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An Antibiotic from *Bacillus thuringiensis* against Gram-Negative Bacteria

Estibaliz Sansinenea* and Aurelio Ortiz

Faculty of Chemistry, Autonomous University of Puebla, Puebla, Pue. 72570, Mexico

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The secondary metabolism is an interesting way to explore new compounds which have great biological activities. This characteristic is the reason why chemists have shown interest in this type of technology opening a gate to a new biotechnology. The wide varieties of compounds that have been found in microbial cultures and plant extracts have economic interest. As many microbial species Bacillus also produces many metabolites with biological activities [1].

The bacillus cereus group of bacteria consists of *B. cereus*, *B. thuringiensis*, *B. mycoides* and *B. anthracis*.

Bacillus thuringiensis is an aerobic and gram-positive bacterium and form endospores at the same time with a crystalline inclusions that are called as crystal proteins or δ-endotoxins. These proteins are selectively toxic against different species of insects. On the other hand, *B. thuringiensis* also secretes secondary metabolites with biological activities. One of these metabolites is Zwittermicin A. This natural antibiotic is a highly polar, water-soluble aminopolyol that was firstly isolated from the soil-born bacterium B. cereus. The rising interest in zwittermicin A as a "green" biopesticide has stimulated studies of its unique biosynthesis, mechanism of action and its organic synthesis [2].

The group of Handelsman has been the pioneer that isolated this antibiotic for the first time. They detected that

B.cereus had a biological effect against the fungal pathogens of plants [3-6]. It protects alfalfa seedlings from damping-off caused by Phytophthora medicaginis, tobacco seedlings from *Phytophthora nicotianae*, cucumber fruits from rot caused by *Pythium aphanidermatum* and peanuts from Sclerotinia minor. When they analyzed the containing of this strain to view which was the active component they reported that zwittermicin A **1** was the responsible of the biological activity of the strain [7]. He et al. [8] further elucidated the structure of zwittermicin A **1** and they reported that is a linear aminopolyol antibiotic, which represented a new class of antibiotics (Figure. 1). Further analyses reported that the unique way to identify the strains that are producers of this antibiotic was the antibiotic activity of this compound against the growth of Erwinia herbicola or to be sensitive to phage P7. [9]

This antibiotic is widespread among different strains of *B. cereus* and *B. thuringiensis* from diverse geographical origins [9], therefore it was a logical to screen in a search for diverse strains with biological control activity. The only accurate method for identifying zwittermicin A **1** production is the test for the antibiotic itself. It was reported that the culture conditions influenced accumulation of the zwittermicin A antibiotic [10]. Maximum accumulation was detected in supernatants of trypticase soy broth cultures after sporulation. Has been proved that zwittermicin A enhances insecticidal activity of crystal protein produced by *B. thuringiensis* [11,12] therefore use of synergists has been proposed as one strategy to enhance the efficacy of *B. thuringiensis*.

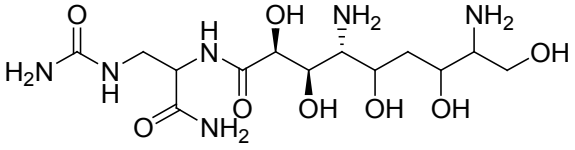

Figure 1: Structure of Zwittermicin A **1**.

The biological activity of this natural antibiotic is very wide. Zwittermicin A has a high activity against the Oomycetes and their relatives, the algal protists, and a moderate activity against some gram-negative bacteria and many plant pathogenic fungi such as Alternaria, Fusarium, Helminthosporium, and Ustilago [13].

The chemists have had an interest to realize the practical syntheses of zwittermicin A **1** due to was difficult to isolate in substantial quantities from the strains, its highly polar, charged nature at physiological pH, and its sensitivity to alkaline conditions [14,15]. However due to its complicated structure with seven stereogenic centers its synthesis has not been easy.

Erwinia herbicola also called *Pantoea agglomerans* is the gram-negative bacterium that is inhibited by this antibiotic [8]. This bacterium is known to be an opportunistic pathogen in the immunocompromised, causing wound, blood, and urinary-tract infections. It is difficult to differentiate *Pantoea spp*. from other members of this family, such as Enterobacter, Klebsiella, and Serratia species. Klebsiella, Enterobacter, and Serratia are closely related gram-negative bacteria that occasionally infect people in hospitals or in long-term care facilities. If Klebsiella pneumonia is acquired in the community, antibiotics, usually a cephalosporin or fluoroquinolone, given intravenously, can cure it. If an infection with any of these three bacteria is acquired in a health care facility, the infection is difficult to treat because bacteria acquired in such facilities are usually resistant to many antibiotics, so Zwittermicin A can be a promising antibiotic against these bacteria.

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***Corresponding author:** Estibaliz Sansinenea, Faculty of Chemistry, Autonomous University of Puebla, Puebla, Pue, 72570, Mexico, E-mail: estisan@yahoo.com

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