Intracellular activity of antibiotics against *S. aureus* internalized by human skin keratinocytes: comparison with THP-1 macrophages

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Intracellular *S. aureus* is a reality …

and you need antibiotics to treat them …
Intracellular S. aureus

- **PULMONARY INFECTIONS ASSOCIATED WITH CYSTIC FIBROSIS**
  
  *Jarry and Cheung, Infect Immun, 2006*

- **COMPLICATED SKIN INFECTIONS**
  
  *Mempel et al, Br J Dermatol., 2002*

- **RECURRENT RHINOSINUSITIS**
  
  *Clement et al, J Infect Dis, 2005*

- **ENDOCARDITIS**
  
  *Sinha and Herrmann, Thromb Haemost, 2005*

- **OSTEOMYELITIS**
  
  *Ellington et al, J Bone Joint Surg Br., 2003*
Aim of the work

Evaluation of the activity of antibiotics against intracellular forms of \textit{S. aureus} (strain ATCC 25923):

- in \textbf{pertinent} cellular models of infection
  (phagocytes vs. skin keratinocytes)

- following a \textbf{pharmacological} approach (dose-response studies)
Dose-response studies

Pharmacological parameters were similar in both cell types

Static dose: ~ 0.7 mg/L

Emax: ~ - 0.9 log cfu (24h)
• Similar effects in both cell types for all drugs, except for rifampicin

• Poor activity of oxacillin, vancomycin, linezolid against intracellular *S. aureus*

• Extensive intracellular activity of moxifloxacin, rifampicin, and quinupristin-dalfopristin
Static doses

- Similar effects in both cell types for all drugs, except for rifampicin.
- Extensive activity of rifampicin and moxifloxacin, probably in relation with their low MICs values and their ability to readily accumulate within cells.
- Poor activity of linezolid and vancomycin.
Conclusion

• Pharmacological parameters were similar in both cell lines (keratinocytes, macrophages) for all drugs, except for rifampicin (more active in keratinocytes)

• In both models, rifampicin, moxifloxacin and quinupristin-dalfopristin show the largest intracellular activity

• These models could be used for fast screening and quantitative assessment of novel antibiotics active against intracellular S. aureus