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Improved transcutaneous delivery of cetirizine hydrochloride for the treatment of post-chemotherapy alopecia: Poke and emulgel approach

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Abstract: **Background**: Chemotherapy-induced alopecia negatively impacts the mental health of cancer patients. Topical minoxidil, a widely recommended drug for hair regrowth, causes scalp irritation and contact dermatitis. Oral minoxidil causes multiple cardiovascular and neurological side effects. Cetirizine hydrochloride, an antihistamine with a better safety profile than minoxidil, may stimulate hair follicle activity by modulating prostaglandin levels. **Objectives**: The present study aimed to develop a cetirizine hydrochloride-loaded emulgel and evaluate its potential, in combination with microneedling, for the treatment of chemotherapy-induced alopecia. **Methods**: Different emulgel formulations comprising cetirizine HCl, liquid paraffin, carbopol 940, propylene glycol, oleic acid, Tween 20, Span 20 and propylparaben were optimized using central composite design and response surface methodology. Physicochemical evaluation of the prepared emulgel included physical examination, determination of pH, viscosity, spreadability, drug content and stability. Interactions and compatibility among formulation constituents were assessed using *In-silico* analysis and Fourier transform infrared spectroscopy. *In-vitro* drug release, *ex-vivo* permeation and *in-vivo* hair growth studies were carried out to evaluate the performance efficiency of emulgel. **Results**: The prepared emulgels exhibited acceptable physicochemical properties and remained stable for 3 months. Constituents were found to be compatible with each other. The optimized formulation F4 released >95% drug at pH 5.5 within 360 minutes. During *an ex-vivo* study, ~94% of the drug permeated across rat skin within 6 hours following application of emulgel on the microneedle-pretreated skin. In cyclophosphamide-induced alopecia in rats, application of emulgel to microneedle-pierced skin for 15 days promoted hair growth. **Conclusion**: The prepared cetirizine HCl-loaded emulgel and microneedle combination may be a promising approach to treating chemotherapy-induced alopecia.

Keywords: Chemotherapy-induced alopecia; Cetirizine hydrochloride; Microneedling; Poke and emulgel approach; Transcutaneous delivery

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INTRODUCTION

Chemotherapy-induced alopecia negatively impacts the mental health and self-esteem of cancer patients. The severity and pattern of chemotherapy-induced alopecia are significantly impacted by the type of drug used. For example, the incidence of alopecia is >80%, 10-50% and ≥60% following chemotherapy using taxanes (e.g., paclitaxel), antimetabolites (e.g., 5-fluorouracil) and alkylating agents (e.g., cyclophosphamide), respectively (Kaufman *et al.*, 2025).

Minoxidil is the most widely recommended pharmacological option for hair regrowth. In case of topical application, minoxidil is converted to minoxidil sulphate (active form) by sulfotransferases; however, ~40-60% of people are reported to lack sufficient levels of these enzymes in their scalp, in turn, reducing treatment efficacy. Topical minoxidil causes scalp irritation and contact dermatitis. Oral minoxidil is metabolized in the liver (which contains abundant sulfotransferases); however, it is associated with several cardiovascular and neurological side effects (Jimenez-Cauhe *et al.*, 2024). Minoxidil primarily acts by extending the anagen phase of the hair growth cycle and increasing follicular vascularization, instead of specifically targeting the inflammatory and prostaglandin-mediated pathways implicated in chemotherapy-associated follicular damage. Cetirizine hydrochloride, a second-generation antihistamine with anti-inflammatory properties, is commonly prescribed for allergic rhinitis and urticaria and may reduce microinflammation of the scalp (a contributing factor in alopecia) and oxidative stress associated with chemotherapy, thereby improving tolerability and patient compliance. It may promote hair growth by reducing prostaglandin D2 (an inhibitor of hair growth) and enhancing prostaglandin E2 (which supports follicular proliferation and anagen maintenance) (Chen *et al.*, 2022; Jiang *et al.*, 2023; Mostafa *et al.*, 2021; Zaky *et al.*, 2021). In a study, significantly greater hair growth was observed in 30 males with alopecia who received a

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topically applied cetirizine solution (1%, 1 ml) compared with a placebo solution in the control group (Zaky *et al.*, 2021). An improvement in hair growth and density was observed in patients suffering from female pattern hair loss following treatment with cetirizine 1% or minoxidil 2% topical solutions. Minoxidil treatment was significantly superior to cetirizine in improving hair density but not in improving hair diameter (Alavi *et al.*, 2023). Traditional formulations, e.g., ointments, creams and lotions, are relatively less effective for treating alopecia due to poor localization of drugs at the target site (Jillani *et al.*, 2022). Emulgels can improve the transcutaneous penetration of drugs due to their composition (containing surfactants, co-solvents, oils, etc.). In addition, the non-greasy gel base of emulgels enhances the spreadability and compliance, particularly in cancer patients who often have sensitive skin (Talat *et al.*, 2021). An advanced technique, e.g., microneedling, which involves using a roller with tiny needles (300-1500 µm) on the affected area, can enhance the permeation and, in turn, the effectiveness of topical formulations.

Oleic acid, a lipophilic sebum-compatible fatty acid, was used for follicular targeting and promoting localized delivery of the active ingredient into the pilosebaceous units (Atef *et al.*, 2022). Propylparaben is commonly used as an antimicrobial preservative (Assaf Vandecasteele *et al.*, 2021). Propylene glycol, a co-solvent and humectant, improves drug solubility in the aqueous phase and drug penetration by softening the stratum corneum (Mistry and Notman, 2024). Liquid paraffin serves as an emollient and occlusive (Nailwal *et al.*, 2019). Carbopol 940, a gelling agent, imparts suitable viscosity to the formulation and enhances spreadability (Arshad *et al.*, 2023a). Span 20 and Tween 20 act as emulsifiers (Ravichandran *et al.*, 2018).

The present study aimed to develop a cetirizine hydrochloride-containing emulgel formulation and evaluate its potential, in combination with microneedling, for treating chemotherapy-induced alopecia. The literature on combining emulgel-based delivery of cetirizine hydrochloride with microneedling is scarce. Addressing this gap can provide valuable insights into improving the therapeutic efficacy of the cetirizine hydrochloride-microneedling combination in treating alopecia. In the present study, microneedles of size 500 µm were used because they are capable of penetrating the stratum corneum (in a minimally invasive manner) and creating channels that can enhance drug diffusion (Gong *et al.*, 2026; Zafar *et al.*, 2023).

MATERIALS AND METHODS

Materials

Cetirizine hydrochloride was kindly donated by Tagma Pharma Private Limited, Lahore, Pakistan. Propylene glycol, oleic acid, Carbopol 940, Span 20, Tween 20, liquid paraffin, propylparaben and triethanolamine were obtained from Merck, Darmstadt, Germany. Double-distilled water was obtained from an in-house facility (Department of Pharmaceutics, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan).

Preparation of cetirizine hydrochloride loaded emulgel

Different cetirizine hydrochloride (1% w/v) loaded emulgel formulations comprising varying concentration of propylene glycol (25-30% w/v), oleic acid (3-4% w/v), Carbopol 940 (2% w/v), Span 20 (0.95% w/v), Tween 20 (0.7% w/v), liquid paraffin (7.5% w/v) and propylparaben (0.01% w/v) were prepared following screening by CCD-RSM (Central composite design-Response surface methodology) approach (Table 1).

Table 1: List of formulations as per central composite design.

Formulation code	X1	X2
F1	X1	X2
F2	0	0
F3	-1	+1
F4	0	+1
F5	+1	0
F6	+1	+1
F7	-1	-1
F8	1	-1
F9	0	-1
F10	-1	0
F11	0	0
F12	0	0
F13	0	0

X1 = Oleic acid (-1, 0 and +1 indicates 3 g, 3.5 g and 4 g, respectively), X2 = Propylene glycol (-1, 0 and +1 indicates 25 g, 27.5 g and 30 g, respectively).

Oleic acid, Span 20 and liquid paraffin were mixed by stirring at 200 rpm and 75±5°C for 10 minutes (oil phase) using a hotplate (UC152, Stuart, Staffordshire, United Kingdom). A solution comprising propylene glycol, propylparaben, Tween 20 and cetirizine hydrochloride was prepared in double-distilled water with continuous stirring at 200 rpm and 75±5°C for 10 minutes (aqueous phase). The oil phase was mixed with the aqueous phase while stirring constantly at room temperature (25±2°C) to prepare the emulsion. The prepared emulsion was added to the gel phase (prepared by dissolving Carbopol 940 in double-distilled water) while stirring continuously. The pH of the emulgels was adjusted to 5-6 using triethanolamine (Khan *et al.,* 2021).

Physicochemical evaluation

Physicochemical evaluation of emulgels included determination of particle size, pH, viscosity, spreadability and stability. A Metasizer 3000 with a Hydro EV unit (Malvern Panalytical Limited, Malvern, United Kingdom)

was used to measure the particle size of the oil phase. The sample was inserted into the instrument; laser obscuration was adjusted to 9.5-10.5% and particle size was assessed at 2400 rpm. The pH of the emulgels was measured at room temperature using a digital pH meter. Emulgels were placed in a beaker and their viscosity was determined by a viscometer (OU7110, AMETEK Brookfield, Massachusetts, United States of America) at 25±1°C and 2.5 rpm. Spreadability was assessed by measuring the change in emulgel diameter under applied weight. The formulation was placed on a marked circular area of a glass slide and covered with another slide. Weight (100 g) was applied and the circle diameter was determined after 5 minutes by using Eq. 1.

$$S = \frac{m \times l}{t} \times 100 \qquad \text{Eq. 1}$$

Where S, m, l and t indicated spreadability, weight of the upper plate with weight applied on the plate, diameter of emulgel after applying weight, and time, respectively. Stability was assessed by storing the emulgels for 3 months at 40±2°C and 75±5% relative humidity. Emulgels were then evaluated for physicochemical features.

Interactions and compatibility studies

Interactions and compatibility among formulation constituents were evaluated using *In-silico* and Fourier transform infrared spectroscopy (FTIR) analyses. For *in-silico* analysis, 3D (three-dimensional) structures of molecules were developed using Chem3D and Sybyl-X 1.3, and their energies were minimized by the Tripos force field and Gasteiger-Hückel charges. Flexible docking simulations were performed to study interactions using the Surflex-Dock module of SYBYL-X 1.3. In Surflex-Dock, default settings were used to create a protomol with a binding site (threshold: 0.50, bloat: 0 Angstroms) (Arshad *et al.*, 2023a). FTIR spectra were recorded at 25±2 °C, over a wavenumber range of 650-4000 cm^{-1} using a spectrophotometer (Alpha Bruker, Massachusetts, United States of America).

In-vitro drug release study

Emulgels (1 g each) were placed in a dialysis membrane (14 kDa cutoff) and attached to the paddle of the Type II dissolution apparatus (UDT-818-12, Logan Instruments, New Jersey, United States of America). Dissolution medium comprised phosphate buffer (pH 5.5) maintained at 32±0.5 °C and 50 rpm. Aliquots were obtained at different time intervals, i.e., 30, 60, 90, 120, 150, 180, 240, 300, 360 minutes. An equal volume of blank medium was added at each sampling time to maintain sink conditions. Aliquots were filtered, their absorbances were measured by a UV-Vis spectrophotometer (U-1800, Hitachi, Tokyo, Japan) at 244 nm, and % drug release was calculated by using a calibration curve. Release profiles were analyzed by applying different models, e.g., zero-order, first-order, Korsmeyer-Peppas and Higuchi (Siepmann and Siepmann, 2013).

Ex-vivo permeation study

Animal studies complied with 'ARRIVE (Animal Research: Reporting of *In-vivo* Experiments) guidelines' and were conducted in accordance with 'Public Health Service Policy on Humane Care and Use of Laboratory Animals'. Wistar rats of either sex, with an average weight of 200-250 grams, were kept under ambient temperature (25±2 °C) and given free access to food and water at least 48 hours before the experiments. Rats (N=6) were sacrificed, dorsal hair was removed, skin tissues were cut using a sterile blade and preserved in formalin till further use.

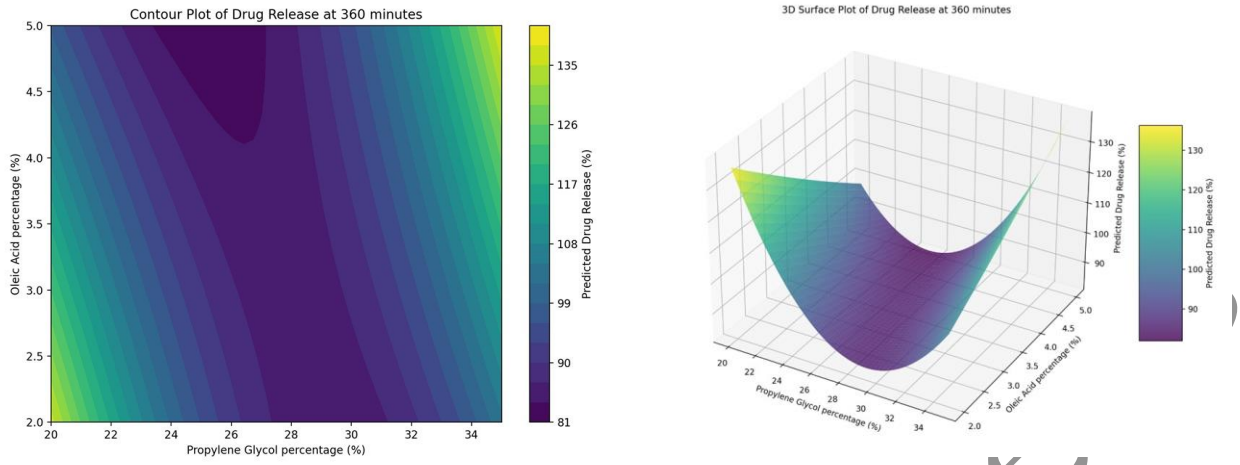
A permeation study was conducted using a Franz diffusion cell apparatus comprising a donor and recipient compartment with a permeation area of 1 cm^2. The experiments were carried out at 50 rpm and 32±0.5°C using 10 ml phosphate buffer (pH 5.5) as a dissolution medium. Skin tissues were divided into two groups (T_{EF} and T_{MEF}) and clamped between the donor and recipient compartments. Group T_{EF} was applied with the emulgel (F4). Group T_{MEF} was pierced for 30 seconds using metal microneedles (ZGTS derma roller; needle size 500 µm), followed by the application of emulgel. Samples (0.5 mL) were drawn at predetermined time intervals (1, 2, 4 and 6 hours) and the same volume of buffer was added to the receptor compartment to maintain sink conditions (Tariq *et al.*, 2025). Absorbance of aliquots was measured at 244 nm with a UV-Vis spectrophotometer, and the % drug permeated across the skin was estimated from a calibration curve.

In-vivo hair growth study

Alopecia was induced in albino rats (N=9, average weight 200-250 grams) by administering an aqueous solution of cyclophosphamide intraperitoneally (125 mg/kg) using a 21-gauge needle (Paus *et al.*, 1994). After developing alopecia, rats were equally divided into 3 groups: U, T_{EF} and T_{MEF}. Group U was not given any treatment. Cetirizine hydrochloride-loaded emulgel was applied to the affected area of group T_{EF}. In the case of group T_{MEF}, the affected regions were first pre-treated with the derma roller, followed by the application of the prepared emulgel. After completion of the study (day 15), skin tissues were obtained by punch biopsy and sliced (~1-2 µm thick) using a microtome. The samples were stained with hematoxylin and eosin (HE) and visualized under a light microscope at 40X magnification.

Statistical analysis

The experiments were performed in triplicate; the mean and standard deviation were calculated. In addition, the data were statistically analyzed using Student's t-test in Microsoft Excel 2016.



(A) (B)

Fig. 1: Plots showing effect of oleic acid and propylene glycol on % drug release (A) contour and (B) three-dimensional (3D) surface.

RESULTS

Preparation of cetirizine hydrochloride-loaded emulgel

The RSM evaluated the combined effects of propylene glycol and oleic acid on drug release at 360 minutes. The experimental data were modeled using a second-order polynomial equation (Eq. 3):

$$y = \beta_0+\beta_1x_1+\beta_2x_2+\beta_{11}x_1^2+\beta_{22}x_2^2+\beta_{12}x_1x_2+\varepsilon \quad \text{Eq. 3}$$

where y represents the predicted drug release at 360 minutes.

A combination of propylene glycol and oleic acid significantly influenced % drug release. The highest predicted drug release (95.38% within 360 minutes) was observed in the region where propylene glycol and oleic acid were at concentrations of 30% w/w and 3.5% w/w, respectively (Fig. 1).

Physicochemical evaluation

The prepared white-colored, homogeneous and smooth-textured emulgels showed acceptable physicochemical features, i.e., particle size (~70.34 µm). pH (5.2-6.1), viscosity (150000-250000 cP) and spreadability (400-550 $g \cdot cm \cdot min^{-1}$). No significant differences were observed in the physicochemical properties of the emulgels over 3 months, suggesting their high stability.

Interactions and compatibility studies

The binding between formulation constituents was assessed by CScores. Cetirizine hydrochloride-oleic acid, cetirizine hydrochloride-Tween 20, cetirizine hydrochloride-liquid paraffin, propylene glycol-propylparaben, propylene glycol-Tween 20, propylparaben-oleic acid, Carbopol 940-tween 20, Span 20-Tween 20 and Tween 20-oleic acid showed the highest binding affinity (CScore = 5.00), suggesting favorable conformity and stable complexation. Interactions between different formulation components are displayed in figure. 2. Distinctive bands shown by pure ingredients, suggesting vibrations of functional groups, are summarised in table 2 (Niu *et al.*, 2017; Pourfarzad *et al.*, 2018; Ravichandran *et al.*, 2018; Senthilkumar and Dash, 2019). Emulgels showed peaks of individual constituents with some blue and red shifts indicating compatibility between ingredients (Fig. 3).

In-vitro drug release study

A calibration curve for cetirizine hydrochloride was successfully established with an R2 of 0.9991 (Fig. 4). All emulgels exhibited a burst release of the drug (25-50%) within the first 30 minutes. In the next 5.5 hours, consistent drug release (total >81%) was recorded. Formulation F4 demonstrated the highest drug release (~95%) (Fig. 5).

Formulation F4 showed rate constant values of 0.348, 0.011, 5.624, 16.603 and 0.003 for zero-order, first-order, Higuchi, Korsmeyer-Peppas and Hixson-Crowell models, respectively. All release profiles showed R^2 values>0.9 (Table 3).

Based on the results of subsections 3.2 and 3.4, emulgel formulation F4 (optimized) was used in the next part of the study.

Ex-vivo permeation study

Drug permeated slowly (~27%) in group T_{EF} within the first 4 hours. In the next 2 hours, this amount increased to ~46%. In the case of group T_{MEF}, a significantly higher amount (~74%) of drug permeated within the first 4 hours (Student's t-test, p-value < 0.05). Over the next 2 hours, this amount reached ~94% (Fig. 6).

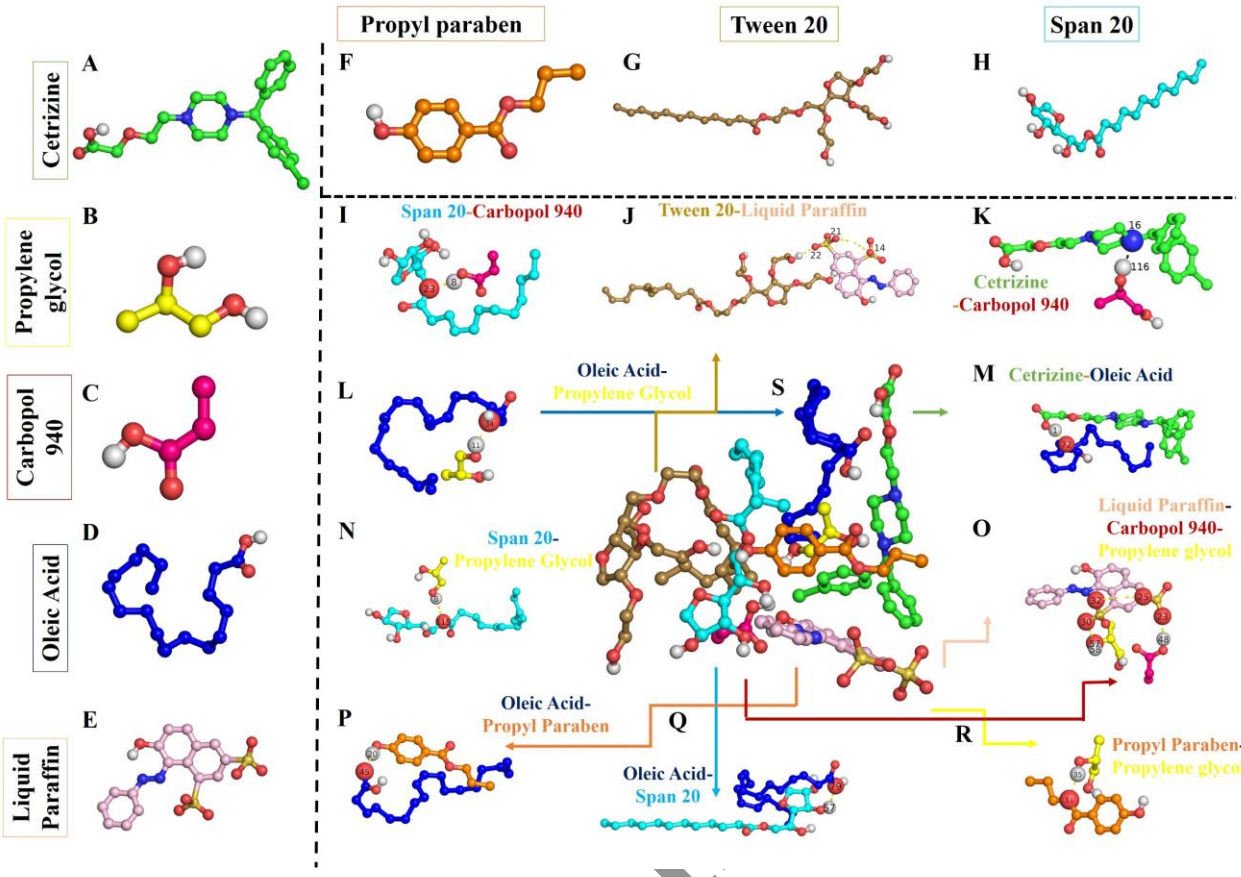


Fig. 2: 3D (three-dimensional) structures of (A, B, C, D, E, F, G, H) ingredients and (I, J, K, L, M, N, O, P, Q, R) different docked conformations. S represents the picture of all ligands, receptors and their binding sites with the complex.

Table 2: Band frequencies in FTIR spectra of pure ingredients.

IR frequencies/wave number (cm^{-1})								Assigned band
Propylene glycol	Tween 20	Span 20	Propyl-paraben	Carbopol 940	Oleic acid	Liquid paraffin	Cetirizine hydro-chloride	
3200-3600	3200-3600	3400	3400	3400	3500-3100	3200-3500	3380-3300	O-H stretch, N-H stretch
2800-3000	2800-3000	2900-3000	2950	2957	3000	2700-3000	2920-2850	C-H stretch
	1700	1700	1750	1702	1700		1750-1700	C=O stretch
					1600			C=C stretch
1450			1400	1408		1465		C-H bend, C-C stretch
1200-900	1100	1200		1150-1250	1000-1300		1250-1000	C-O stretch, O-H bend, C-H stretch, C-N stretch
			700-900				800-600	C-H bend, C-Cl stretch

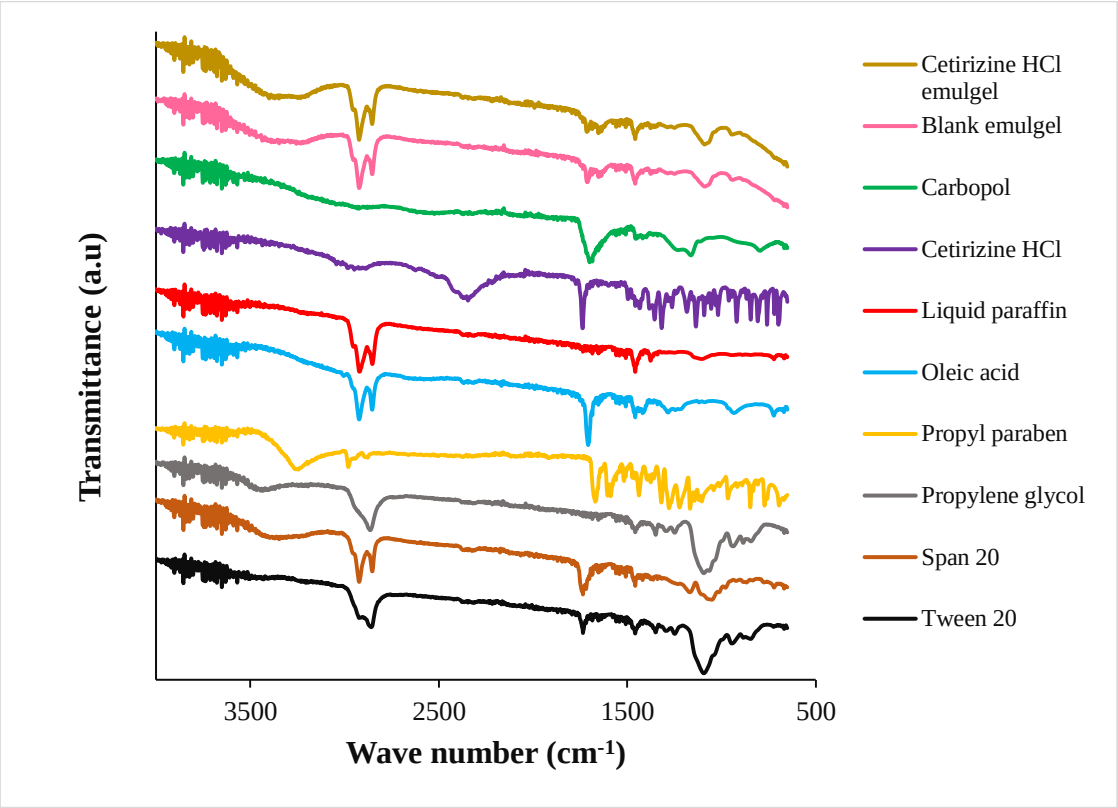


Fig. 3: Fourier transform infrared (FTIR) spectra of pure ingredients and optimized blank and drug loaded emulgels (F4).

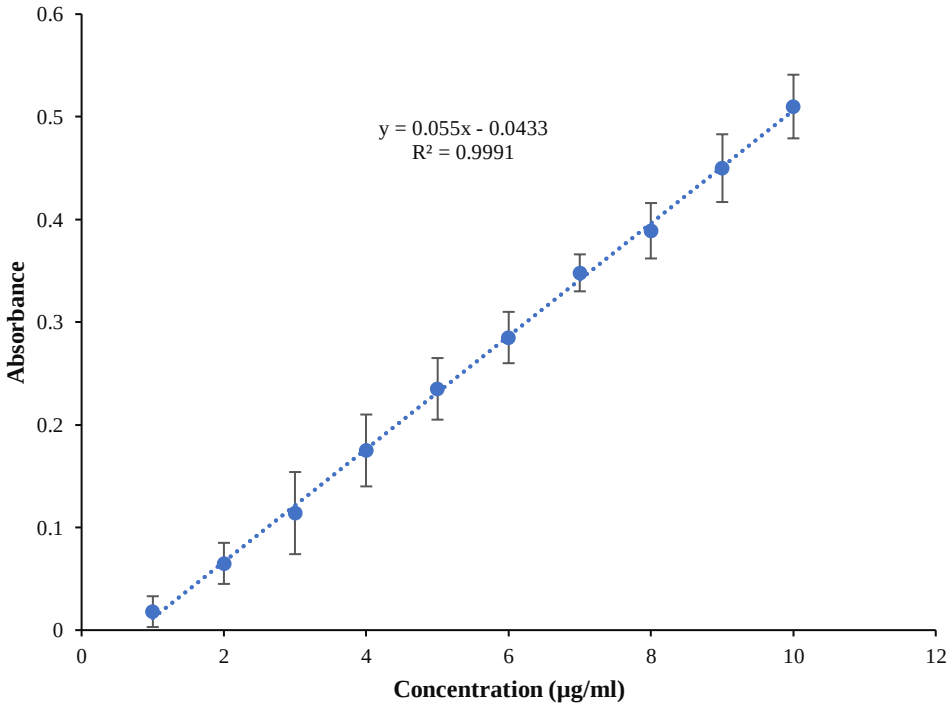


Fig. 4: Calibration curve of cetirizine hydrochloride.

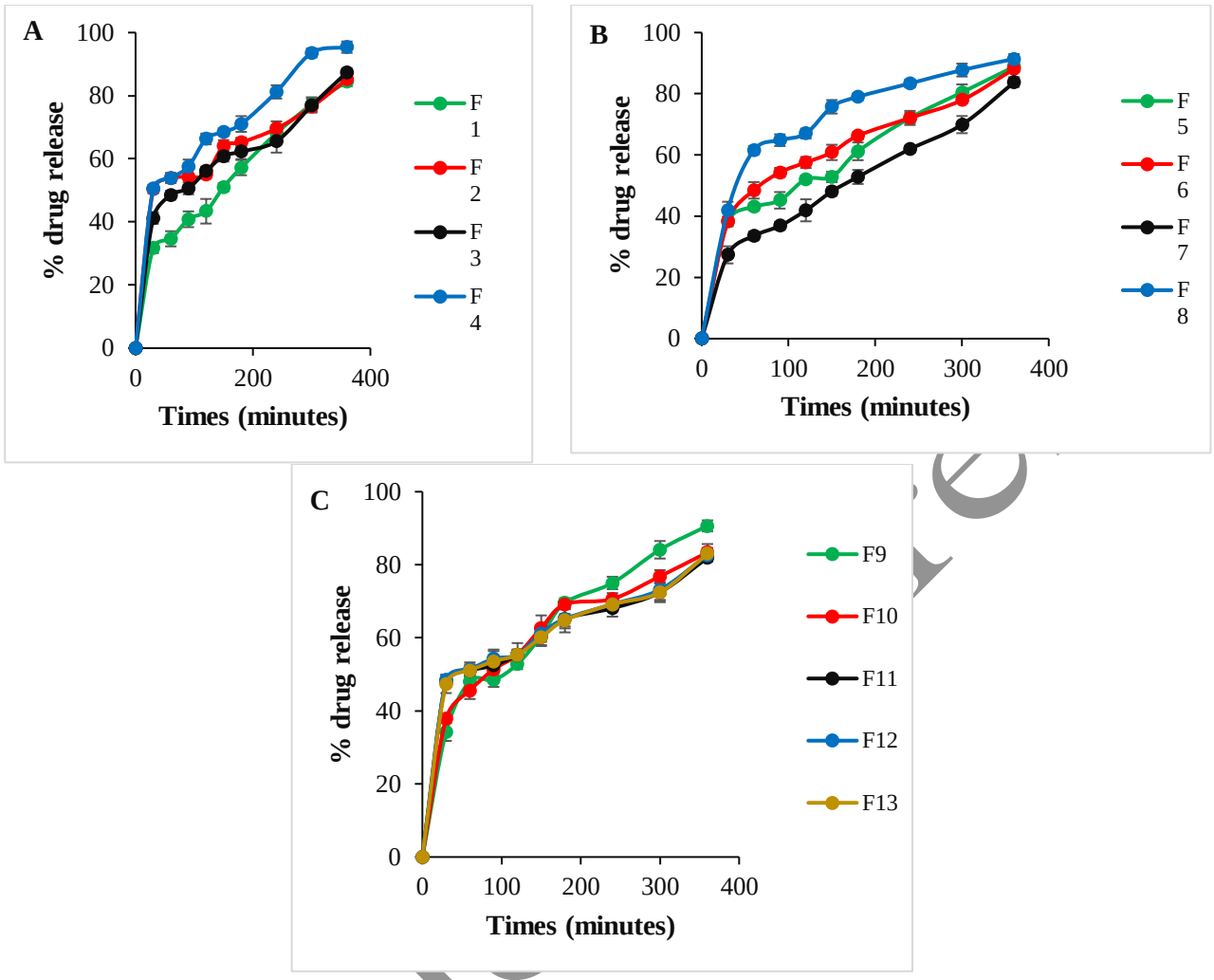


Fig. 5: % release of cetirizine hydrochloride from different emulgels at specified time intervals (A) F-F4, (B) F5-F8 and (C) F9-F13.

Table 3: Rate constant (k) and coefficient of determination (R^2) values for different dissolution models applied on the release profiles of prepared formulations (details of formulations are given in Table 1).

Formulations	Models									
	Zero order		First order		Higuchi		Korsmeyer-Peppas		Hixson-Crowell	
	k_0	R^2	K_1	R^2	k_H	R^2	k_{KP}	R^2	k_{HC}	R^2
F1	0.281	0.9974	0.005	0.9717	4.416	0.9828	5.978	0.9784	0.001	0.9840
F2	0.307	0.9884	0.008	0.9008	5.050	0.9593	25.211	0.9190	0.002	0.9218
F3	0.301	0.9908	0.007	0.9429	4.874	0.9763	16.460	0.9558	0.002	0.9573
F4	0.348	0.9835	0.011	0.9379	5.624	0.9885	16.603	0.9800	0.003	0.9412
F5	0.301	0.9969	0.007	0.9503	4.787	0.9769	10.029	0.9636	0.002	0.9673
F6	0.309	0.9800	0.008	0.9809	4.982	0.9963	12.894	0.9939	0.002	0.9847
F7	0.264	0.9984	0.005	0.9756	4.128	0.9829	4.720	0.9810	0.001	0.9854
F8	0.350	0.9356	0.012	0.9809	5.711	0.9792	18.480	0.9879	0.003	0.9792
F9	0.316	0.9847	0.007	0.9755	5.031	0.9930	9.258	0.9895	0.002	0.9837
F10	0.303	0.9726	0.007	0.9893	4.894	0.9948	13.210	0.9936	0.002	0.9929
F11	0.296	0.9927	0.008	0.9297	4.877	0.9695	24.058	0.9322	0.002	0.9503
F12	0.300	0.9945	0.008	0.9380	4.927	0.9780	23.735	0.9471	0.002	0.9555
F13	0.298	0.9938	0.008	0.9328	4.901	0.9730	23.356	0.9389	0.002	0.9519

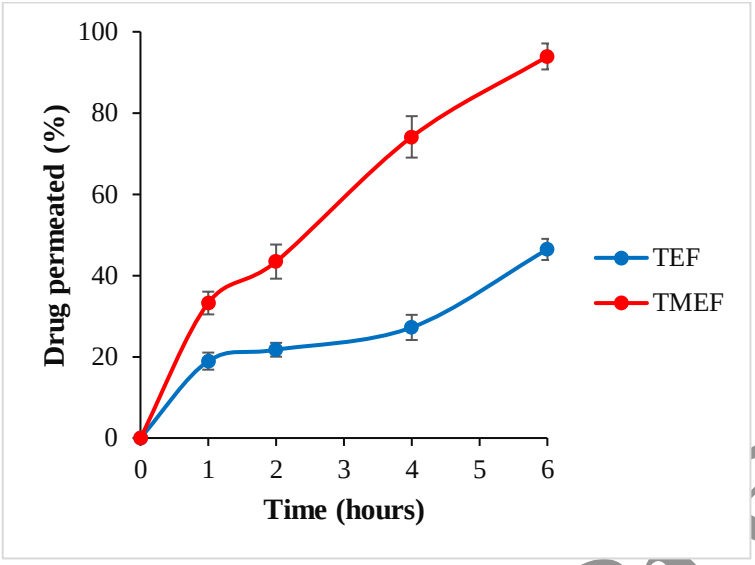


Fig. 6: % cetirizine hydrochloride permeated across rat skin of groups T_{EF} (treated with emulgel) and T_{MEF} (applied with emulgel on microneedle pre-pierced skin) (Statistically significant difference between the two groups indicated by student t test, p value <0.05)

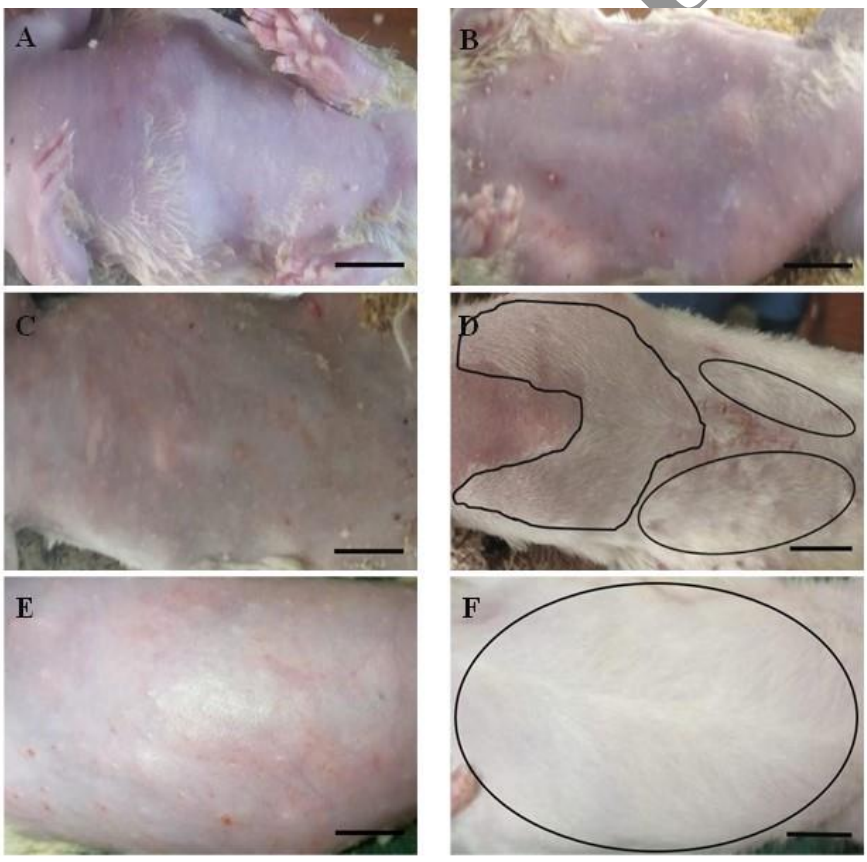


Fig. 7: Physical images of (A and B) untreated (U), (C and D) emulgel treated (T_{EF}) and (E and F) microneedle pretreated emulgel applied (T_{MEF}) rat skin at day 1 (A, C and E) and 15 (B, D and F) (scale bar = 2 cm).

In-vivo hair growth study

On day 1 (alopecia development day), the skin surface was bald. In the untreated group (U), no significant recovery or hair growth was observed after 15 days. The treated group T_{EF} exhibited hair growth; however, some bald regions were also recorded. In group T_{EF}, no bald regions were observed and the hair appeared relatively denser than the group T_{EF} counterpart (Fig. 7).

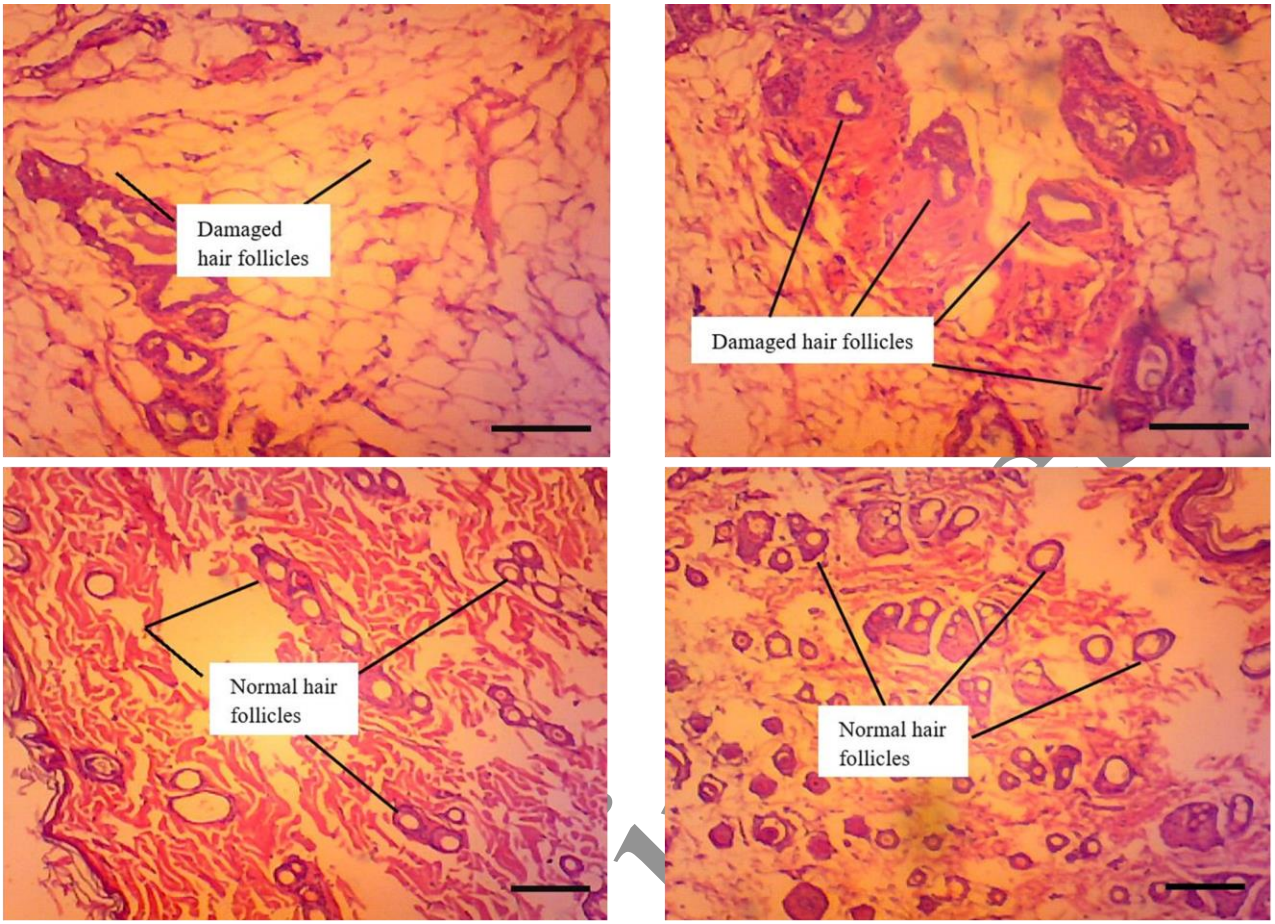


Fig. 7: Microscopy images of H and E-stained (top left) alopecia affected, (top right) untreated (U), (bottom left) emulgel treated (T_{EF}) and (bottom right) micropierced emulgel applied (T_{MEF}) skin (scale bar = 100 µm).

In the alopecia-affected skin, normal follicular architecture was absent. No significant hair follicle regeneration was observed in the untreated group (U). Hair follicles with improved follicular density were recorded in groups T_{EF} and T_{MEF} (Fig. 8).

DISCUSSION

Chemotherapy-induced alopecia affects the self-esteem of cancer patients. Topical minoxidil is widely recommended for hair regrowth; however, it is reported to cause scalp irritation and contact dermatitis. Cetirizine hydrochloride, an antihistamine with anti-inflammatory properties, may reduce micro inflammation of the scalp and oxidative stress associated with chemotherapy, thereby improving tolerability. Emulgels can improve the transcutaneous penetration of drugs due to their composition (surfactants, co-solvents, oils, etc.) compared with traditional topical preparations, e.g., creams and lotions. Micro needling, an advanced technique, can enhance the permeation and, in turn, the effectiveness of topical preparations.

In the present study, a cetirizine hydrochloride-containing emulgel formulation with acceptable physicochemical properties (e.g., particle size, pH, viscosity, spreadability) was prepared. *In-silico* and FTIR analyses indicated interactions between the formulation constituents. The emulgel exhibited a burst release of the drug (~50%) within the first 30 minutes, likely due to the highly hydrophilic gel phase and the presence of propylene glycol (a co-solvent and humectant that increases the solubility of the drug in the aqueous phase). Optimized formulation F4 demonstrated ~95% drug release within 6 hours.

A low amount (~27%) of cetirizine hydrochloride permeated from emulgel across rat skin within 4 hours, possibly because the free drug present in the aqueous phase diffused slowly across the stratum corneum. In the next 2 hours, this amount increased to ~46%, which might be due to an increased availability of surfactant-bound drug. Application of emulgel on microneedle-treated rat skin resulted in the permeation of a significantly higher amount (~94%) within 6 hours (Student's t-test, p-value < 0.05). A possible reason for this significantly higher permeation was the movement of the drug through the channels generated in the skin layers by needles, as reported in the literature (Arshad *et al.*, 2023b). During *in-vivo* study in rats, hair follicles with improved follicular density were recorded following application of

cetirizine hydrochloride emulgel on microneedle pre-treated skin. Emulgel promoted hair growth by inhibiting the release of prostaglandin D2 (which causes hair to move into the catagen phase) and stimulating the release of prostaglandin E2 (responsible for the transition of hair follicles into the anagen phase) (Chen *et al.*, 2022).

In group T_{MEF}, synergistic action of the drug and micropiercing simulated hair growth. Microneedles enhanced transdermal permeation of the drug. Moreover, microneedling promoted vascularization, release of growth factors and stimulated follicular stem cells, in turn, improving hair regrowth. The literature suggests that microneedling promotes hair growth by activating the wingless-related integration site (Wnt)/β-catenin pathway and VEGF (vascular endothelial growth factor) (Xiao *et al.*, 2025). The literature also reports significant improvements in hair density following application of a topical formulation to microneedle-pretreated skin compared with the topical formulation alone (English *et al.*, 2021).

CONCLUSION

Cetirizine hydrochloride-loaded emulgel F4, with acceptable physicochemical properties, released >95% drug at pH 5.5 within 6 hours. Almost 94% of the drug permeated through the emulgel across microneedle-treated skin within 6 hours. In rats, a 15-day application of a drug-loaded emulgel to microneedle-treated skin promoted hair growth. The prepared cetirizine hydrochloride-loaded emulgel and microneedling combination showed potential and warrants further clinical investigation. Chemotherapy induced alopecia in humans involves complex hormonal, genetic and inflammatory mechanisms that may not be fully reproduced in preclinical animal models. Therefore, further investigations using human scalp models and clinical studies would be required to establish the safety, efficacy and translational applicability of the developed emulgel and micro needling combination system.

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Author's contributions
Sana Hassan: Validation, Investigation, formal analysis, writing–original draft, methodology, data curation; Sadia Jafar Rana: Writing–review and editing, methodology, formal analysis, software and investigation; Saman Zafar: Writing – original draft, methodology, validation, formal analysis, software and investigation; Tahir Ali Chohan: Validation, writing, review, editing and formal analysis; Qalander Khan: Validation, formal analysis, writing, review and editing and methodology; Khizar Abbas: Formal analysis, writing, review and editing; Muhammad Sohail Arshad: Validation, methodology, conceptualization, writing, review, editing, supervision and formal analysis. All the authors have reviewed and approved the final version for publication.

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Data availability statement
All data generated or analysed during this study are included in this published article.

Ethical approval
Experiments involving animals (rats) were carried out after seeking permission from the University Research Ethical Committee, Bahauddin Zakariya University, Multan, Pakistan (vide letter number 33/UREC/2025). This study was performed in adherence with the ARRIVE guidelines. See supplementary file for the ARRIVE checklist.

Conflict of interest
The authors declare no conflict of interest.

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