Influence of Iron on Production of the Antibacterial Compound Tropodithietic Acid and Its Noninhibitory Analog in Phaeobacter inhibens - DTU Orbit (08/11/2017)

Influence of Iron on Production of the Antibacterial Compound Tropodithietic Acid and Its Noninhibitory Analog in *Phaeobacter inhibens*

Tropodithietic acid (TDA) is an antibacterial compound produced by some *Phaeobacter* and *Ruegeria* spp. of the *Roseobacter* clade. TDA production is studied in marine broth or agar since antibacterial activity in other media is not observed. The purpose of this study was to determine how TDA production is influenced by substrate components. High concentrations of ferric citrate, as present in marine broth, or other iron sources were required for production of antibacterially active TDA. However, when supernatants of noninhibitory, low-iron cultures of *Phaeobacter inhibens* were acidified, antibacterial activity was detected in a bioassay. The absence of TDA in nonacidified cultures and the presence of TDA in acidified cultures were verified by liquid chromatography-high-resolution mass spectrometry. A noninhibitory TDA analog (pre-TDA) was produced by P. inhibens, *Ruegeria mobilis* F1926, and *Phaeobacter* sp. strain 27-4 under low-iron concentrations and was instantaneously converted to TDA when pH was lowered. Production of TDA in the presence of Fe³⁺ coincides with formation of a dark brown substance, which could be precipitated by acid addition. From this brown pigment TDA could be liberated slowly with aqueous ammonia, and both direct-infusion mass spectrometry and elemental analysis indicated a [Fe^{III}(TDA)₂]_x complex. The pigment could also be produced by precipitation of pure TDA with FeCl₃. Our results raise questions about how biologically active TDA is produced in natural marine settings where iron is typically limited and whether the affinity of TDA to iron points to a physiological or ecological function of TDA other than as an antibacterial compound.

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