Stereochemical synthesis of Lugdunin – An antimicrobial cyclic peptide

The consequence of overuse of antibiotics is that the bacteria have developed a various mechanism to overcome the effect of these molecules, which we now address as antibiotic resistance. In fact, antibiotic resistance has become a serious issue in hospitals where the local microbial flora has evolved under constant selection pressure from the various antibiotics in use. The Center for Disease Control has developed an extensive list of many multi-drug resistant bacteria. This includes many bacteria, which otherwise would be simple to treat, but because of acquired resistance have become a serious threat. *e.g*. *Methicillin-resistant Staphylococcus aureus* (MRSA). In efforts to combat antibiotic resistance, researchers are constantly trying to identify new antibiotics or design better antimicrobial agents. Recently, Zipperer *et. al.* have found that a bacteria (*Staphylococcus lugdunensis*) found in the nose of humans make a cyclic peptide (lugdunin) that shows promise against a variety of Gram-positive bacteria, including opportunistic pathogens such as *MRSA* and vancomycin-resistant *Enterococcus*. Lugdunin, when isolated from the bacteria, is a mixture of two cyclic peptides that only differ in the orientation of a single bond in space. This mixture of stereoisomers of lugdunin has never been resolved and their individual activities are unknown. It is common knowledge in medicinal chemistry that stereoisomers of the same molecule can have vastly different activity. In fact, in some cases, one stereoisomer can either partially or completely inhibit the activity of the other. In our study, we are working on a strategy to chemically synthesize lugdunin as pure stereoisomers. The chemical synthesis of individual isomers will allow us to better understand their specific activity. This poster highlights our efforts in achieving stereochemical control in the synthesis of lugdunin.

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