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Original Article

Translational evaluation of magnetized saline water combined with ciclopirox olamine and piroctone olamine against *Malassezia* species and scalp seborrheic dermatitis

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Abstract

Yeasts of the *Malassezia* genus are implicated in numerous skin conditions, including seborrheic dermatitis, pityriasis versicolor, and folliculitis. While ciclopirox olamine (CPO) and piroctone olamine (OCT) are effective anti-*Malassezia* agents, the activity of magnetized water against pathogenic yeasts remains unclear. The aim of this study was to examine the in vitro efficacy of magnetized saline water (MSW), alone or combined with CPO plus OCT, against three *Malassezia* species (*M. furfur*, *M. globosa*, and *M. restricta*) using broth microdilution to determine minimal inhibitory concentrations (MICs). A proof-of-concept study evaluating a shampoo containing MSW 30% + CPO 0.5% + OCT 1.0% in 20 patients with scalp seborrheic dermatitis (SSD) was subsequently conducted. Participants applied the shampoo four times per week for 12 weeks; efficacy was assessed by changes in a validated 16-point SSD severity score. The triple combination demonstrated additive-to-synergistic activity, with MIC values of 3.91 mg/L across all three species, representing a 2.0- to 4.0-fold MIC reduction compared to CPO + OCT alone, and synergy (FIC=0.31) for *M. furfur*. The total SSD score decreased by 33.9% after 12 weeks ($p<0.001$), with improvements in pruritus (49.0%), erythema (54.3%), and scaling (24.2%); all p values remained significant after Bonferroni correction ($\alpha=0.0125$). These findings support MSW as a vehicle to potentiate the anti-yeast activity of CPO and OCT while reducing the chemical load, potentially offering a novel strategy for *Malassezia*-associated skin disorders. The open-label, single-arm design limits causal attribution, and larger controlled trials are needed.

Keywords: *Malassezia*, magnetized saline water, ciclopirox olamine, synergy, scalp seborrheic dermatitis

Introduction

Lipophilic yeasts of the genus *Malassezia* (comprising at least 17 recognized species) represent a significant component of the normal human cutaneous microbiota, particularly in sebum-rich areas where they metabolize host-derived lipids [1]. Under normal physiological conditions, *Malassezia* yeasts exist as commensals on healthy skin, residing primarily on the outer cutaneous surface and follicular infundibulum [2]. Various host and environmental factors can trigger pathogenic behavior, leading to *Malassezia* invasion of the epidermis and interaction with resident cells, including keratinocytes, Langerhans cells, and melanocytes [3]. This dual

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commensal-pathogenic nature has established *Malassezia* species as key agents in the pathogenesis of numerous dermatological conditions [4], including seborrheic dermatitis, pityriasis versicolor, folliculitis, and head-and-neck dermatitis, a specific phenotype of atopic dermatitis characterized by type I hypersensitivity reactions to the invading *Malassezia* yeasts [5]. Among the currently recognized *Malassezia* species, at least three (*M. furfur*, *M. globosa*, and *M. restricta*) have emerged as clinically significant in dermatology [1,6]. Specifically, *M. furfur* is among the species commonly associated with pityriasis versicolor and seborrheic dermatitis [7], where it can release significant amounts of biologically active indolic compounds [8]. In contrast, *M. globosa* and *M. restricta* represent the dominant yeast flora isolated in patients with head-and-neck dermatitis [9]. These species-specific colonization patterns and distinct pathogenic mechanisms highlight the complexity of *Malassezia*-host interactions.

Current management strategies for *Malassezia*-associated dermatoses rely predominantly on topical antifungal therapy, with azoles (particularly ketoconazole) [10] and hydroxypyridones (notably ciclopirox olamine (CPO) [11] and piroctone olamine (OCT) [12]), representing the therapeutic mainstays. These agents operate through distinct mechanisms: azoles inhibit ergosterol biosynthesis by targeting the fungal cytochrome P450 enzyme lanosterol 14α-demethylase [13] while CPO and OCT act largely through metal chelation (notably iron), which can impair metal-dependent cellular processes and inhibit fungal mitochondrial energy metabolism [14]. Despite their known clinical efficacy, these conventional approaches may face significant limitations, including incomplete *Malassezia* eradication, rapid recolonization following treatment discontinuation, and high recurrence rates [15]. Another increasingly important challenge lies in the development of azole resistance through upregulation of drug efflux pumps and mutations in cytochrome P450 enzymes [16].

Recent advances in non-pharmacological strategies targeting pathogenic microorganisms have sparked growing interest in physical water treatment modalities. Magnetized water, produced by exposing water to controlled magnetic fields, has demonstrated several distinctive physicochemical properties, including increased conductivity and pH, reduced density, lower evaporation temperature, and decreased surface tension [17-19]. These modifications have been attributed to magnetic field-induced alterations in water clustering as well as to altered water-ion interactions [17,18]. Notably, such properties can exert notable antibacterial and antifungal effects. Prior research has shown that using magnetized water as a mouthwash significantly reduces the colony count of *Streptococcus mutans* in children [20]. In a separate study, magnetized water exhibited efficacy comparable to chlorhexidine in managing periodontal and gingival infections [21]. More recently, magnetized water treatment was found to reduce the number of viable *Pseudomonas fluorescens* cells in biofilms by 2.46 $\log_{10}$ colony-forming units/cm^2 after 15 days of treatment, likely due to the magnetic field impact on ionic metabolic processes [22]. Regarding fungi, magnetized water has demonstrated inhibitory effects against the plant pathogen *Fusarium oxysporum* in tomato plants and, when combined with salicylic acid, can protect cucumber plants from *Pythium aphanidermatum* [23].

Given the limitations of current anti-yeast therapies and the promising antimicrobial effects of water exposed to magnetic fields, it was hypothesized that magnetized saline water (MSW), prepared from a proprietary mineral-enriched saline solution containing trace amounts of Zn^{2+} and Al^{3+}, could amplify the antifungal activity of CPO and OCT against *Malassezia* species via additive and/or synergistic potentiation. The present study was therefore designed with a dual goal: first, to evaluate the individual and combined antifungal efficacy of MSW and CPO plus OCT against three clinically significant *Malassezia* species (*M. furfur*, *M. globosa*, and *M. restricta*) using standardized in vitro testing; and second, to translate these laboratory findings into clinical practice by assessing the therapeutic potential of an MSW/CPO/OCT-formulated shampoo in patients with scalp seborrheic dermatitis (SSD).

Methods

Malassezia strains and culture conditions

M. furfur ATCC-14521, *M. globosa* ATCC-MYA-4612, and *M. restricta* ATCC-MYA-4611 were obtained from the American Type Culture Collection (ATCC, Manassas, VA, USA). All strains were maintained on modified Dixon agar (mDixon) containing 3.6% malt extract, 0.6% peptone,

2% desiccated ox bile, 1% Tween 40, 0.2% oleic acid, 0.2% glycerol, 0.05% chloramphenicol, and 1.2% agar. Cultures were incubated at 30°C under aerobic conditions for five days prior to testing.

Test formulations

The following five formulations were tested against *Malassezia* species: (1) MSW 30%, (2) CPO 0.5% + OCT 1.0%, (3) MSW 30% + CPO 0.5% + OCT 1.0% (hereafter, the triple combination), (4) ketoconazole 2% (positive control), and (5) tap water (negative control). The MSW production process used a proprietary saline solution (Aquavis S.r.L, Brescia, Italy) containing 0.9% NaCl, 0.011% KCl, 0.009% $CaCl_2$, 0.007% $MgCl_2$, 0.007% $ZnCl_2$, and 0.007% $AlCl_3$, which was subsequently exposed to a fixed magnetic field of 3000 gauss for 2 h [24]. The magnetic field was generated using a permanent neodymium magnet assembly and verified with a calibrated gaussmeter prior to each preparation. The resulting MSW was stored at room temperature and used at a 30% concentration within three months of preparation. The 30% MSW concentration was selected because it represented the maximum amount that could be incorporated into the surfactant-based shampoo vehicle while preserving formulative stability, adequate foaming properties, and an appropriate pH (5.5); higher MSW concentrations compromised the surfactant phase and reduced product acceptability. This concentration differs from the 95% MSW used in previously reported leave-on formulations [18,24], in which the absence of a surfactant base allowed a greater proportion thereof. The CPO 0.5% + OCT 1.0% solution (Sigma Aldrich, St. Louis, MO, USA) was prepared by dissolving CPO and OCT in sterile distilled water with gentle stirring until complete dissolution. A separate combination solution was prepared containing a final concentration of MSW 30%, CPO 0.5%, and OCT 1.0%. Ketoconazole 2% solution (Sigma Aldrich, St. Louis, MO, USA) was prepared in 10% dimethyl sulfoxide and used as the positive control, whereas tap water served as the negative control. For the clinical shampoo formulation, MSW 30%, CPO 0.5%, and OCT 1.0% were incorporated into a standard surfactant base (pH 5.5), without additional antimicrobial preservatives, to ensure that the observed effects were attributable solely to the active components. The microbiological stability of each shampoo batch was verified by aerobic plate count at baseline and at weeks 4 and 8, confirming the absence of microbial contamination throughout the study period.

In vitro susceptibility testing

Minimal inhibitory concentrations (MICs) were determined using the broth microdilution method [25], adapted with minor modifications. Assays were conducted in mDixon broth, prepared according to the standard recipe for Dixon agar but omitting the agar (Condalab, Madrid, Spain). Yeast inocula were generated from five-day-old cultures by suspending colonies in sterile saline and adjusting the turbidity to a 0.5 McFarland standard using spectrophotometry. The suspension underwent further dilution in mDixon broth to achieve a final inoculum concentration of 1×10^5 cells/mL. Two-fold serial dilutions of the test formulations were subsequently prepared in 96-well microtiter plates, with each well containing a final volume of 100 µL. An equal amount of the standardized fungal inoculum was added to each well, yielding final test concentrations ranging from 0.1 to 500 mg/L. For MSW 30%, the reported MIC values refer to the concentration of the whole magnetized saline solution (expressed as mg of solution per liter of broth), not to any individual dissolved ion or salt. Growth control wells contained fungal inoculum in broth without the test formulations, whereas sterility control wells contained broth only. Each formulation was tested in triplicate wells per concentration within each of three independent experiments. Plates were incubated at 30°C for five days with continuous orbital shaking at 100 rpm. MICs were defined as the lowest concentration of the test formulations that completely inhibited visible yeast growth compared to the growth control. MIC endpoints were determined by visual inspection by two independent observers. As is inherent to the two-fold serial dilution method [25], all reported MIC values carry an intrinsic measurement uncertainty of ±1 dilution step.

Proof-of-concept clinical study

An open-label, single-arm, proof-of-concept clinical study was conducted at two Italian private clinical practices (Studio Rivetti and Studio Minoretti, Italy) between January and June 2025. Volunteers (n=20) with newly diagnosed SSD were consecutively recruited from patients

presenting at routine consultations. Based on a two-sided paired *t*-test (α=0.05, expected effect size *d*=0.80, power=0.80), a minimum of 17 subjects was required; twenty patients were enrolled to account for potential dropouts. The cohort comprised 10 women and 10 men (age range: 27 to 49 years; mean age: 38.1±7.1 years). Inclusion criteria required the presence of at least one erythematous plaque with characteristic yellow scaling consistent with the SSD diagnosis [26]. Exclusion criteria comprised subjects under 18 years of age, pregnant or lactating women, and individuals presenting exclusively with dandruff. Eligible subjects received a shampoo containing MSW 30% + CPO 0.5% + OCT 1.0% and were instructed to apply the product four times per week for a total of 12 weeks. All clinical assessments were performed at baseline and 12 weeks thereafter. The outcome of interest was the change from baseline in a 16-point SSD severity scale [27]. The instrument includes three subscales: scaling (scored 0–10), erythema (scored 0–3), and pruritus (scored 0–3), and has been previously validated [27]. A categorical severity framework was also applied based on the total SSD score, as follows: mild SSD (0–5 points); moderate SSD (6–9 points); and severe SSD (10–16 points) [27]. At each study visit, patients were actively queried regarding local adverse effects, including burning, stinging, dryness, and worsening of erythema or pruritus. *Malassezia* species-level identification on patient scalps was not performed in this proof-of-concept study. The research adhered to the Declaration of Helsinki and received approval from the Institutional Review Board of Studio Minoretti. Prior to participation, all individuals provided written informed consent.

Statistical analysis

Continuous data are expressed as means ± standard deviations (SDs). For the in vitro study, statistical comparisons were performed using one-way analysis of variance (ANOVA) followed by Tukey post hoc tests. Interactions between MSW 30% and CPO 0.5% plus OCT 1.0% against *Malassezia* species were assessed using a simplified two-component fractional inhibitory concentration (FIC) index [28]. Because CPO and OCT were co-formulated at a fixed ratio in the shampoo base, they were treated as a single pharmacological unit; therefore, this approach cannot capture potential three-way interactions among the individual agents. The FIC index was calculated according to the following formula: FIC Index = FIC_{MSW} + $FIC_{CPO+OCT}$, where FIC_{MSW} represents (MIC of MSW in combination with CPO and OCT) / (MIC of MSW alone) and $FIC_{CPO+OCT}$ represents (MIC of CPO and OCT in combination with MSW) / (MIC of CPO plus OCT alone). FIC index values were interpreted as follows: ≤0.5, synergy; >0.5 to ≤1.0, additive effect; >1.0 to ≤4.0, indifferent interaction; and >4.0, antagonism. In the clinical study, baseline and 12-week scores on the SSD severity scale (i.e., total score and three subscales) were compared using paired Student *t*-tests. Effect sizes were estimated using Cohen *d* for paired samples (calculated as the *t*-statistic divided by the square root of *n*). To account for multiple comparisons across four clinical endpoints, a Bonferroni-corrected significance threshold of α=0.0125 was applied to paired *t*-tests. The distribution of SSD severity categories before and after application of the shampoo formulated with the triple combination was analyzed using a McNemar-Bowker test. All calculations were performed using SPSS, version 20.0 (IBM, Armonk, NY, USA).

Results

In vitro susceptibility profiles of *Malassezia* species

The susceptibilities of the three *Malassezia* species to the five tested formulations are summarized in **Table 1**. As expected, tap water showed no inhibitory activity against any strain (MIC >500 mg/L), confirming its suitability as a negative control and the absence of contamination. MSW 30% demonstrated moderate activity with a uniform MIC of 62.5 mg/L across all three species. *M. globosa* showed identical susceptibility to MSW, as did *M. furfur* and *M. restricta* (all MIC=62.5 mg/L). The CPO 0.5% + OCT 1.0% formulation exhibited significant anti-*Malassezia* activity with notable species-specific differences. *M. restricta* and *M. globosa* showed identical susceptibility (MIC=7.81 mg/L), whereas *M. furfur* demonstrated approximately two-fold lower sensitivity (MIC=15.63 mg/L). The triple combination demonstrated superior activity with a uniform MIC of 3.91 mg/L across all three species, representing a statistically significant improvement over the CPO 0.5% + OCT 1.0% formulation

(p<0.001). As anticipated, ketoconazole 2% (included as a positive control) demonstrated the highest potency among the tested formulations, with MICs of 0.49–0.98 mg/L, consistent with previously published data for *Malassezia* species [29].

Table 1. Antifungal susceptibilities of *Malassezia* species to the five test formulations (MIC values in mg/L)

Species	MSW 30%	CPO 0.5% + OCT 1.0%	MSW 30% + CPO 0.5% + OCT 1.0%	Ketoconazole 2%	Tap water	FIC index
M. furfur	62.5	15.63	3.91*	0.98	>500	0.31 (S)
M. globosa	62.5	7.81	3.91*	0.49	>500	0.56 (A)
M. restricta	62.5	7.81	3.91*	0.49	>500	0.56 (A)

CPO: ciclopirox olamine; FIC: fractional inhibitory concentration; MSW: magnetized saline water; OCT: piroctone olamine
FIC Index interpretation: S: synergy (≤0.5); A: additive (>0.5 to ≤1.0)
*Statistically significant at p<0.001 versus CPO 0.5% + OCT 1.0%

In vitro additive and synergistic interactions between magnetized saline water, ciclopirox olamine, and piroctone olamine

The triple combination demonstrated significant potentiation of anti-yeast activity across all three tested *Malassezia* yeasts. The combination yielded a uniform MIC of 3.91 mg/L for all three species, representing a 2.0- to 4.0-fold improvement compared with CPO 0.5% + OCT 1.0% alone (p<0.001 for all species). FIC index analysis revealed a clear synergistic interaction for *M. furfur* (FIC=0.31), whereas additive effects were observed for *M. globosa* and *M. restricta* (both FIC=0.56).

Clinical efficacy in patients with scalp seborrheic dermatitis

After 12 weeks of treatment with a shampoo formulated with the triple combination, statistically significant reductions in the total SSD severity score and in all individual domain scores, including scaling, erythema, and pruritus, were observed (**Table 2**). The mean total SSD severity score decreased from 11.65±2.10 at baseline to 7.70±2.40 at week 12 (t=7.851, p<0.001, Cohen d=1.76). The scaling score showed a significant reduction from 7.45±2.24 to 5.65±2.90 (t=4.451, p<0.001, Cohen d=1.00), while the pruritus score declined from 2.45±0.50 to 1.25±0.70 (t=8.527, p<0.001, Cohen d=1.91). A significant decrease was also documented for the erythema score, which declined from 1.75±0.60 at baseline to 0.80±0.45 at week 12 (t=7.842, p<0.001, Cohen d=1.75). Following the 12-week treatment period, a notable shift in the distribution of SSD severity categories was observed among the 20 study participants. At baseline, 14 patients (70%) were classified as having severe SSD (score 10–16), 5 (25%) had moderate disease (score 6–9), and 1 (5%) had mild disease (score 0–5). After the intervention, the number of patients with severe SSD decreased to 5 (25%), those with moderate SSD increased to 10 (50%), and 5 patients (25%) achieved the mild disease category (p=0.014). No participant discontinued treatment due to adverse local or systemic effects.

Table 2. Changes in scalp seborrheic dermatitis (SSD) severity observed over the 12-week study period among seborrheic dermatitis treated with the triple combination of magnetized saline water, ciclopirox olamine and piroctone olamine

Measure	SSD severity score (means ± SD)		t	p-value	Cohen d
	Baseline	12 weeks			
Total score	11.65±2.10	7.70±2.40	7.851	<0.001	1.76
Scaling score	7.45±2.24	5.65±2.90	4.451	<0.001	1.00
Erythema score	1.75±0.60	0.80±0.45	7.842	<0.001	1.75
Pruritus score	2.45±0.50	1.25±0.70	8.527	<0.001	1.91

Cohen d was calculated as $t/\sqrt{n}$ (paired-samples method using the standard deviation of within-subject differences)

Discussion

In this study, the efficacy of MSW combined with CPO and OCT against *Malassezia* yeasts was examined, first through in vitro susceptibility testing and subsequently in a proof-of-concept clinical investigation of patients with SSD. The in vitro results demonstrated a significant

potentiation of anti-yeast activity when MSW 30% was combined with CPO 0.5% and OCT 1.0% against three dermatologically relevant *Malassezia* species. Accordingly, the triple combination yielded a uniform MIC of 3.91 mg/L across all three species, representing a 2.0- to 4.0-fold improvement compared to CPO 0.5% + OCT 1.0% alone. This apparent convergence toward a single MIC value is attributable to the limited resolution inherent to the two-fold serial dilution method, which constrains MIC values to discrete concentration steps and cannot capture differences smaller than one dilution increment. FIC index analysis indicated true synergy for *M. furfur* (FIC=0.31), while the interaction with *M. globosa* and *M. restricta* was classified as additive (FIC=0.56 for both; threshold for synergy ≤0.5) [28]. The most pronounced synergistic effect was observed for *M. furfur* (FIC=0.31), a species frequently associated with SSD, seborrheic dermatitis, and pityriasis versicolor [30]. Although the interaction did not reach the conventional synergy threshold for *M. globosa* and *M. restricta*, the consistent MIC reduction across all species indicates meaningful potentiation. While the MIC of the MSW/CPO/OCT combination (3.91 mg/L) remained 4.0- to 8.0-fold higher than those of ketoconazole 2% (0.49–0.98 mg/L), it was substantially lower than CPO/OCT alone (7.81–15.63 mg/L), confirming meaningful potentiation of anti-yeast activity.

While the precise mechanisms underlying this interaction remain to be fully characterized, it can be hypothesized that the biophysical alterations of MSW (characterized by reduced surface tension and modified ionic interactions) [17-19] may create a stressful microenvironment that could destabilize fungal cell membranes [23], potentially increasing their fluidity and permeability. Enhanced penetration of CPO and OCT within *Malassezia* cells could, in turn, lead to accelerated intracellular metal chelation and mitochondrial dysfunction. These mechanisms are entirely hypothetical at present, and direct experimental validation (including membrane permeability assays and intracellular drug accumulation studies) will be required to substantiate this model. This caveat notwithstanding, the 12-week proof-of-concept clinical evaluation in patients with moderate-to-severe SSD suggested that the in vitro additive/synergistic effects may translate into measurable clinical benefits. Accordingly, treatment with the investigational shampoo (MSW 30% + CPO 0.5% + OCT 1.0%) resulted in a statistically significant 33.9% reduction in total SSD scores. A component analysis revealed that all three subscales demonstrated significant improvements, with erythema showing the most dramatic reduction (54.3%), followed by pruritus (49.0%) and scaling (24.2%). The reduction in overall SSD severity observed in this study is consistent with efficacy data previously reported for other established topical antifungal therapies used in this condition, including the ketoconazole 2% reference standard [31,32]. Notably, the shift in disease severity distribution (with 70% of patients presenting with severe SSD at baseline compared to only 25% at week 12) provides further preliminary evidence of the formulation clinical efficacy.

The pronounced reduction in the pruritus subscale observed in SSD patients represents a particularly noteworthy finding. From a clinical perspective, rapid pruritus relief may serve as a critical driver of treatment adherence, a factor that directly influences therapeutic outcomes. While the anti-yeast activity of the CPO/OCT combination likely contributes to symptomatic relief by reducing *Malassezia*-driven inflammation, MSW itself may provide a direct anti-pruritic effect, potentially through modulation of cutaneous sensory pathways or activation of autophagy mechanisms [33]. Complementing these clinical benefits, the formulation demonstrated an excellent tolerability profile, with no patient discontinuing product application over the 12-week study period due to adverse effects. This observation is particularly significant for a chronic and relapsing condition like SSD, where the necessity for long-term management makes patient adherence a cornerstone of clinical effectiveness [34]. Although the present study did not test lower concentrations of CPO and OCT, the observed in vitro potentiation raises the hypothesis that MSW-based formulations might allow reduced concentrations of conventional antifungal agents while maintaining therapeutic efficacy. This dose-sparing hypothesis, along with the environmental and economic implications of such formulations, warrants dedicated investigation in future studies.

Several limitations must be acknowledged when interpreting these findings. The open-label, single-arm design of the proof-of-concept clinical study is the most significant limitation, as it cannot distinguish the specific contribution of MSW from the established effects of CPO and OCT.

Specifically, the absence of both a CPO/OCT monotherapy arm and an MSW-only vehicle control prevents quantification of the incremental clinical benefit of MSW. Nonetheless, this caveat is at least partially offset by the clear demonstration of MSW/CPO/OCT additive/synergistic interactions through rigorous in vitro susceptibility testing, which establishes biological plausibility for clinical observations. The small sample size (n=20) limits the statistical power and the generalizability of the findings. The 12-week duration, while sufficient for an initial efficacy assessment, may be inadequate to assess long-term effectiveness or recurrence rates following treatment cessation, a critical consideration given the characteristically relapsing course of SSD. An important additional consideration is that the proprietary saline solution used to prepare MSW contains trace concentrations of Zn^{2+} and Al^{3+}, which may exert independent antifungal effects. Future studies should compare MSW prepared from standard 0.9% NaCl with the current proprietary formulation to isolate the contribution of magnetic field exposure from that of mineral composition. The temporal stability of the physicochemical properties of MSW was not formally assessed, and it remains unclear whether the antifungal-enhancing properties of MSW are maintained over prolonged storage periods. Moreover, the absence of quantitative microbiological assessment (e.g., culture or molecular analysis of scalp *Malassezia* burden) prevents direct confirmation that clinical improvement resulted from reduced yeast colonization rather than from anti-inflammatory or other non-antifungal effects of the formulation components. Finally, species-level identification of *Malassezia* present on patient scalps was not performed, precluding correlation between in vitro species-specific additive/synergistic profiles and individual clinical responses.

Conclusion

The present study provides preliminary evidence that combining MSW 30% with CPO 0.5% and OCT 1.0% represents a well-tolerated and effective strategy for managing SSD. This triple combination demonstrated additive-to-synergistic anti-*Malassezia* activity in vitro, with synergy against *M. furfur* (FIC=0.31) and additive effects against *M. globosa* and *M. restricta* (FIC=0.56), achieving a 2.0- to 4.0-fold reduction in MIC compared to CPO and OCT alone. While the in vitro data confirmed meaningful pharmacological potentiation, the clinical arm provided preliminary evidence of the formulation therapeutic potential; the single-arm design precludes quantification of the individual contribution of MSW to the observed clinical improvements. The observed in vitro potentiation suggests that this formulation could potentially allow for the use of lower concentrations of conventional antifungal agents while maintaining or even improving efficacy against *Malassezia* yeasts, a hypothesis that warrants further testing. Notably, the observed shift in disease severity distribution, with 75% of patients achieving moderate or mild disease status at week 12 versus 30% at baseline, underscores the clinical relevance of these findings. Based on these proof-of-concept results, further research is justified, ideally through a randomized, vehicle-controlled trial that includes separate arms for CPO/OCT alone, MSW vehicle, and the triple combination.

Ethics approval

The Institutional Review Board of Studio Minoretti, Italy, has reviewed and approved the study protocol (reference: MW2501). Prior to participation, all individuals provided written informed consent.

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None.

Competing interests

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

No artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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