



Neem Biotech Presents Data Showing Effectiveness of the Quorum Sensing Inhibitor Ajoene Against Spread of Infection in Preclinical Models at ASM Microbe 2019

Ajoene found to reduce virulence factor secretion, destabilise mature bacterial biofilms, allowing re-sensitisation to antibacterial agents

Neem Evaluating Drug Candidates based on Ajoene for Clinical Evaluation Against Wound Infections

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Neem Biotech, a company focused on developing novel solutions to address antimicrobial resistance, announced today the presentation of data demonstrating the effectiveness of Ajoene against the spread of infection in chronic wounds at ASM Microbe 2019 in San Francisco (20-24 June). Ajoene is a quorum sensing inhibitor found naturally in garlic. Quorum sensing (QS) pathways regulate microbial motility, virulence factor production, and the formation and maturation of biofilms, providing a potential mode of therapeutic intervention. Neem has identified and synthesised novel compounds inspired by Ajoene. These candidate compounds are being evaluated for clinical studies.

“There is an urgent need for new avenues of treatment in chronically-infected wounds. So far, the ability to prevent biofilm formation, disruption of mature biofilms, reduction of virulence factors and thus the spreading of infection remains clinically elusive,” said Dr. David Houston, Senior Scientist and wound project lead at Neem Biotech. “The antibacterial properties of Ajoene are well known. This research provides insight into the mechanism behind this activity as well as multiple potential targets for therapeutic drug discovery.”

Study Details

In the studies, the effects of Ajoene on planktonic bacteria and biofilms of *Pseudomonas aeruginosa* (Pa) and *Staphylococcus aureus* (Sa) were tested using QS inhibition, biofilm formation and eradication assays. Ajoene was also tested against novel biofilm skin and chronic wound spreading infection models using a mature Pa + Sa biofilm consortium.

Ajoene inhibited QS in Pa (80% at 75 μ M) and Sa (33 mm zone of inhibition at 3 mM) and inhibited the formation of biofilms of Pa (IC_{50} 31 \pm 10 μ M) and Sa (1 \pm 0.5 μ M). Pre-treatment with Ajoene enhanced the susceptibility of Pa and Sa iodine, *in vitro*. Ajoene reduced the secretion of hemolysin in Sa of lasB, RL, pyocyanin and proteases in Pa. Ajoene reduced microbial viability in a biofilm infection model of *ex-vivo* porcine skin (>5 log reduction of colony forming units of both Pa and Sa). A clinically relevant Ajoene-loaded hydrogel

prevented the spread of bacteria from the initial inoculation site in the chronic wound *ex vivo* model.

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About Biofilms and Quorum Sensing Inhibition

Biofilms are complex bacterial communities formed during the natural infection process as a protection mechanism and controlled by bacterial quorum sensing. Biofilm communities allow infections to spread by producing toxins that inhibit the body's immune system, generating exopolysaccharide and changes in metabolic state that reduce the efficacy of antibiotics and activating virulence factors that drive the spread of infection. Biofilms and quorum sensing allow infections to spread acutely and to become chronic. Inhibiting acute and chronic spread of infection by inhibition of quorum sensing has potential to manage a wide range of infection including not only wounds but also respiratory infection such as cystic fibrosis without the risk of generating antimicrobial resistance.

NX-AS-911 is a series of compounds synthesised by Neem based on its Ajoene research that hold potential for the treatment for wound infection. The incidence of wounds is set to rise as more of us live longer and the effects of chronic lifestyle-related diseases, such as diabetes and obesity, take hold. Treatment of these wounds is often complicated by the presence of infection. The NX-AS-911 compounds are quorum sensing inhibitors of *Pseudomonas aeruginosa* and *Staphylococcus aureus* that have shown potential *in vitro* to inhibit the spread of acute infection and support management of chronic infection.

About Neem Biotech

Neem Biotech is a Wales-based biotechnology company with a vision to enhance the life expectancy of patients, and the quality of life of both patients and their families. Leveraging significant expertise in the biology and chemistry of bioactive compounds, Neem Biotech transforms these naturally-inspired compounds into novel non-traditional antibiotic treatments that can aid in the fight against the global threat of antimicrobial resistance. Neem Biotech are studying the management of bacterial biofilms in cystic fibrosis and inhibition and treatment of wound infection, against which the company has drug candidates. For further information visit: www.neembitech.com.