TITLE: DETERMINATION OF THE ANTIMICROBIAL ACTIVITY OF SYNTHETIC SUBSTANCES DERIVED FROM B-LAPACHONE.

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ABSTRACT:

The development of antimicrobial agents has dramatically reduced mortality and morbidity rates caused by microbial diseases. However, in the last decades, a change in this scenario due to the emergence and the dissemination of resistance to commercial drugs among the microorganisms is increasing. Based on this problem, it is necessary to search for new and more effective alternatives in the treatment of infections caused by these microbial agents. β - lapachone is an ortho-naphthoquinone that can be extracted from several plant species of the Bignoniaceae family, widely distributed in Brazil, highlighting *tabebuias* and trees popularly known as ipês. Although β-lapachone is the primary antimicrobial substance isolated from these plant species, its high toxicity compromises its establishment as a therapeutic alternative to treat microbial diseases. This project aims to develop synthetic antimicrobial substances with selective toxicity to pathogenic microorganisms derived from β-lapachone. Imidazoles are essential examples of derived β – lapachone substances with several antimicrobial activities. The methodology for the synthesis of twenty-six β-lapachone based substances was the Radziszewski reaction. This part integrates a previous work, in which among the twenty-six synthesized substances, nine were investigated based on their antimicrobial potential. In this continued study, antimicrobial activity was evaluated using the minimum inhibitory concentration (MIC) assay against Candida albicans, Cryptococcus neoformans, Escherichia coli, and Staphylococcus aureus. As results, β-lapachone derivatives showed good antimicrobial activity with MICs varying from 3,9 µg/mL to 15,6 µg/mL for Cryptococcus neoformans, Staphylococcus aureus, and Candida albicans. Though, no activity against Escherichia coli was detected to 250 µg/mL. The hemolytic activity of the synthesized substances was determined in vitro using human erythrocytes. As results, β-lapachone derivatives (100 µg/mL)showed weak hemolytic activity varying from <1% to 6,5% of hemolysis. The prospects for the present work are that the synthetic substances derived from β-lapachone will be promising for applications in new antimicrobial therapeutic methods. Additional studies are being conducted to determine their mechanisms of action.

Keywords:microorganisms, antimicrobial, β-lapachone.

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