree of lymphocyte proliferation in mice. In the current study, the spleen index was evaluated for all mice. The result demonstrated a significant increase in the spleen index after topical application of IMQ

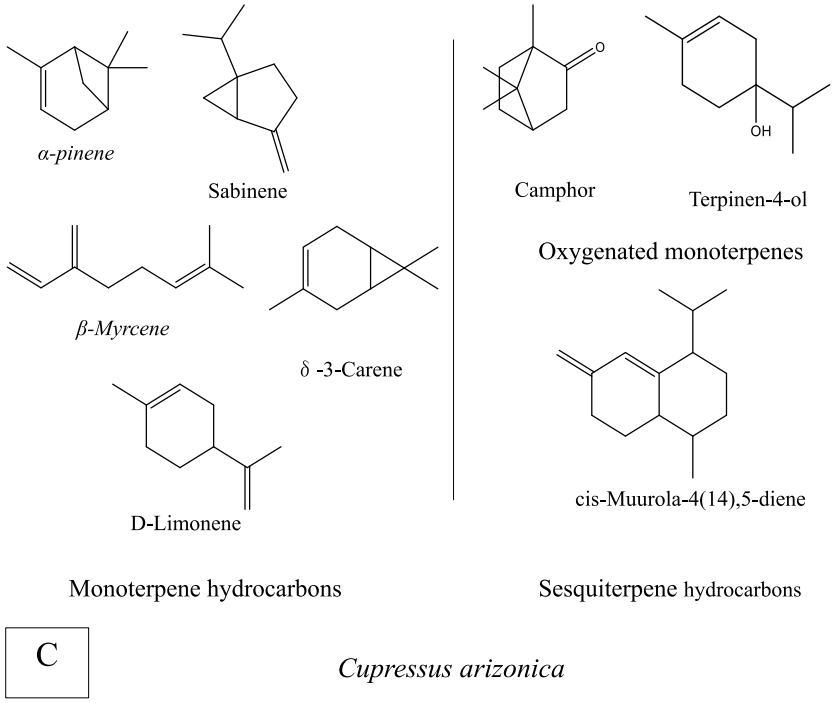

Fig. 3. (*continued*).

cream ($p < 0.0001$) by 1.4-folds as compared to the control group, meanwhile, topical treatment with PC essential oil (5 and 10%) as well as CL essential oil (10%) decreased the spleen index by 32, 37 and 26%, respectively as compared to the insult ($p < 0.0002$). In contrast, the other three topical treatments of CL essential oil (5%), and CA essential oil (5 & 10%) failed to decrease the spleen index. Noteworthy, the spleen index of PC essential oil (5 and 10%) showed no significant difference when compared to the mometasone group, on the other hand, the spleen index of CL and CA essential oils demonstrated a significant difference when compared to standard treatment, therefore PC essential oil is more effective than the CL and CA essential oils in alleviating of IMQ-Induced Psoriasis-like symptoms.

Since the results showed that PC essential oil (5 and 10%), as well as CL essential oil (10%), showed a significant difference as compared to the insult, therefore, PC (5 and 10%), and CL (10%) essential oils were selected to examine the biochemical mechanism for anti-psoriasis activity.

3.2.3. *Attenuation of inflammatory biomarkers in IMQ-induced psoriasis in serum*

The pathogenesis of psoriasis is attributed to the stimulation of dendritic cells, as well as macrophages. Activation of dendritic cells and macrophages creates an inflammatory status by the production of a massive amount of proinflammatory cytokines such as IL-23, IL-1β, and IL-6 (Dobrzyńska et al., 2020), which in turn promote the differentiation of T-helper 17 (TH-17) cells to secrete IL-17 and other mediators that increase epidermal cell proliferation and promotes the activation of nuclear factor kappa of B cells (NF-κB) (Fakhri et al., 2022; Zhou et al., 2018). The stimulation of NF-κB provokes the development of psoriatic lesions together with the elevation of proinflammatory cytokine levels in the blood (Sun et al., 2017). In the current study, ELISA kits were used to evaluate IL-23, and IL-17A levels in the serum of the selected groups. In the IMQ-induced psoriasis group, the levels of IL-23 and IL-17A were increased by 4 and 4.7 folds, respectively as compared to the control group. On the other hand, topical treatment with essential oils of CL (10%), and PC (5% and 10%) displayed a significant reduction in IL-23 level (74, 60 and 55%, respectively) as well as IL-17 level (56, 48 and 47%, respectively), as compared to the insult group. Moreover, the results of PC essential oil (5 & 10%) were comparable to the standard treatment Fig. 7.

4. Discussion

According to the World Health Organization, psoriasis is a serious non-communicable disease that affects people of all ages and has no preference for gender. It can affect the skin, nails, and joints and is linked to several complications (Michalek et al., 2017). The pathophysiology of psoriasis is attributed to a massive release of proinflammatory cytokines and chemokines, that lead to epidermal hyperproliferation, skin erythema, and scaly skin plaques (Liu et al., 2007). The conventional treatments for psoriasis include phototherapy and immunosuppressive drugs such as methotrexate and cyclosporine (Koo, 1999) which may cause severe adverse effects (Hany A. El-Shemy, 2017). Indeed, systemic therapy with methotrexate and cyclosporine impairs liver and kidney functioning and decreases RBCs, WBCs, and Platelets counts (Agrawal et al., 2010). Further, their topical use is associated with poor permeation through the skin because of its hydro-solubility and greater molecular weight (Chen et al., 2015; Pinto et al., 2014). Therefore, finding a natural plant resource with therapeutic effects against psoriasis is a global demand. In previous studies, the essential oil of different organs of *P. canariensis* C.Sm., *C. lusitanica* Mill. and *C. arizonica* Greene, a natural medicinal resource, have been confirmed for their antioxidant (Koutsaviti et al., 2021) and anti-inflammatory activities (Fakhri et al., 2022). Hence, the current study investigated -for the first time-the anti-inflammatory activities of EOs extracted from these three coniferous plants (PC, CA, and CL) against IMQ-induced psoriasis in BAIB/c mice. Moreover, the aim was extended to delineate the possible mechanisms involved.

By comparing the peak area % of the identified components, the composition and proportions of the compounds detected in PC oil were in line with those previously published data (Gad et al., 2021; Visan et al., 2021) who reported that monoterpene and sesquiterpene hydrocarbons were the major classes with α-pinene (72–74%) as a major component. However, in contrast to Moroccan needles oil, monoterpenes were minor (8%) (Hmamouchi et al., 2001). Similarly, the major components found in CA oil were comparable to those detected in

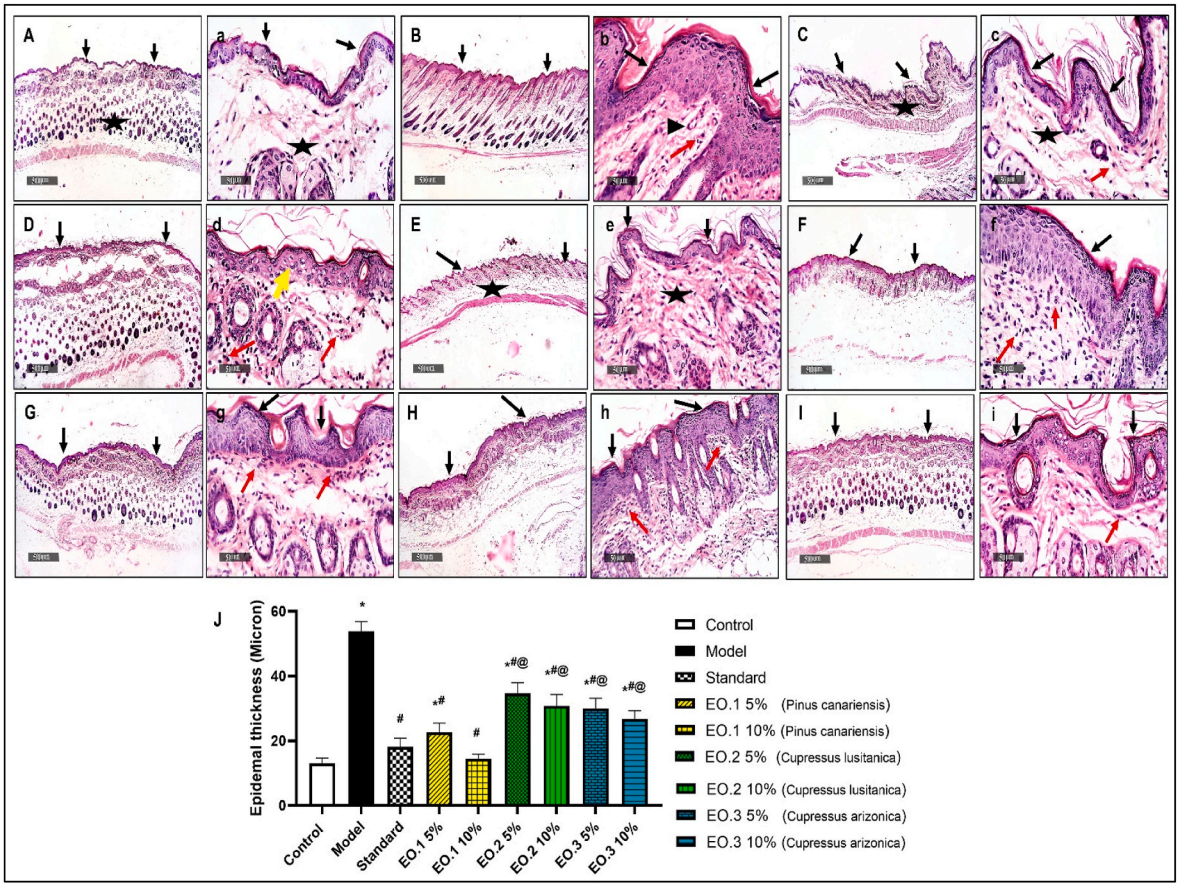

Fig. 4. Histological evaluation of *Pinus canariensis* C.Sm., *Cupressus lusitanica* Mill. and *Cupressus arizonica* Greene essential oil against IMQ-induced psoriasis in BALB/c mice. Photomicrographs represent H&E staining from control group [A, a], IMQ-group [B, b], mometasone group [C, c], *Pinus canariensis* C.Sm. EO 5% group [D, d], *Pinus canariensis* C.Sm. EO 10% group [E, e], *Cupressus lusitanica* Mill. EO 5% group [F, f], *Cupressus lusitanica* Mill. EO 10% group [G, g], *Cupressus arizonica* Greene EO 5% group [H, h], and *Cupressus arizonica* Greene 10% group [I, i]. Panel [J] represents epidermal thickness in microns. Scale bar = 50 μm. **Black arrow:** skin epidermal layer; **black star**: intact dermal layer with well-organized collagen fibers and hair follicles; **arrow ahead**: congested and dilated subepidermal blood vessels; **red arrow**: inflammatory cell infiltration; **yellow arrow**: focal vacuolization of epidermal keratinocytes. EO refers to essential oil. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 3
Score records of histologically examined skin lesions after topical application of *Pinus canariensis* C.Sm., *Cupressus lusitanica* Mill. and *Cupressus arizonica* Greene essential oils against IMQ-induced psoriasis in BALB/c mice.

	Control	IMQ	Mometasone	*Pinus canariensis* C.Sm. 5%	*Pinus canariensis* C.Sm. 10%	*Cupressus lusitanica* Mill. 5%	*Cupressus lusitanica* Mill. 10%	*Cupressus arizonica* Greene 5%	*Cupressus arizonica* Greene 10%
Epidermal thickening	–	+++	–	+	+	++	++	++	++
Dermal inflammatory cell infiltrates	–	++	+	+	+	++	+	++	++
Congested blood vessels	–	++	–	–	–	–	–	–	–

Tunisian oil (Chéraif et al., 2007) but in contrast to results on Italian, Algerian, and American CA oil which revealed lower/higher percentages of α-pinene (Chéraif et al., 2007). Likewise, Kenyan CL leaves revealed oil rich in monoterpene components that differed in proportion to the oil under study (Bett et al., 2016). These varying results may be attributed to climatic, geographical, and organ-specific factors (Mehalaine and Chenchouni, 2021).

The IMQ–treated mouse model is considered one of the most widely used models to study psoriasis (Chamcheu et al., 2016). The reason is that it closely resembles human plaque-type psoriasis concerning skin erythema, thickening, scaling, as well as to inflammatory infiltrate (van der Fits et al., 2009). IMQ results in inducing an immune response in the body by acting as an agonist of (TLR) 7/8 (Zhou et al., 2021). This stimulation triggers lymphocyte activity that may lead to splenomegaly. Additionally, IMQ promotes the release of inflammatory factors such as IL-17 and IL-23 (Su et al., 2022) leading to psoriasis-like symptoms in the skin, including erythema, scaling, and epidermal thickening. The data presented in this study showed for the first time the anti-inflammatory activities of topical application of PC 5, 10%, and CL 10% essential oils and their effect on serum reduction of IL-23 and IL-17A levels. Also, they showed significant improvement of dorsal skin erythema with a reduction in scaling and epidermal thickness as

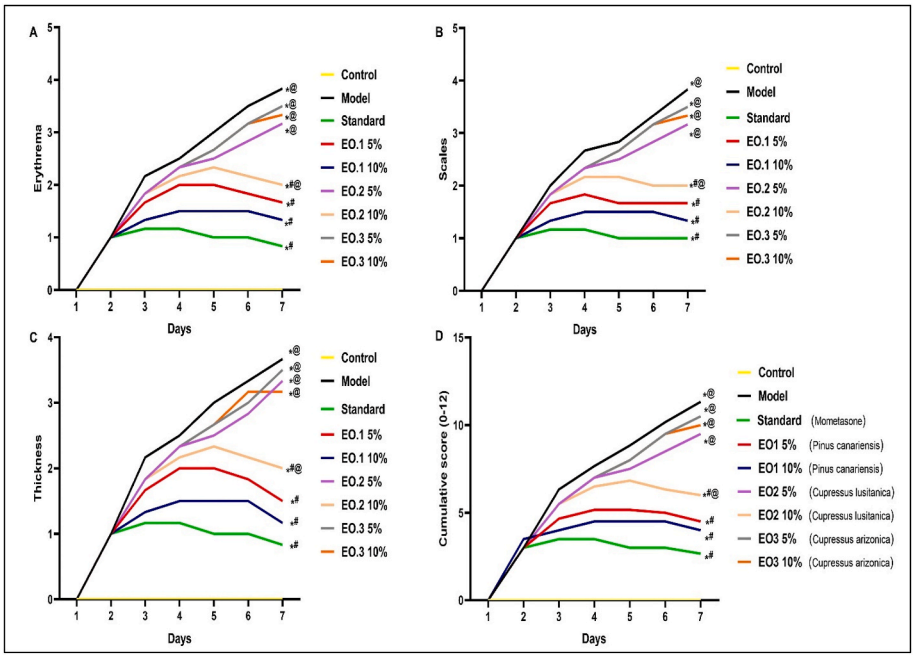

Fig. 5. PASI score of EO.1: *Pinus canariensis* C.Sm. 5 &10%, EO.2: *Cupressus lusitanica* Mill. 5 &10%, and EO.3: *Cupressus arizonica* Greene 5 &10% essential oil against IMQ-induced psoriasis in BALB/c mice. Photomicrographs represent skin erythema [A], scaling [B], epidermal thickness [C], and cumulative score [D] in each group from day one to day seven. All data were expressed as mean ± SD (n = 6), using two-way ANOVA followed by Tukey's post hoc test; $p < 0.05$. * Vs control group, # vs IMQ group, @ vs mometasone group. EO refers to essential oil.

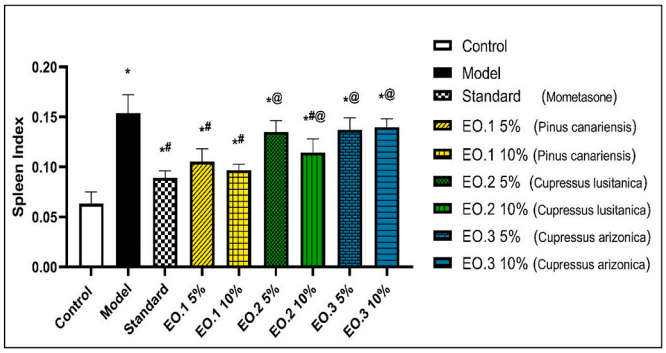

Fig. 6. Spleen index of EO.1: *Pinus canariensis* C.Sm. 5 &10%, EO.2: *Cupressus lusitanica* Mill 5 &10%, and EO.3: *Cupressus arizonica* Greene 5 &10% essential oil against IMQ-induced psoriasis in BALB/c mice. All data were expressed as mean ± SD (n = 6), using one-way ANOVA followed by Tukey's post hoc test; $p < 0.05$. * Vs control group, # vs IMQ group, @ vs mometasone group. EO refers to essential oil.

observed in the PASI score. Moreover, they decreased dermal inflammatory cells infiltration. Indeed, the effect of topical treatment of PC essential oil (5 and 10%) is comparable to the standard treatment (mometasone) (Figs. 4–7).

The observed anti-psoriasis activity of PC, CL, and CA EOs could be attributed to the activity of the major compounds (*α*-pinene, *β*-pinene, *δ*-3-Carene, D-limonene, camphor, umbellulone, *cis*-muurola-3,5-diene, and germacrene D), either singly or synergistically. *α*-pinene and *β*-pinene were quantified in EOs (13.74–47.16 and 0.24–10.79, respectively). These oils obtained from the woods of 4 conifers, *P. densiflora, P. koraiensis, Chamaecyparis obtusa,* and *Larix kaempferi,* showed an anti-inflammatory effect by inhibition of degranulation of mast cells and reduction of cytokines expression by decreasing the gene expression of IL-4 and IL-13 in lipopolysaccharide (LPS)-induced RBL-2H3 mast cells (Yang et al., 2019). Moreover, Mahdieh Khoshnazar et al. reported that *α*-pinene (100 mg/kg) attenuated the neuro-inflammation *via* reducing both gene and protein expression of tumor necrosis factor (TNF)-α and IL-1β in the hippocampus, cortex, and striatum (Khoshnazar et al., 2020). Furthermore, *α*-pinene significantly decreased LPS-induced production of IL-6, TNF-α, and nitric oxide (NO) in LPS-stimulated macrophages (Kim et al., 2015a). In addition, *α*-pinene prevented Ultraviolet-A (UVA)-induced oxidative stress, inflammation, DNA damage, and apoptosis in human skin epidermal keratinocytes

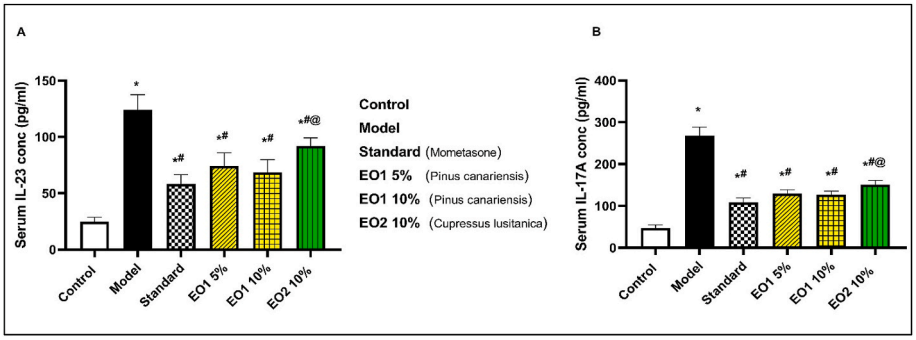

Fig. 7. Effect of EO1: *Pinus canariensis* C.Sm. EO 5 &10%, and EO2; *Cupressus lusitanica* Mill. EO 10% on serum [A] IL-23 level and [B] IL-17A level against IMQ-induced psoriasis in BALB/c mice. All data were expressed as mean ± SD (n = 6), using one-way ANOVA followed by Tukey's post hoc test; $p < 0.05$. * Vs control group, # vs IMQ group, @ vs mometasone group. EO refers to essential oil.

(Karthikeyan et al., 2018). Importantly, δ-3-carene, α-pinene, linalool-acetate, β-phellandrene, β-pinene, limonene, and (E)-caryophyllene were the major compounds detected in the EO extracted from three *Pinus* species. These compounds exerted an anti-inflammatory activity through the reduction of IL-6 secretion by up to 60% in an LPS-stimulated macrophage model (Basholli-Salihu et al., 2017). D-limonene, α-pinene and β-pinene, germacrene D and α-cadinol were detected in *Liquidambar styraciflua* EO which showed an inhibitory effect against 5-Lipoxygenase (5-LOX) activity and Prostaglandin E2 (PGE2) production in LPS stimulated hepatic cells in a dose-dependent manner (El-Readi et al., 2013). Interestingly, limonene was reported to suppress inflammation by targeting the NF-κB pathway which played an important role in pro-inflammatory signaling transduction (Younis et al., 2023). Added to that, *Lavandula intermedia* EO topical application with camphor (21.2%), exhibited anti-psoriasis activity by inhibiting cell proliferation and decreasing the number of T-cells, macrophages, and lymphocytes in mice ear skin with Imiquimod-induced inflammation (Sosnowska et al., 2022).

Furthermore, Tunisian EO of *C. sempervirens* cones which mainly composed of monoterpene hydrocarbons (65%) with **α**-pinene as the major constituent (47.51%) showed anti-oxidant effects against the 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) with IC_{50} 151 **μ**g/mL and 176.454 **μ**g/mL, respectively (Ben Nouri et al., 2015). A monoterpene-rich Iranian *C. arizonica* Greene fruits oil with α-pinene (71.92%), myrcene (6.37%), δ-3-carene (4.68%), β-pinene (3.71%), and limonene (3.34%) showed anti-nociceptive and anti-inflammatory activity against carrageenan-induced paw edema (Fakhri et al., 2022). Moreover, α-pinene as a single component had an anti-inflammatory effect by decreasing the LPS-induced production of IL-6, tumor necrosis factor-α (TNF-α), and nitric oxide (NO), in addition to inhibition of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) expressions in a dose-dependent manner. Additionally, it attenuated mitogen-activated protein Kinase (MAPKs) and NF-κB activation (Kim et al., 2015b).

In this context, we can summarize that PC EO is more effective than CL in alleviating IMQ-induced psoriasis symptoms, such effect could be attributed to the activity of major compounds that present in PC EO [α-pinene (71%) and β-pinene (13%)]. On the other hand, CL essential oil showed low concentrations of α-pinene (15.3%) and β-pinene (1.4%). Also, the lack of anti-psoriasis activity of CA could be attributed to the low content of sesquiterpene hydrocarbons (8.42%) and oxygenated sesquiterpenes (2.71%), as sesquiterpenes exert an anti-inflammatory effect. So, it would be interesting to verify whether the activity observed in the present study is due to these compounds or not by further future studies.

5. Conclusion and recommendations

In conclusion, our findings supported the traditional uses of the EO of *P. canariensis* and *C. lusitanica* aerial parts, as a natural plant resource, in the treatment of psoriasis as they attenuated both the immune and inflammatory responses. Further studies are recommended to evaluate the biological activity of the major identified compounds, either individually as isolated ones or in combinations.

CRediT authorship contribution statement

Rania M. Kamal: performed the phytochemical study, Data curation, Formal analysis, Writing – original draft, and editing. **Manal M. Sabry:** Supervision, Writing – review & editing. **Ali M. El-Halawany:** Conceptualization, Supervision, Writing – review & editing. **Mostafa A. Rabie:** performed the animal experiment, Formal analysis, Writing – biological part and editing. **Nesrine S. El Sayed:** Conceptualization, Formal analysis, Writing – review & editing. **Mohamed S. Hifnawy:** Supervision, Conceptualization, All authors approved the final manuscript. **Inas Y. Younis:** Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

List of abbreviations

AMDIS	Automated Mass spectral Deconvolution and Identification
ANOVA	One-way analysis of variance
ELISA	Enzyme-linked Immunosorbent Assay
EOs	essential oils
IL	Interleukin
IMQ	Imiquimod
5-LOX	5-Lipoxygenase
LPS	Lipopolysaccharide
MH	Monoterpene hydrocarbons
MS	Mass Spectra
PASI	Psoriasis Area and Severity Index
PGE2	Prostaglandin E2
RI	Retention Index
TNF-α	Tumor Necrosis Factor-Alpha

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