Lipogenic activity of Selenium Sulfide (SeS_2) and its role in enhancing lipid production in Meibomian Glands

Abstract # 3533514

Yair Alster, MD, Hila Epstein-Barash, PhD, Hadas Rapaport, DVM; Omer Rafaeli, MD
Azura Ophthalmics Limited, Tel Aviv Israel

BACKGROUND

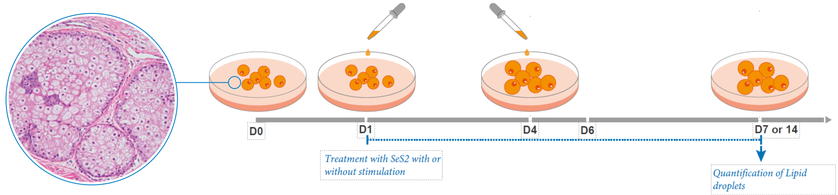
- Meibomian Gland Dysfunction (MGD) is the leading cause of Dry Eye Disease (DED). Reduced secretion of lipids due to obstructive MGD leads to instability of the tear film and drying of the ocular surface.
- SeS_2, a potent keratolytic agent, has improved glandular function in patients with MGD in several studies.
- Beyond it's ability to alleviate the obstruction it has been suggested that SeS_2 may further Beyond it's ability to alleviate glandular obstruction, it has been suggested that SeS2 may also increase lipid availability. Patients treated with SeS_2 medicated shampoo for seborrheic dermatitis often complain of excessive oil on their scalp. Using a sebometer to measure increased amounts of sebum over the skin following treatment with SeS_2 shampoo confirmed patient do experience increased oil production.
- Meibocytes and Sebocytes originate from the same embryonic origin and share strong similarities in their development, structure and holocrinic mode of lipid secretion. Thus, increased lipid from Sebocytes may indicate that such an effect is possible in Meibocytes.

OBJECTIVES

Test the hypothesize that SeS_2 can directly induce lipid production in lipid producing cells.

METHODS

The ability of SeS_2 to enhance lipid secretion was evaluated in two human sebocytre models: **3-D** and **2-D** cultures (SEBO662 SEBO662AR, respectively; BioAlternative, France).

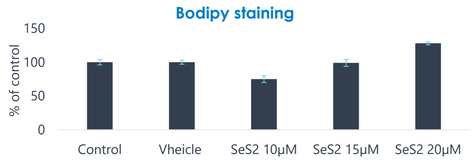


Step one: Cytotoxicity assay, using a standard MTT reduction assay

Step two: Stimulation with SeS_2 and one or two known lipid stimulators (Lipogenic mix [Bioalternative proprietary] and Testosterone). The treated cultures were incubated for 7 or 14 days. Bodipy or Oil-Red-O stained culture sections were evaluated to determine lipid production , in 2D and 3D cell culture, respectively

RESULTS: 2-D Sebocytes

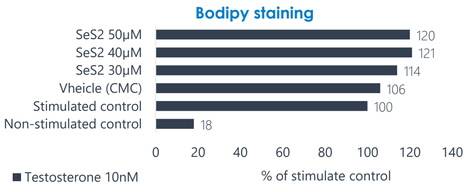
Without stimulant



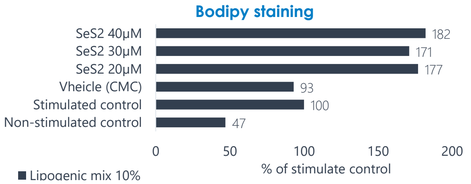
Bodipy staining

A. Lipid production increased by 28% with 20 µM SeS2 without stimulation (P<0.01) .

With stimulant

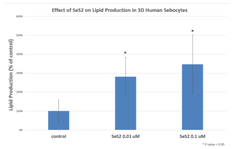


B. Following stimulation with testosterone and treatment with SeS2 at 40 and 50µM lipid detection increase by 20-21%, above base stimulation control (P<0.01)



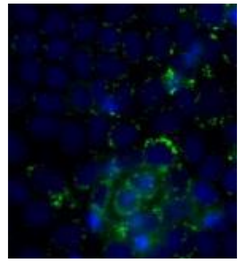
C. Following stimulation with lipogenic mix and treatment with SeS2 at 20 to 40µM lipid detection increase by 71 to 82%, above base stimulation control (P<0.01)

RESULTS: 3-D Sebocytes

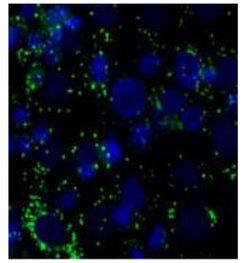


Lipid production was significantly increased by 282% with 0.01 µM SeS2 and by 348% with 0.1 µM SeS2 (P< 0.05)

Lipogenic Mix Stimulation; Green dots = more lipid

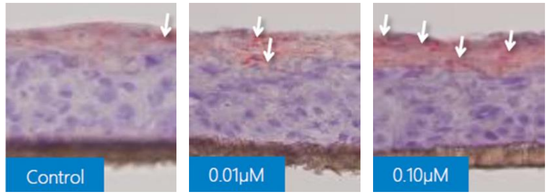


Stimulated Control



SeS2 + CMC
30µM + 1.5 x 10^{-4}%

Oil-Red-O staining



DISCLOSURES

Yair Alster- Azura Ophthalmics; I, E, P&S
Hila Epstein-Barash – Azura Ophthalmics; I, E&P
Hadas Rapaport - Azura Ophthalmics; I, E&P
Omer Rafaeli - Azura Ophthalmics; I, E&P

CONCLUSIONS

Through their lipid secretion the Meibomian glands play a crucial role in maintaining a healthy ocular surface and its optical quality. Located in the upper and lower eyelids, the oil-producing Meibomian glands are modified sebaceous glands and are responsible for secreting the lipid layer (meibum) that forms the outermost layer of the tear film. The lipid layer plays a crucial role in maintaining a healthy ocular surface and its optical quality. These in-vitro results suggest that selenium sulfide has the potential to improve Meibomian Glands' function by pushing cells to their maturation state and therefore increasing lipid production. Such outcome is likely to play a role in the observed benefit of SeS_2 in improving the clinical outcome of MGD patient