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Mycobacterium abscessus cell wall and plasma membrane characterization by EPR spectroscopy and effects of amphotericin B, miltefosine and nerolidol

Lais Alonso [a], Laryssa Ketelyn Lima Pimenta [b], André Kipnis [b], Antonio Alonso [a]

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Highlights

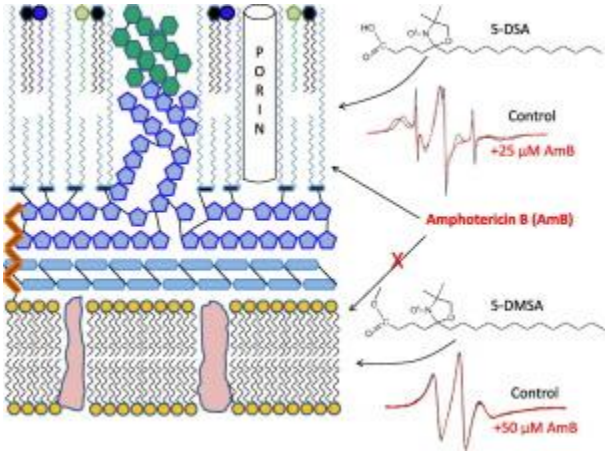
- Amphotericin B (AmB) reduced the cell wall fluidity of *Mycobacterium abscessus*.
- AmB enters the cell wall but does not reach the mycobacterial plasma membrane.
- Miltefosine and nerolidol increase the fluidity of cell envelope membranes.
- Nerolidol is shown to extract lipids from the mycobacterial cell wall.

Abstract

Spin label electron paramagnetic resonance (EPR) spectroscopy was used to characterize the components of the *Mycobacterium abscessus massiliense* cell envelope and their interactions with amphotericin B (AmB), miltefosine (MIL), and nerolidol (NER). Spin labels analogous to stearic acid and phosphatidylcholine (PC) were distributed on an envelope layer with fluidity comparable to other biological membranes, probably the

mycobacterial cell wall, because after treatment with AmB a highly rigid spectral component was evident in the EPR spectra. Methyl stearate analogue spin labels found a much more fluid membrane and did not detect the presence of AmB, except for at very high drug concentrations. Unlike other spin-labeled PCs, the TEMPO-PC spin probe, with the nitroxide moiety attached to the choline of the PC headgroup, also did not detect the presence of AmB. On the other hand, the steroid spin labels were not distributed across the membranes of *M. abscessus* and, instead, were concentrated in some other location of the cell envelope. Both MIL and NER compounds at 10 μM caused increased fluidity in the cell wall and plasma membrane. Furthermore, NER was shown to have a remarkable ability to extract lipids from the mycobacterial cell wall. The EPR results suggest that the resistance of mycobacteria to the action of AmB must be related to the fact that this drug does not reach the bacterial plasma membrane.

Graphical abstract



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Keywords

Mycobacterium abscessus; Amphotericin B; Miltefosine; Nerolidol; Spin label; Electron paramagnetic resonance

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