Selenium disulfide: a key ingredient to rebalance scalp microbiome and sebum quality in the management of dandruff

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INTRODUCTION

Dandruff is a milder form of seborrheic dermatitis (SD). It usually presents as scaliness on the scalp without any visible signs of inflammation.[1] Several extrinsic and intrinsic factors have been related to the development of dandruff/SD: the activity of the sebaceous gland and sebum composition, epidermal barrier function, host immune function, colonization by fungi (Malassezia yeasts), and the host-inhabitant interplay.[2, 3] *Malassezia spp.* metabolize and oxidize sebum-derived lipids such as triglycerides, squalene and fatty acids into inflammatory compounds and produce indole derivatives which may trigger skin inflammation.[4,5] Next generation sequencing based studies have shown that bacterial scalp microbiota changes have been associated with the pathogenesis of dandruff/SD in addition to *Malassezia spp.*[6-8]

Selenium disulfide (SeS_2) is effective in managing both dandruff and scalp SD. It reduces flakes, itching, irritation and redness of the scalp. It has shown a full spectrum antimicrobial action against *Malassezia* yeasts and bacterial species.[9, 10]

OBJECTIVES

The objective of this work was to evaluate the clinical benefits of a shampoo containing SeS_2 on scalp dandruff and its impact on the scalp microbiota and surface lipids.

MATERIAL AND METHODS

STUDY 1: SINGLE BLIND VEHICLE-CONTROLLED DESIGN

Study population

50 adults with an adherent dandruff score of more than 2.5 and total dandruff score (adherent + non-adherent) ≥4.5 (ranging from 0=none to 10=very severe) were recruited for this study. Adherent dandruff was scored from 0 (no dandruff) to 5 (very severe) using a visual dandruff severity scale. Subjects washed their hair 3 times/week with the vehicle shampoo for 3 weeks and then with either the SeS2 or the vehicle shampoo 3 times/week for 28 days. Subjects then reverted back to the vehicle shampoo for 28 days.

Clinical assessments

Adherent and non-adherent dandruff scores were assessed at Day (D) -21, D0 baseline and at D21, D28, D35 and D56.

Bacterial diversity

Culture-independent next-generation sequencing methods assessed the bacterial diversity. The alpha diversity was assessed using the Shannon index. The Bray-Curtis index was used to quantify the OTU composition dissimilarity between 2 different groups or sites. Scalp microbiome samples were collected at baseline and on the same scalp area after 4 weeks, and after 5 and 8 weeks.

Quantification of microbial scalp species

qPCR using specific primers and MGB probes targeting a specific region of bacterial 16S rDNA, or fungal ITS-28S; rDNA quantified *Staphylococcus spp.* and *Cutibacterium spp.* and the major fungal genus *Malassezia spp.* determined potential changes in the abundance of specific microbial species at both lesional and non-lesional zones in both groups at baseline (D0), at D28, D35 and D56.

STUDY 2: OPEN LABEL DESIGN

Study population

32 adults with mild to severe scalp desquamation and mild to severe pruritus were included in this 10-week open-label study. Subjects washed their hair 3/week during the 2 weeks preceding study start with a bland shampoo. SeS_2 was used 3 times/week for 28 days, followed by a 42-day period using a bland shampoo 3 times/week.

Clinical and instrumental assessments

Adherent and non-adherent dandruff scores were assessed using scores from 0 (none) to 5 (very severe). Subjects self-assessed the severity of scaling, pruritus and scalp greasiness from 0 (none) to 9 (very severe).

Trans Epidermal Water Loss (TEWL) was assessed at D-3, D31, D73.

Lipid analysis

Scalp sebum lipids were sampled at D0 and D31.

• LOCAL TOLERANCE

Local tolerance was assessed for all subjects included in both studies.

RESULTS

STUDY 1: VEHICLE-CONTROLLED

53 subjects with adherent dandruff scores of at least 2.5 and 6 subjects with a score between 2.0 and 2.5, all having total dandruff scores of at least 4.5, were included. Mean age was 42.4 years; 58% were women.

Clinical efficacy

Both groups had similar adherent dandruff scores at baseline. SeS_2 significantly reduced adherent dandruff scores at all post-baseline visits, with reductions ranging from 40.8% to 58.3% compared to baseline (all $p<0.001$, **Figure 1**) with a maintenance of the clinical benefit until D56. Compared to baseline, no significant change was observed with the vehicle throughout the study.

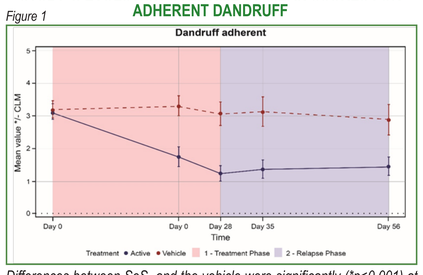
Bacterial diversity of the scalp

The Shannon index showed that SeS_2 and the vehicle maintained the microbiota diversity (**Figure 2**).

SeS_2 induced a global change in the distribution of the abundance relatives of the OTUs at lesional zones, as measured by the Bray-Curtis Index. There was no change with the vehicle (**Figure 3**). A notable increase in the OTU distribution returning to initial diversity levels was observed at D56.

STUDY 1: EVOLUTION OVERTIME OF MEAN SCORES FOR ADHERENT DANDRUFF

Figure 1



Differences between SeS_2 and the vehicle were significantly ($p<0.001$) at all post-baseline (D0) visits for mean adherent dandruff scores.*

STUDY 1: SCALP BACTERIAL DIVERSITY USING THE SHANNON INDEX FOR LESIONAL AND NON-LESIONAL ZONES

Figure 2a

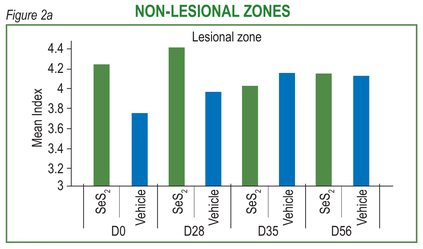
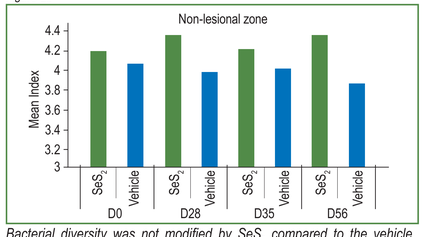


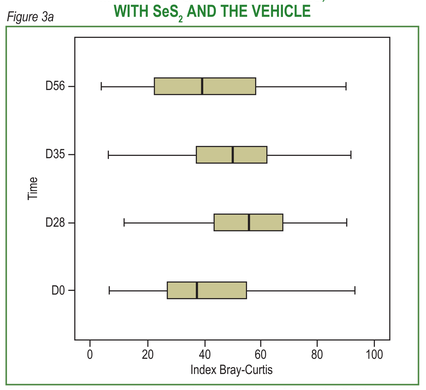
Figure 2b



Bacterial diversity was not modified by SeS_2 compared to the vehicle, either during the active phase or the follow-up period, at both lesional and non-lesional zones

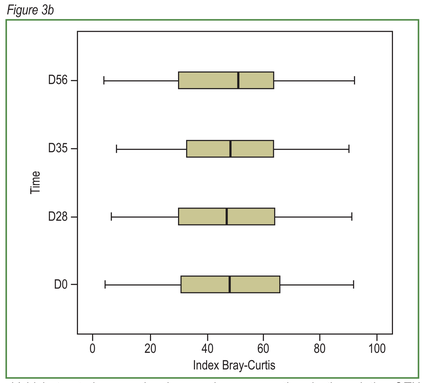
STUDY 1: BACTERIAL OTU COMPOSITION DISSIMILARITY AS MEASURED USING BRAY-CURTIS, WITH SeS_2 AND THE VEHICLE

Figure 3a



SeS_2 caused changes in the relative distribution of bacterial OTUs towards greater diversity, at D28 and D35. This variation returned to baseline levels after 56 days.

Figure 3b



Vehicle-treated group showing no change over time in the relative OTU distribution

Bacterial species quantification

Staphylococcus spp. were significantly reduced by ~-1Δlog at both lesional and non-lesional zones at D28 ($p<0.001$) returning to baseline levels at D56 with SeS_2 shampoo only. *Cutibacterium spp.* levels were not different between both treatment groups, except at D56 at the lesional zone, where levels increased by ~0.4Δlog with SeS_2 ($p<0.001$).

Malassezia quantification

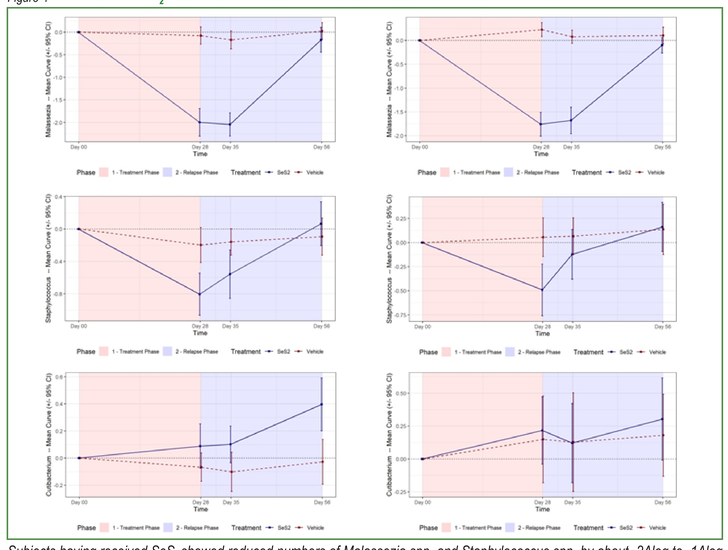
After 4 weeks of treatment, *Malassezia spp.* was significantly reduced by ~-2Δlog ($p<0.001$) at both zones following the use of SeS_2 while there was no such effect observed with the vehicle. A maintenance effect with SeS_2 was observed at D35 which was not anymore observed at D56 (**Figure 4**).

Between-species Ratios

The ratio Malassezia/Cutibacterium spp. was highly increased in lesional zones compared to non-lesional zones. At lesional zones receiving SeS_2, this ratio was significantly decreased compared to baseline level, after 4 weeks of treatment and also at D35 ($p<0.001$) whereas no effect was observed with the vehicle (**Figure 5**).

STUDY 1: SeS_2 REDUCES NUMBERS OF *MALASSEZIA SPP.* AND *STAPHYLOCOCCUS SPP.*

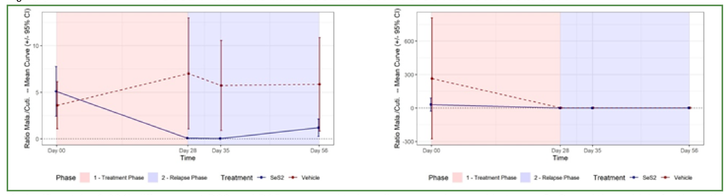
Figure 4



Subjects having received SeS_2 showed reduced numbers of Malassezia spp. and Staphylococcus spp. by about -2Δlog to -1Δlog respectively, at D28 and 35 at both lesional and non-lesional zones ($p<0.001$) when compared to D0 and the vehicle group. By D56, the number of these 2 microorganisms had returned to near-D0 levels. Cutibacterium spp. numbers did not vary at D35 and between the SeS_2 and the vehicle group for both lesional and non-lesional zones. Cutibacterium spp. numbers were significantly increased by ~+04Δlog with SeS_2 treatment ($p<0.001$), but only at the lesional zone at D56.

STUDY 1: RATIO *MALASSEZIA SPP.* VS *CUTIBACTERIUM SPP.*

Figure 5



A significant ($p<0.001$) difference at D28 and D35 compared to baseline were observed between SeS_2 and the vehicle for the ratio of number of Malassezia spp. Cutibacterium spp.

STUDY 2: OPEN LABEL

24 women and 8 men aged between 29 and 42 years and with mild to severe dandruff participated.

Clinical assessments

Figure 6 summarizes changes over time of the total dandruff severity. During the follow-up phase (D31-D73), a slow increase in dandruff severity was observed, with a maintenance of a significant benefit compared to baseline still present at D73 ($p<0.01$). **Figure 7** illustrates mean severity scores for self-perceived scaling, itch and scalp greasiness integrating an additional self-assessment at D3.

Lipid Analysis

After 4 weeks SeS_2 significantly increased the total squalene content ($p<0.05$) and decreased squalene peroxide at D31 by almost 50%. Between D0 and D31, the ratio TG/FFA had significantly increased ($p<0.0001$) corresponding to decrease of the lipasic activity of *Malassezia spp.* The ratio of SQOOH/SQ was significantly decreased ($p<0.0001$) after 4 weeks, correlating with the decrease of peroxide squalene with SeS_2.

Skin barrier markers

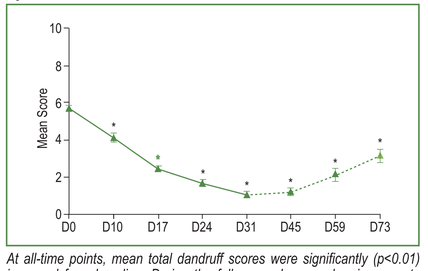
The use of SeS_2 significantly ($p<0.02$) led to a drop by 4.91 units ($g/m^2/h$) of TEWL during the active phase, returning to baseline values during the follow-up phase.

LOCAL TOLERANCE

No local tolerance issues were reported for SeS_2, in any of the 2 studies.

STUDY 2: CHANGES OVER TIME OF MEAN TOTAL DANDRUFF SEVERITY SCORES

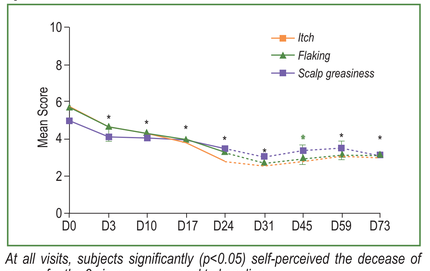
Figure 6



At all-time points, mean total dandruff scores were significantly ($p<0.01$) improved from baseline. During the follow-up phase a slow increase to baseline values was observed, with a maintenance of a significant ($p<0.01$) clinical benefit.

STUDY 2: CHANGES OVER TIME OF THE MEAN SCORES IN THE SELF-PERCEPTION OF THE SEVERITY OF FLAKING, ITCH AND SCALP GREASINESS

Figure 7



At all visits, subjects significantly ($p<0.05$) self-perceived the decease of scores for the 3 signs as compared to baseline.

CONCLUSION

SeS_2 in a shampoo is effective and well tolerated in dandruff due to its rebalancing effect on the equilibrium between the main bacterial and fungal populations and on sebum composition, and helps to restore a healthy scalp.

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Conflict of interest

All authors are employees of L'OREAL Research & Innovation, France.

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