

## **Streszczenie w j. angielskim**

Antimicrobial resistance (AMR) is a major concern in clinical settings, that has been related to the misuse and overuse use of antibiotics, as well as crisis in the development of novel antimicrobial agents. Ceragenins (CSAs) are promising candidates for the founding of novel antibiotics. These non-peptide mimics of endogenous antimicrobial peptides (AMPs) are bactericidal and broad-spectrum antimicrobials with immunomodulatory properties. In addition, antibacterial activity and biocompatibility of ceragenins may be improved by their attachment on the surface of nanomaterials, such as gold nanoparticles (AuNPs).

The objective of this research was to study the antibacterial efficacy of ceragenins alone and in combination with peanut-shaped gold nanoparticles (AuP NP@CSA) against the leading etiological agents of middle ear infection – *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Enhanced antibacterial activity, reduction of the proinflammatory cytokine IL-8 secretion, and improved biocompatibility with host cells characterized the tested ceragenin-based nanosystems. Remarkably, the antibacterial activity of ceragenins was not affected by human cerumen (earwax).

In vitro experiments with induction of resistance to ceragenin CSA-13 and colistin in an emerging hospital pathogen – *Enterobacter hormaechei* subsp. *steigerwaltii* (ST89) were used to investigate the potential mechanisms of resistance to these compounds. Notably, despite the common cationic nature of both agents, the prolonged exposure of *E. hormaechei* to CSA-13 induced only moderate level resistance to this ceragenin, compared to the high level of resistance to colistin observed in *E. hormaechei* upon exposure to this antibiotic. Furthermore, the whole-genome (WGS) and transcriptome (RNA-seq) analyses revealed that molecular mechanisms responsible for the high level of resistance to colistin developed by the studied *E. hormaechei* strain have no impact on its susceptibility to ceragenin CSA-13. Additionally, several novel mechanisms that directly or indirectly may contribute to the development of resistance to ceragenin CSA-13 and/or colistin in *E. hormaechei* have been identified.