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Nerolidol Inhibits the LOX-1 / IL-1 β Signaling to Protect Against the Aspergillus Fumigatus Keratitis Inflammation Damage to the Cornea

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Abstract

Purpose: Nerolidol, a naturally occurring sesquiterpene has both anti-microbial and anti-inflammatory properties. The current study aims to investigate the antifungal and the anti-inflammatory effects of nerolidol against mouse *Aspergillus fumigatus* (*A. fumigatus*) keratitis.

Methods: The minimum inhibitory concentration (MIC) and cytotoxicity tests were used to study the

ity. For in vivo and in vitro studies, the mouse corneas and the human corneal epithelial cells infected with *A. fumigatus* spores were intervened with nerolidol or phosphate buffered saline. Thereafter, the effect of the nerolidol on the response against inflammation was analyzed using the following parameters: recruitment of the neutrophils or macrophages and the expression of

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Feedback

oxidized low density lipoprotein receptor-1 (LOX-1) and interleukin 1 β (IL-1 β). Techniques used were the slit lamp, immunofluorescence, myeloperoxidase (MPO) detection, quantitative real-time polymerase chain reaction (qRT-PCR) and Western blot.

Results: Nerolidol directly inhibits the growth of *A. fumigatus*. The administration of nerolidol reduced the severity of fungal keratitis with infiltration of fewer inflammatory cells and reduced levels of the LOX-1, as well the anti-inflammatory cytokines such as IL-1 β were reduced compared with the PBS group. Additionally, in vitro studies showed that treatment with nerolidol inhibited the production of the LOX-1 / IL-1 β levels in *A. fumigatus* stimulated HCECs.

Conclusion: Nerolidol attenuated the *A. fumigatus* keratitis inflammatory response by inhibiting the growth of *A. fumigatus*, reducing the recruitment of the neutrophils and the macrophages, and inhibiting the LOX-1/ IL-1 β signaling.

Keywords: *Aspergillus fumigatus*; IL-1 β ; Keratitis; LOX-1; Nerolidol.

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Maresin1 Regulates Neutrophil Recruitment and IL-10 Expression in *Aspergillus Fumigatus* Keratitis

Q Tang et al. *Int Immunopharmacol* 69, 103-108. Apr 2019. PMID 30690344.

Taken together, these findings demonstrate that treatment with maresin1 moderates corneal inflammation through reducing neutrophil recruitment and levels of the chemokine ...

Inhibition of LOX-1 Alleviates the Proinflammatory Effects of High-Mobility Group Box 1 in *Aspergillus fumigatus* Keratitis

JQ Jiang et al. *Int J Ophthalmol* 12 (6), 898-903. 2019. PMID 31236343.

In fungal keratitis, HMGB1 is a proinflammatory factor in the first line of immune response. HMGB1 mainly stimulates neutrophils and macrophages to produce inflammatory c ...

Osteopontin Contributes to Effective Neutrophil Recruitment, IL-1 β Production and Apoptosis in *Aspergillus Fumigatus* Keratitis

G Zhao et al. *Immunol Cell Biol* 96 (4), 401-412. Apr 2018. PMID 29359350.

Fungal keratitis is a major cause of corneal ulcers, resulting in significant visual impairment and blindness. A phosphorylated glycoprotein secreted by immunocompetent c ...

Wedelolactone Suppresses IL-1 β Maturation and Neutrophil Infiltration in *Aspergillus Fumigatus* Keratitis

M Cheng et al. *Int Immunopharmacol* 73, 17-22. Aug 2019. PMID 31078922.

Present findings indicated that wedelolactone reduced host immune responses by attenuating neutrophil recruitment and IL-1 β maturation in *Aspergillus fumigatus* keratitis. ...

Wnt5a Contributes to dectin-1 and LOX-1 Induced Host Inflammatory Response Signature in Aspergillus Fumigatus Keratitis

C Che et al. Cell Signal 52, 103-111. Dec 2018. PMID 30172652.

Fungal keratitis causes devastating corneal ulcers which can result in significant visual impairment and even blindness. As a ligand that activates the non-canonical Wnt ...

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Morphogenesis control in *Candida albicans* and *Candida dubliniensis* through **signaling** molecules produced by planktonic and biofilm cells.

Martins M, et al. Eukaryot Cell 2007.

Both planktonic cells and biofilm supernatants of *C. albicans* and *C. dubliniensis* contained isoamyl alcohol, 2-phenylethanol, 1-dodecanol, E-**nerolidol**, and E,E-farnesol. ...Overall, these results reveal a group of alcohol extracellular **signaling** molecules that are biologically active with *C. albicans* and *C. dubliniensis* morphogenesis...

Next result

(3R,6E)-**nerolidol**, a fertility-related volatile secreted by the queens of higher termites (Termitidae: Syntermitinae).

Havlíčková J, et al. Z Naturforsch C J Biosci 2019.

We show that primary queens of four higher termites from the subfamily Syntermitinae (*Embriatermes neotenicus*, *Silvestritermes heyeri*, *Labiotermes labralis*, and *Cyrrillitermes angulariceps*) emit significant amounts of the sesquiterpene alcohol (E)-**nerolidol**. ...In spite of technical difficulties encountered in long-term experiments with the studied species, (3R,6E)-**nerolidol** remains among eventual candidates for the role in queen fertility **signalling**...

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