

Ultraviolet A photosensitivity profile of dexchlorpheniramine maleate and promethazine-based creams: Anti-inflammatory, antihistaminic, and skin barrier protection properties

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Summary

Background: Unwanted side effects such as dryness, hypersensitivity, and cutaneous photosensitivity are challenge for adherence and therapeutical success for patients using treatments for inflammatory and allergic skin response.

Aims: In this study, we compared the effects of two dermatological formulations, which are used in inflammatory and/or allergic skin conditions: dexchlorpheniramine maleate (DCP; 10 mg/g) and promethazine (PTZ; 20 mg/g).

Methods: We evaluated both formulations for phototoxicity potential, skin irritation, anti-inflammatory and antihistaminic abilities, and skin barrier repair in vitro and ex vivo using the standard OECD test guideline n° 432, the ECVAM protocol n° 78, and cultured skin explants from a healthy patient. Ultraviolet A was chosen as exogenous agent to induce allergic and inflammatory response.

Results: Both PTZ and DCP promoted increases in interleukin-1 (IL-1) synthesis in response to ultraviolet A (UVA) radiation compared to control. However, the increase observed with PTZ was significantly greater than the DCP, indicating that the latter has a lower irritant potential. DCP also demonstrated a protective effect on UVA-induced leukotriene B₄ and nuclear factor kappa B (NF-κB) synthesis. Conversely, PTZ demonstrates more robust UVA antihistaminic activity. Likewise, PTZ promoted a significantly greater increase in the production of involucrin and keratin 14, both associated with protective skin barrier property.

Conclusion: In conclusion, these data suggest possible diverging UVA response mechanisms of DCP and PTZ, which gives greater insight into the contrasting photosensitizing potential between DCP and PTZ observed in the patients.

KEYWORDS

antihistamines, anti-inflammatory, dexchlorpheniramine, phototoxicity, promethazine, skin barrier

1 | INTRODUCTION

Topical H₁-antihistamines (tAH) are widely used for presenting an immediate effect in reducing the pruritus in patients with

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eczematous dermatitis, xerotic skin, insect stings, among others.¹ In addition to promptly alleviating symptoms, it has been shown that a single application of tAH suppressed histamine for at least 2 hours.² As a consequence of the widespread use, self-medication, and the low cost of this therapeutic class, the dissemination of tAH has resulted in an increase incidence of side effects.²

Several case reports and studies are described in the literature on adverse reactions and even worsening of symptoms after using tAH, especially with phenothiazine- and piperazine-derived compounds. Hydroxyzine and cetirizine are among the most referenced with respect the induction of sensitization or allergic reactions after topical application^{3,4}; however, other classes are indicated in hypersensitivity (Table 1).⁵⁻⁷

The main reactions reported are as follows: urticaria, contact dermatitis, maculopapular eruption, palmar erythema, desquamation, and others cutaneous eruptions.⁵⁻⁹ Photosensitive contact dermatitis, reported as phototoxicity and photoallergy, was also observed after topical application of diphenhydramine and promethazine.^{7,8} It was reported, in a review of the literature, that topical doxepin is the most topical preparation implicated in causing contact dermatitis.¹⁰ H₁-Antihistamines administered orally also produce similar and generalized cutaneous reactions, such as diffuse erythema and pustules, morbilliform eruption, pruritus, toxicoderma, and exanthematous pustulosis.^{3,4,6}

As the name indicates, antihistamines block histamines by acting as a competitive inhibitor of the H₁-receptor site. Hence, in addition to concomitant with antipruritic effects of antihistamines, secondary effects are expected due to the presence and function of H₁ receptors in a variety of cell types.¹ Some have suggested mechanisms for hypersensitivity reactions caused by the oral AH such as IgE-mediated reaction, immunoreactivity of the drug itself, and conformational changes of H₁ receptor.^{3,5} However, others have implicated pharmaceutical formulations and not the active compounds as direct causes for hypersensitivity.¹¹ The role of tAH in skin sensitization is left unclear.

In order to contribute to the understanding of the effects of the tAH in skin metabolism, this study was conducted to evaluate the effects of two dermatological formulations—dexchlorpheniramine maleate (DCP; 10 mg/g) and promethazine (PTZ; 20 mg/g) regarding the phototoxicity potential, skin irritation, anti-inflammatory, and antihistaminic abilities, as well as skin barrier repair, using the widely accepted standards from Organization for Economic Cooperation

and Development (OECD) test guideline n° 432,¹² the European Centre for the Validation of Alternative Methods (ECVAM protocol n° 78),¹³ and cultured skin explants from a healthy patient. The use of these methods, besides adhering to accepted ethical standards, is also considered the preferred method for testing the use of topical pharmaco/cosmetic formulations.¹⁴

2 | MATERIAL AND METHODS

2.1 | Test substances

Test substances dexchlorpheniramine maleate (DCP; 10 mg/g; Polaramine®; INCI names: dexchlorpheniramine maleate, allantoin, methylparaben, glycerin, sorbitol, mineral oil, glyceryl stearate, cetyl esters, cetyl alcohol, Lavandula Officinalis flower oil, acetylated lanolin alcohol, aqua; Mantecorp Indústria Química e Farmacêutica Ltda, Rio de Janeiro, Brazil) and promethazine (PTZ; 20 mg/g; Fenegan®; INCI name: stearic acid, cetareth-20, sodium lauryl sulfate, cholesterol, lanolin oil, TEA-salicylate, glycerin, methylparaben, propylparaben, Lavandula Angustifolia (Lavender) flower oil; Sanofi-Aventis Farmacêutica Ltda, São Paulo, Brazil) were purchased in drugstores in the form of dermatological cream.

As they are commercially available products, the use of a placebo formulation without active ingredients becomes unfeasible, because the companies do not provide information about the pharmacotechnical design. This information is confidential.

2.2 | Prediction of phototoxicity potential

The phototoxicity assay was based on the OECD test guideline n° 432 and the ECVAM protocol n° 78.^{12,13} A permanent mouse fibroblast cell line BALB/c 3T3 clone A31 was obtained from BCRJ (Banco de Células do Rio de Janeiro, Rio de Janeiro, RJ, Brazil) and routinely grown in Dulbecco's modified Eagle's medium (Sigma-Aldrich, St Louis, MO, USA) containing glucose (4.5 g/L), L-glutamine (Sigma-Aldrich), antibiotics (penicillin 100 IU/mL; streptomycin 100 µg/mL; Thermo Fisher Scientific, Waltham, MA, USA), and 10% heat-inactivated fetal bovine serum (Cultilab, Campinas, SP, Brazil) in a 5% CO₂ humidified atmosphere at 37°C. Cells were seeded in 96-well (Nalge Nunc International, Rochester, NY, USA) plate at 1×10⁴ cells per well. Duplicate 96-well monolayers of 3T3 fibroblasts were pretreated with eight different concentrations (range: 10–0.00316 mg/mL) of DCP and PTZ in HBSS medium (Thermo Fisher Scientific) during 60 minutes. These concentrations were defined by cytotoxicity test (MTT; 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; Sigma-Aldrich). The test substances were diluted in culture medium containing polysorbate 20 (0.03%; Sigma-Aldrich). As a negative control, culture medium containing 0.03% of polysorbate 20 was used and it not presented phototoxicity potential. As a positive control, a known chemical phototoxic—chlorpromazine (Sigma-Aldrich)—was tested concurrently.

One of the plates was exposed to a noncytotoxic 5 J/cm² ultra-violet A (UVA) radiation dose using the UVA Cube 400, SOL 500,

TABLE 1 Classification of topical antihistamines formulation implicated in causing hypersensitivity

Antihistamine Class	Preparations	Cutaneous side effects
Piperazine	Hydroxyzine, cetirizine, levocetirizine	Pruritus, papules, erythema
Phenothiazine	Promethazine	Photosensitive dermatitis
Piperidine	Desloratadine, ketotifen, azelastine, levocabastine	Urticaria, erythema, edema
Ethanolamine	Diphenhydramine	Photosensitive dermatitis
Others	Doxepin	Contact dermatitis

H1 filter e UV Meter (Honle UV America Inc., Marlborough, MA, USA), while the other plate was kept in the dark. In both plates, the treatment medium was then replaced by fresh culture medium and cell viability was determined by neutral red uptake (In Cytotox Neutral Red; Xenometrix AG, Allschwil, Switzerland) after 24 hours of incubation. Cell viability was expressed as percentage of untreated controls and was calculated for each test concentration.

The prediction of phototoxicity was given by the ratio between the IC_{50} (inhibitory concentration) of the nonexposed cells and exposed to UVA radiation. Test substance is considered nonphototoxic if the photoirritation factor (PIF) is <2 , possibly phototoxic if $PIF >2$ to <5 and phototoxic if $PIF >5$. Another parameter that must also be considered is the mean photoeffect (MPE) based on comparison of the complete concentration response curves. In this case, the substance is nonphototoxic if MPE is <0.1 ; probably phototoxic if $MPE >0.1$ and <0.15 and phototoxic if MPE is >0.15 .^{12,13}

2.3 | Treatment and irradiation protocol for skin cultures

The skin fragments were originating from one (01) healthy subject, female, skin type III, 54, who underwent elective plastic surgery in the abdominal region (abdominoplasty). After the surgical procedure, the skin fragments were collected in plastic vials containing 0.9% saline and kept in refrigeration for up to 24 hours. This project did not include the storage and stockpiling of biological material for future use, and the spare fragments were disposed of appropriately as infectious residue. The use of human skin fragments from elective surgeries for this study was approved by the Ethics Committee of the University São Francisco—SP, Brazil (CAAE 29286914.8.0000.5514).

Skin fragments were fractionated into pieces of approximately 2-cm², weighed, incubated in 24-well plate (Nalge Nunc) with DMEM containing glucose, L-glutamine, penicillin, streptomycin, and fetal bovine serum. To simulate an inflammatory response in the test system, skin fragments were subjected to a dose of 10 J/cm² ultraviolet A radiation using the UVA Cube 400, SOL 500 H1 filter e UV Meter (Honle) for three consecutively days. After the last exposure period, skin fragments were treated with DCP and PTZ, directly from the packing to the surface of the skin fragments, at a ratio of 2 mg/cm² for additional three consecutively days. This strategy, as mentioned above, can mimic the actual conditions of use.¹⁴

2.4 | Quantification of mediators released by skin culture

Forty-eight hours after the last day of skin culture treatment with DCP and PTZ, supernatant was collected and fragments were dissociated process to obtain tissue homogenate, using the Medimachine (BD Biosciences, Bruino, Italy). IL-1 α , prostaglandin E₂ (PGE₂), leukotriene B₄ (LTB₄), β -endorphin, and histamine were analyzed in the skin culture supernatant, while transient receptor potential cation channel, subfamily V, member 1 (TRPV-1), involucrin, and keratin 14 were analyzed in tissue homogenate by commercial ELISA kit (Uscn

Life Sciences, Wuhan, China; R&D Systems, Inc., Minneapolis, MN, USA; Cayman Chemical, Ann Arbor, MI, USA; Phoenix Pharmaceuticals, Inc., Burlingame, CA, USA) according to the manufacturer's protocol. Nuclear factor kappa B (NF- κ B) was measured in nuclear protein fraction using a commercially available extraction kit (Cayman Chemical). Three independent experiments were performed.

2.5 | Statistical analysis

Statistical analysis was performed using ANOVA test (GraphPad Prism 6, Version 6.01, GraphPad Software, Inc., La Jolla, CA, USA) to measure the variation of the results, comparing data between all the groups. We also applied Tukey post-test which strengthened and made the results more precise. The statistical significance was considered as $P < .05$. Data were expressed as mean $\pm$ SD.

3 | RESULTS

In this study, experiments were undertaken to investigate the comparative effects of both dermatological formulations dexchlorpheniramine maleate (DCP; 10 mg/g) and promethazine (PTZ; 20 mg/g) regarding the phototoxicity potential, skin irritation, anti-inflammatory and antihistaminic abilities, and skin barrier function. The following mediators were measured using in vitro and ex vivo techniques: interleukin-1 alpha (IL-1 α), eicosanoids PGE₂ and LTB₄, transcriptional factor NF- κ B, histamine, neuropeptide β -endorphin, TRPV1, and envelope proteins involucrin and keratin 14.

3.1 | Phototoxicity Potential: DCP and PTC demonstrate low phototoxicity in vitro

3T3 fibroblasts were pretreated with eight different concentrations of DCP and PTZ (range: 10-0.00316 mg/mL). The phototoxicity to 3T3 cells was measured by NRU in the presence and absence of UVA and was shown in Figure 1.

The IC_{50} for cell viability and the photoirritant factor (PIF) in nonirradiated and irradiated conditions were calculated using a concentration curve of drug response and showed in Table 2. Our results demonstrate that DCP and PTZ are nonphototoxic ($PIF < 3$). Data for the positive control (chlorpromazine) indicated it was phototoxic, as well as validated the experimental design.

3.2 | DCP shows greater protective anti-inflammatory and anti-irritant activity than PTZ on UVA-exposed skin ex vivo

As expected, UVA produces increases of 28.5%, 6.8%, and 10.4% in the release of PGE₂, LTB₄, and NF- κ B, respectively, when compared to the control group (Figure 2).

The test substance DCP was able to significantly protect skin explants from UVA-induced increases in LTB₄ by 5.1% and NF- κ B by 10.5% as compared to nonirradiated control group. Suppressed

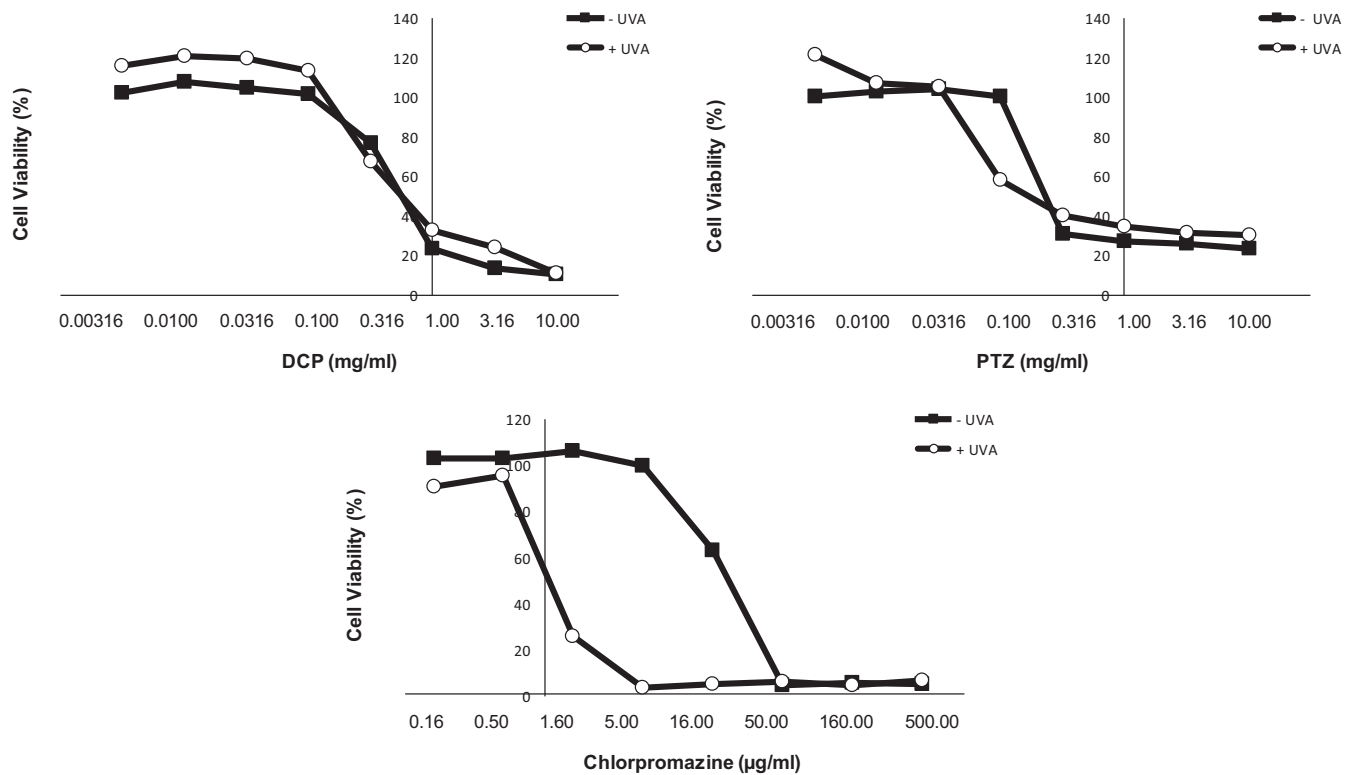


FIGURE 1 The phototoxicity potential of dexchlorpheniramine maleate (DCP), promethazine (PTZ) and chlorpromazine on 3T3 mouse fibroblasts measured by NRU assay

TABLE 2 IC50 and PIF of DCP, PTZ, and chlorpromazine

Test substance	IC ₅₀ non-irradiated	IC ₅₀ irradiated	PIF
DCP	0.586 mg/mL	0.359 mg/mL	1.365
PTZ	0.270 mg/mL	0.112 mg/mL	2.449
Chlorpromazine	18.089 µg/mL	1.419 µg/mL	12.754

Concentration of DCP, PTZ, and chlorpromazine that inhibits 50% of cell viability in nonirradiated and irradiated conditions (IC₅₀); PIF, photorritant factor was given by the ratio between the IC₅₀ of the nonexposed cells and exposed to UVA radiation; PTZ, promethazine.

PGE₂ production was also observed on DCP treated skin, but were not statistically significant.

PTZ-treated skin also showed a downward trend in the levels of LTB₄. However, unlike DCP, PTZ did not protect UVA-exposed skin from increasing NF-κB and PGE₂ productions (*P*<.001, in relation to control group).

These results are consistent with those obtained in skin irritation assay, measured by IL-1α and histamine synthesis (Figure 3). UVA radiation promoted a significant increase in the production of IL-1α and histamine (5.9-fold and 33.2%, in relation to respective control groups).

The production of IL-1α was further elevated by treatment with both test substances. The increase observed in PTZ-treated skin was significantly higher than that obtained in DCP treated skin, indicating that DCP has a lower irritation potential.

As expected, both substances promoted downregulation histamine. However, the antihistamine potential of PTZ-treated,

UVA-irradiated skin was more pronounced, with a 47% reduction as compared to DCP treated, UVA-irradiated skin.

3.3 | DCP, but not PTZ, protects against UVA-induced cutaneous hypersensitivity via β-endorphin signaling in ex vivo skin model

Figure 4 shows the effect of DCP and PTZ on the synthesis of β-endorphin and TRPV1 receptor on human skin subjected to UVA radiation. The exposure of skin explants cultures to UVA radiation promoted reduction in β-endorphin synthesis (decrease in 11.1-fold). On the other hand, skin explants treated with DCP maintained pre-irradiated levels of this neuropeptide as compared to the control group. PTZ did not protect against UVA-induced changes in β-endorphin levels.

Contrary to expectation, UVA radiation promoted a decrease in 21.1% in the synthesis of TRPV1 receptor, when compared to control group. Interestingly, the treatment of irradiated skin explants with PTZ stimulated significant decrease in TRPV1 when compared to the UVA group. DCP did not alter the levels of TRPV1 in relation to UVA group.

3.4 | PTZ promotes skin barrier function better than DCP in UVA-irradiated skin ex vivo

UVA radiation promotes a significant reduction in the production of involucrin and keratin 14, reaching 24.05% and 28.02%, respectively, compared to control group (Figure 5).

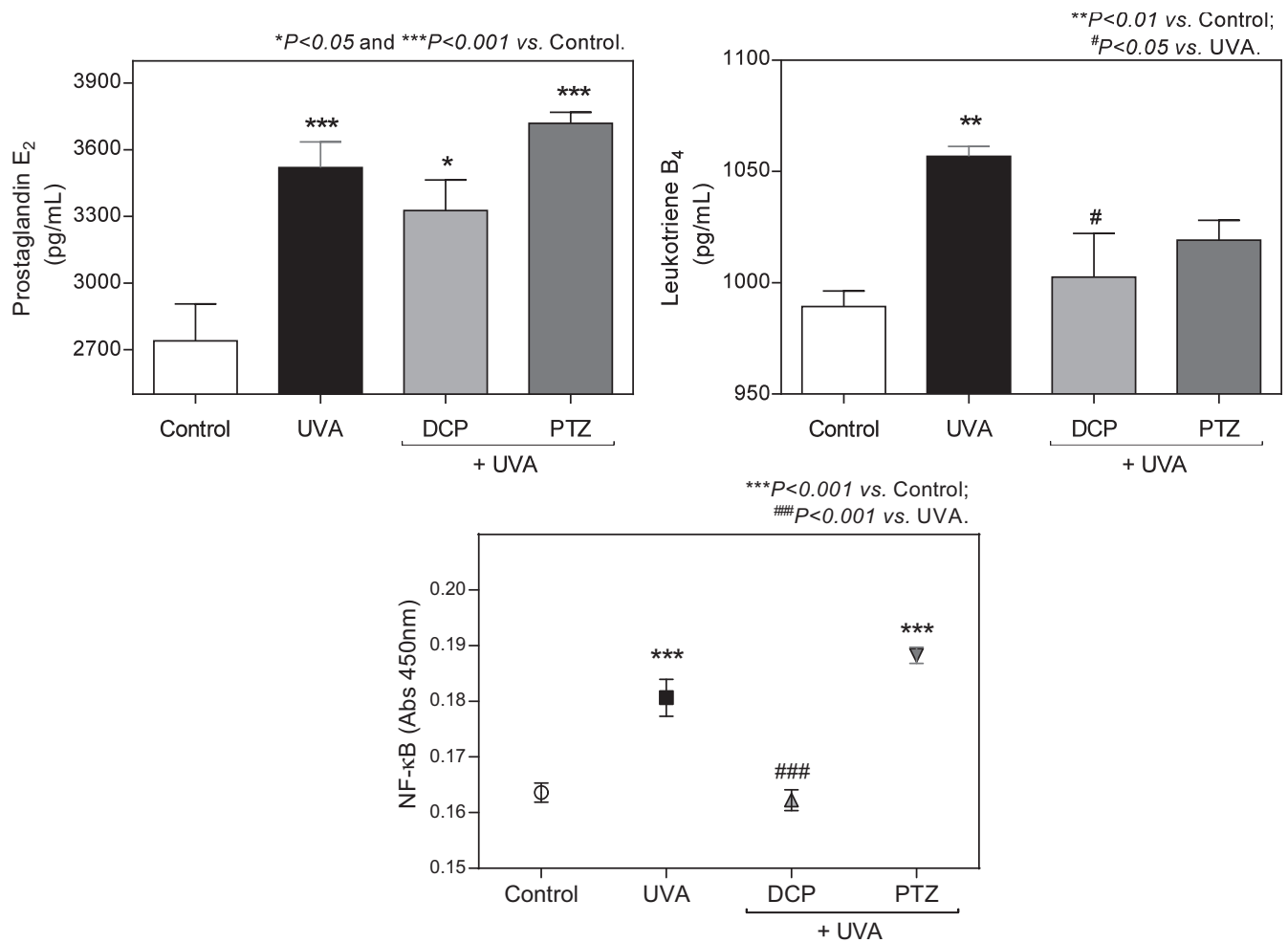


FIGURE 2 Ex vivo effects of dexchlorpheniramine maleate (DCP) and promethazine (PTZ) on the production of prostaglandin E₂, leukotriene B₄, and NF-κB in human skin explants subjected to ultraviolet A (UVA) radiation. Data are presented as mean±SD of three independent experiments (n=6) (ANOVA, Tukey)

Skin explants treated PTZ promoted significant increases in the levels of both involucrin and keratin when compared to UVA group and when compared to the control group. Involucrin levels increased significantly by 1.9- and 4.5-fold, respectively, for DCP and PTZ. A significant increase in keratin 14 production was observed only in PTZ-treated skin explants (2.4-fold increase compared to only irradiate group).

4 | DISCUSSION

The availability of an effective topical treatment for either inflammatory and allergic skin conditions, associated with the absence or minimization of unwanted side effects, can be a key differentiator to ensure adherence to and success outcome such treatment. Unfortunately, finding treatment for inflammatory skin conditions can be frustrating, considering the number of unwanted side effects caused by topical antihistamine H1 (tAH).¹

In this work, we investigate and compared promethazine (PTZ; 20 mg/g), a clinically photo-hypersensitivity tAH, with another tAH,

dexchlorpheniramine maleate (DCP; 10 mg/g), to gain mechanistic insight into tAH-related photo-hypersensitivity.

Depending on the topographical location and environmental influences, skin shows an exceptional structural and functional diversity. It is resulted from the effect of being constantly exposed to external aggressions, such as solar radiation, mechanical stimuli, climate changes, and either chemical or biological damages. The essential function of the skin is to protect the body against these harmful environment insults and, simultaneously, minimizing barrier dysfunction. Therefore, the maintenance of structural skin integrity is critical and must provide immediate mechanisms of epidermal barrier restoration.¹⁵

A decrease in stratum corneum (SC) water content is shared by a large number of dermatosis, such as atopic dermatitis, psoriasis, eczema, hereditary ichthyosis, and senile xerosis. The natural barrier of the SC critically depends on its composition, represented mostly by proteins, of which about 5% corresponds to a structural portion called cornified cell envelopes (CCE). The CCE is formed by a set of proteins highly insoluble and resistant, which involve externally keratinocytes, being fundamental in the structure and organization of

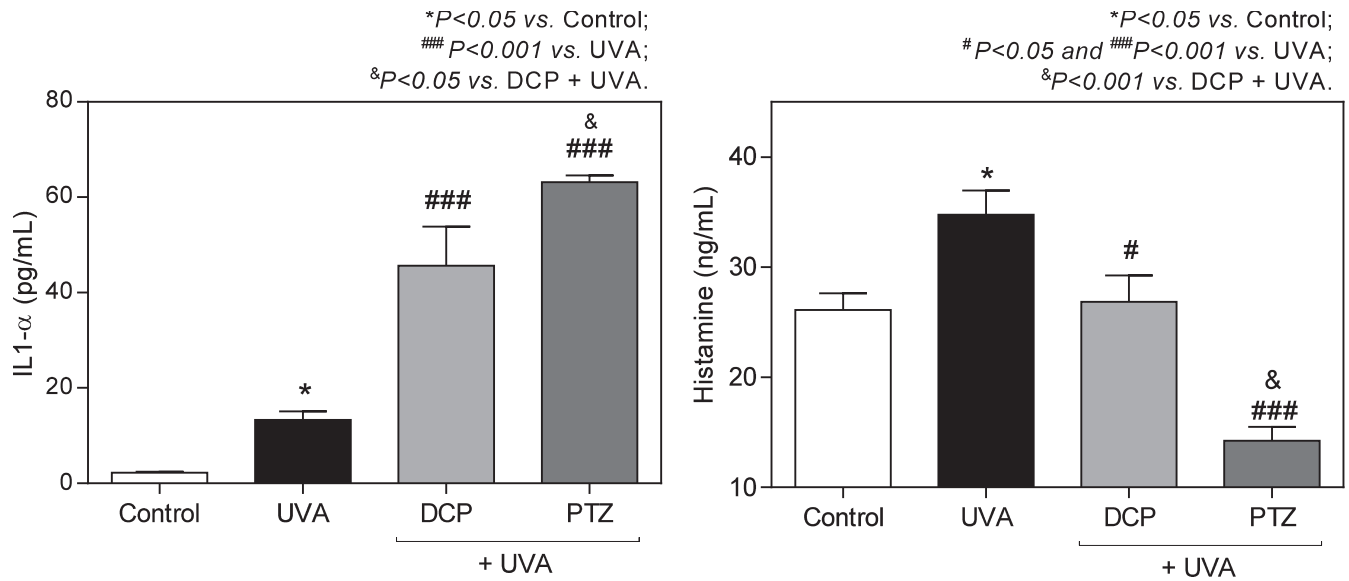


FIGURE 3 Ex vivo effects of dexchlorpheniramine maleate (DCP) and promethazine (PTZ) on the production of IL-1 α and histamine in human skin explants subjected to ultraviolet A (UVA) radiation. Data are presented as mean $\pm$ SD of three independent experiments (n=6) (ANOVA, Tukey)

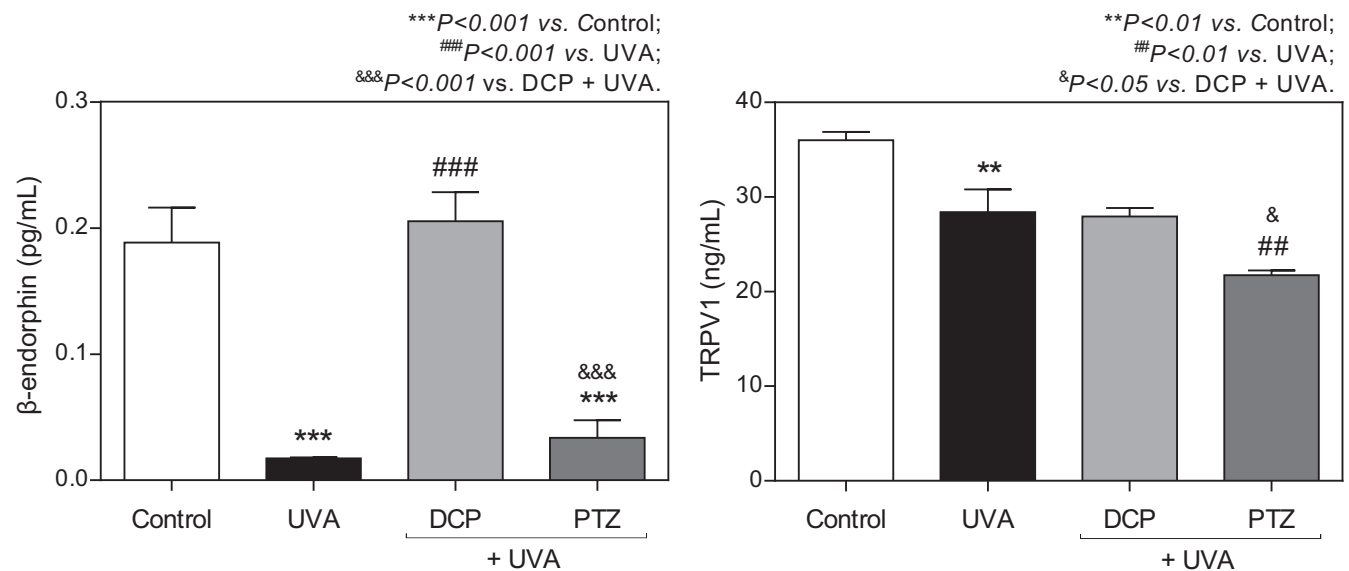


FIGURE 4 Ex vivo effects of dexchlorpheniramine maleate (DCP) and promethazine (PTZ) on the production of β -endorphin and transient receptor potential cation channel, subfamily V, member 1 (TRPV-1) in human skin explants subjected to ultraviolet A (UVA) radiation. Data are presented as mean $\pm$ SD of three independent experiments (n=6) (ANOVA, Tukey)

intracellular lipids. Profilaggrin, filaggrin, involucrin, and loricin are proteins that compose the CCE, responsible for the association of intermediate keratin filaments and consequent increase in cohesion among corneocytes. In fact, it is already well known that ultraviolet light irradiation is capable to interfere on human skin barrier, disrupting both its structure and function, being skin moisturizing directly affected by such external agents.^{16,17}

Our results show that both DCP and PTZ were able to prevent UVA-induced reduction in involucrin levels, demonstrating a positive action on cornified cell envelopes (CCE) formation. PTZ produced a

stronger response by elevating involucrin amount compared to DCP. Additionally, PTZ increased keratin 14 levels, indicative of cell proliferation potential, particularly in the basal layer. Keratin 14 is also essential for the formation and maintenance of integrity of the skin barrier.¹⁸ However, our findings suggest that PTZ protects skin barrier function better than DCP, also indicating a smaller role of improvement in tAH-related photo-hypersensitivity.

Associated with the integrity of skin barrier, local production of neuropeptides, such as substance P, CGRP (calcitonin-related peptide gene), and proopiomelanocortin (POMC)—represented, for example,

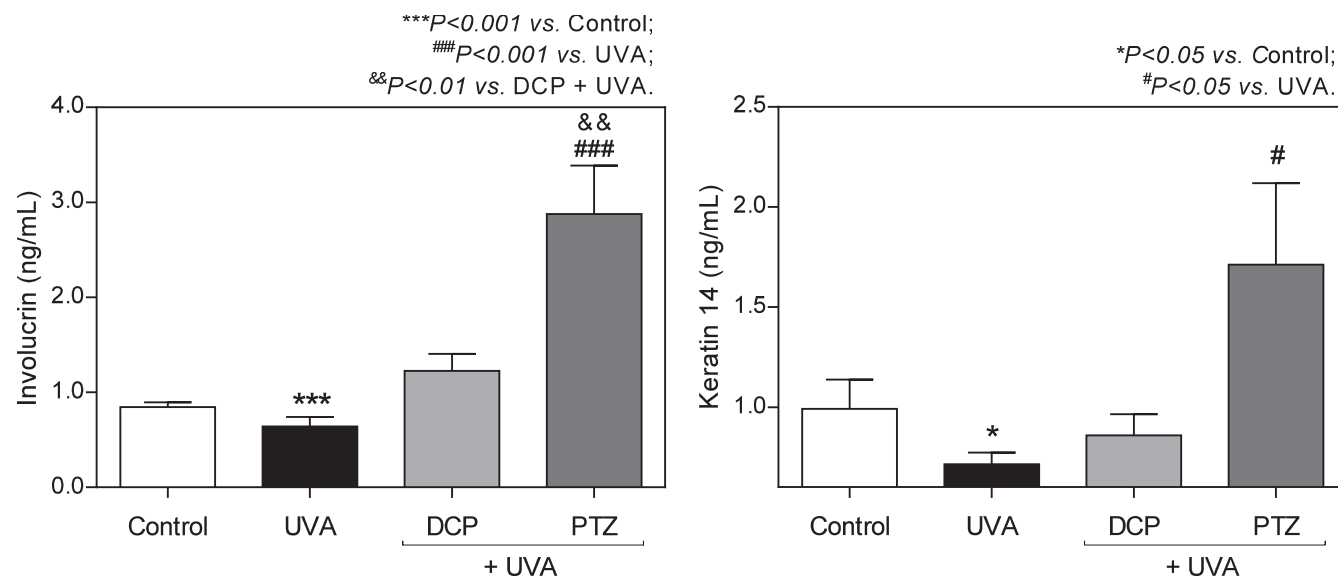


FIGURE 5 Ex vivo effects of dexchlorpheniramine maleate (DCP) and promethazine (PTZ) on the production of involucrin and keratin 14 by human skin explants subjected to ultraviolet A (UVA) radiation. Data are presented as mean $\pm$ SD of three independent experiments ($n=6$) (ANOVA, Tukey)

by β -endorphin and enkephalin—promote regulation of skin immune response and tissue repair. Neurohormones and neuropeptides play an important immunomodulatory function and are associated with physiopathology of some skin disorders.¹⁹ In addition to intrinsic factors, neuropeptides are regulated by environmental factors particularly by UVA and UVB radiation. Unlike UVB, UVA affects deeper into the skin, and 50% of the energy reaches dermis.¹⁷ The intensity of neuroendocrine activation exerted to solar radiation is determined by individual susceptibility, more specifically by the skin pigmentation. UVA radiation causes an increase in gene expression POMCs with subsequent production of α -MSH (melanocyte-stimulating hormone) and ACTH (adrenocorticotrophic hormone) in keratinocytes and human endothelial cells.²⁰ In response, an increase in melanogenesis process may be observed.²¹ The photoexposure also influences the immune response, and particularly UVA exerts an immunosuppressive effect.²²

It is important to be pointed up that POMC peptides have important cutaneous actions, which include downregulation of adhesion molecules and reduction of inflammatory process through the modulation of interleukin-10 production, contributing to the cutaneous neurosensory comfort.²³ β -Endorphin is involved in the process of re-epithelialization, tissue regeneration, and wound healing. The loss of the ability of keratinocytes to synthesize POMC generates deleterious effects on the skin, including inability to perfect restoration of skin barrier, reducing the ability to repair tissue, reduced proliferative capacity of dermal and epidermal cells, as well as reducing the stimulation of protein synthesis.²⁴

As expected, we found that UVA radiation promoted a significant downregulation in the production of POMC β -endorphin. DCP, but not PTZ, protected skin explants against UVA-induced reduction in β -endorphin, indicating a stronger role for neuropeptides with regard to the contrasting photosensitivity between DCP and PTZ.

The formulations containing DCP showed superior UVA protection and anti-inflammatory activity to that containing PTZ. DCP reduced of UVA-induced NF- κ B and leukotriene B₄, whereas PTZ was more effective at reducing the production of histamine ex vivo. These results prove to be aligned with the assay for assessment of skin irritation, which was measured by IL-1 α production in skin explants. In this test, the formulation containing DCP was less irritating than the one containing PTZ, once DCP induced a lower production of IL-1 α ; however, both PTZ and DCP have produced increasing above those initially instigated by UV radiation. Future studies should also investigate the role of TNF α .

Skin irritation is a process that refers to the production of reversible damage to skin following the application of substances resulting in the formation of erythema and edema.²⁵ The irritation process involves a chain of cellular and biochemical responses with the release of various cytokines and eicosanoids; among those cytokines produced by keratinocytes, only the IL-1 α and tumor necrosis factor alpha (TNF- α) activate a sufficient number of effector mechanisms that trigger the skin clinical manifestation.²⁶

Interleukin-1 alpha is constitutively produced by keratinocytes and is retained in the intracellular compartment, being released immediately at any sign of tissue damage, signaling the production of other cytokines, and initiating the inflammatory process.²⁷ Hence, the measurement of IL-1 α is an established method for the appointment of the irritation potential of a substance topically applied.^{14,25}

Despite expectations in the parameter hypersensitivity, we observed that UVA irradiation was not able to increase the functional expression of the nociceptor TRPV1. Peculiarly, this exogenous insult promoted a decrease in TRPV1, which somehow compromises the regulation of inflammatory process.²⁸ Further treatment of skin fragments with PTZ promoted an additional reduction

in this receptor, in comparison with that produced by the group submitted only to UVA radiation.

Considering that reports already published correlate some tAH to either phototoxicity or photoallergy,⁸ we carried out a comparative testing of formulations containing DCP and PTZ to estimate the phototoxic potential of the test substances. In fact, we wondered to know laboratorial differences related to both DCP and PTZ, because both have also already been described with dermatitis.

A widespread alternative photoassay, in vitro 3T3 neutral red uptake phototoxicity test (3T3 NRU),^{12,13} was used. The principle of this phototoxicity assay is a comparison of the reduction in cell viability of a test substance when measured in the presence and absence of a noncytotoxic dose of ultraviolet A (UVA) light. According to our results, none of the tested formulations was found to be predictive of acute phototoxicity that could have arisen from combined action of a chemical and light.

In summation, it was observed that, for anti-inflammatory activity, the formulation containing DCP proved to be more protective against UVA-induced inflammation signaling, whereas the greater antihistamine action and skin barrier protection of PTZ suggest smaller roles for these biomarkers in PTZ's clinically observed photosensitivity.

5 | CONCLUSION

This study aimed to contribute to dermatological research in order by providing insight regarding the biological effects of topical H₁-antihistamines DCP and PTZ when exposed to UVA. Considering these results, DCP seems to be less photosensitizing than PTZ by offering better protection against UVA-induced signaling alterations in the skin.

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CONFLICT OF INTEREST

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