ANTIBIOTIC AND THEORETICAL PROFILES OF 4-ANILINE-1H-PIRAZOLO[3,4-*b*]PIRIDINES AND 4-ANILINE-TIENE[2,3-B]PIRIDINES DERIVATIVES

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The rapid emergence and spread of resistant bacteria involves different biochemical mechanisms from enzymes and targets mutation to the antibiotic chemical modification by new bacteria enzymes. Therefore, new agents need to be developed in response to the increased antimicrobial resistance. The present study reports the synthesis, biological and theoretical evaluation of new 4-aniline-1H-pyrazolo[3,4-*b*]pyridine-5-carboxylic acids derivatives against *Staphylococcus epidermidis*, an important clinical bacteria. Our data showed that most of the active compounds are the *meta*-substituents, which pointed this position as important to determine the biological activity while *para* position is aparently restrictive. The determinations of the minimal inhibitory concentrations (MIC) showed that **2**, **4**, **6** and **7** presented a greater activity than chloranfenicol and similar antibacterial activity than oxacillin, which are currently used as clinical antibiotics. The SAR studies involving the MEP of pyrazolo[3,4-b]pyridine derivatives suggested that the electron density region present in the phenyl ring reduces the activity profile of these system. Interestingly, derivatives **2**, **4**, **6** and **7** containing electronegative atoms as substituents (metoxi, chlorine, fluorine and bromine, respectively) showed the best results in all experiments. Importantly, our data pointed **2**, **4**, **6**, and **7** as potential lead compounds for the development of new antimicrobial drugs against *S. epidermidis*.