

## Application of Antibiotics for Control of Citrus Huanglongbing

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### Editorial

Citrus Huanglongbing (HLB) is the most devastating disease of citrus. HLB has spread to most of the citrus growing areas in the world and causes significantly decline in both citrus production and citrus industry economic output. HLB is caused by three species of fastidious, phloem-resided alpha proteo bacteria: '*Candidatus Liberibacter asiaticus*' (Las), '*Candidatus Liberibacter americanus*' (Lam), and '*Candidatus Liberibacter africanus*' (Laf) [1-3], which are transmitted by the insect vectors, the African citrus psyllid, *Triza erytraea* [4] or Asian citrus psyllid *Diaphorina citri* [5]. Control of HLB in the field is urgently needed but difficult to achieve due to the lack of resistant citrus species and cultivars as well as effective integrated management. Chemotherapy is considered to be an effective short-term strategy for control of HLB. With the finding that prokaryotic organisms were associated with HLB, antibiotics have been applied by injecting into trees in several countries or regions in attempt to control citrus HLB [6]. Currently, many antibiotics have been screened and evaluated by our team and several were determined to be effective or partly-effective in combating HLB.

Beta-lactam antibiotics such as Ampicillin (Amp), and Penicillin (Pen), can inhibit the growth of sensitive bacteria by inactivating enzymes located in the bacterial cell membrane, known as penicillin binding proteins, which are involved in cell wall synthesis [7]. In our previous studies, it was reported that Amp or Pen can eliminate Las bacteria in HLB-affected periwinkle and citrus when applied via root drench, foliar spray, or trunk injection [8-10]. In graft-based assays, Amp and Pen also displayed the greatest antimicrobial activity against Las showing no phyto-toxicity on citrus [11]. In addition as a response to Amp and Pen treatments, the microbial community and structure within the citrus leaf, which is important factor in how Las affects HLB progression, was modified [12,13]. Furthermore, Amp and Pen is easily taken up by citrus [11,12]. Therefore, Amp and Pen have so far been shown to be the most effective antimicrobial compounds against Las. However, due to the public concerns on the emergence of antibiotic-resistant bacteria and the potential side effect on human beings, application of ampicillin and penicillin has not yet been approved to be used on crops by the Environmental Protection Agency (EPA) or other regulatory agencies. It may be a considerable, optional strategy to use Amp or Pen as an emergency use agent for control of HLB.

Sulfonamide antibiotics (sulfadimethoxine sodium, sulfamethoxazole, sulfathiazole sodium) are organic sulfur compounds containing the radical  $-SO_2NH_2$  (the amides of sulfonic acids). Its molecular structure is similar to p-aminobenzoic acid (PABA), a substrate of the enzyme dihydropteroate synthetase required for the synthesis of tetrahydrofolic acid in bacteria [14,15]. In graft-based assays, sulfonamide antibiotics were shown to be effective against Las

and appear and appear to have very little phytotoxicity to citrus [11]. Sulfonamide antibiotics have been reported to alter the root morphology and functionality in carrot, lettuce, alfalfa, and barely [16]. The root system of HLB-affected citrus are often poorly developed. Sulfonamide antibiotics, in addition to killing Las, may potentially aid the health and function of the diseased the root system.

Tetracycline was evaluated by direct injection into the trunks of HLB-affected citrus trees in South Africa, China, Reunion Island, and the Philippines [17-20]. These works demonstrated that tetracycline treatment significantly reduced symptoms in treated trees. However, this control practice was later discontinued because tetracycline is only bacteriostatic, not bactericidal, requiring treatment to be repeated each year. In addition, after several trunk injections, the phytotoxicity of the antibiotic became apparent in the injected citrus trees [21]. Although tetracycline is not commercially feasible for citrus production, this antibiotic can suppress Las bacterial titers. Modification of tetracycline may also reduce phytotoxicity.

Other antibiotics such as Rifamycins, Zhongshengmycin and Validamycin A also displayed effectively or partly effectively results against Las [11]. These antibiotics also can be selected as candidate compounds for control of HLB.

Due to the presence of pathogen "*Ca. L. asiaticus*" in citrus phloem, antibiotics often fail to kill the pathogen, since only a small portion of the effective compounds ever reach the target sites [22]. In the future, application of these effective antibiotics for control of HLB in citrus production should focus on enhancing efficient delivery methods of antibiotics.

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