TITLE: IRON ACQUISITION AND SIDEROPHORE PRODUCTION IS INFLUENCED BY pH IN *Staphylococcus saprophyticus*

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ABSTRACT:

The genus *Staphylococcus* is composed by Gram-positive cocci divided in two distinct groups, according to the presence or absence of coagulase activity: *Staphylococcus* coagulase negative (SCN) and *Staphylococcus* coagulase positive (SCP). Several species of bacteria may form part of the human microbiota. Despite the symbiotic relationship, there are bacteria that may act as pathogens in specific situations. Among them, *Staphylococcus saprophyticus* is an important species of *S*CN that can cause urinary tract-genital infections (UTIs) in humans. UTIs are common causes of morbidity and can affect men and women in all age groups. In addition to proteins produced as a virulence factor in pathogens, there are also molecules acquired from the extracellular medium that are important for the establishment and success of the infection. One of these molecules is iron, that can be acquired by permeases or by siderophores synthesized according to the availability of iron. We performed proteomic analysis of *S. saprophyticus* in acid and alkaline pH (5.5 and 9.0) and we detected proteins related to iron metabolism regulated in both conditions. The acid pH led to a decreased level of proteins related to iron acquisition and storage, since the availability of soluble iron (Fe^{2+}) is higher in acidic conditions. In contrast the alkaline pH led to increased levels of proteins related to xenosiderophore acquisition and decreased levels of iron-dependent proteins since the presence of insoluble iron (Fe^{3+}) is optimized. It is important to point that human urine presents acidic pH (5-6) and when infection by *S. saprophyticus* is initiated the pH increases (8-9). Therefore, the *S. saprophyticus* adaptation to varying iron levels is crucial to the establishment of the infection in bladder. In order to evaluate the production of siderophores by *S. saprophyticus* we cultured bacterial cells in chemically defined medium SSD with and without iron and we detected siderophore production compatible with carboxylates after 48 hours of culture in SSD without iron. The siderophores produced by the bacteria are being characterized in order to confirm the classification. In addition, we performed *in silico* analysis and we detected four permeases that can act capturing iron molecules. We designed oligonucleotides to perform Real Time-PCR in order to detect if transcripts encoding these permeases are regulated by iron deprivation in *S. saprophyticus* cells cultured in SSD medium without iron.

Keywords: Proteomics, pH, siderophores, iron, urinary tract infection.

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