

TITLE: ANTIBACTERIAL COMBINATION OF OREGANO ESSENTIAL OIL AND BIOLOGICAL SILVER NANOPARTICLES AGAINST STRAINS OF CLINICAL IMPORTANCE

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ABSTRACT

Infections due to multidrug-resistant bacteria have become a clinical and public health problem, making therapeutic decisions more challenging. Therefore, it is crucial the research and development of new drugs with potential to prevent the selection of multidrug-resistant bacteria and kills such microorganisms. Antimicrobial combination, compounds derived from plants and nanodrugs have been proposed as alternative antimicrobials. This study showed the antibacterial effect of biological silver nanoparticles combined with oregano essential oil (OEO) against Gram positive and negative bacteria, including multidrug-resistant strains. Biological silver nanoparticles (AgNP-bio) were obtained after reduction of ionic silver by *Fusarium oxysporum*. Diameter and zeta potential were determined using Zetasizer NanoZS (Malvern). OEO was obtained from commercial source. Antimicrobial assays were performed against four reference strains (ATCC) and three multidrug-resistant strains as follows: methicillin-sensitive *Staphylococcus aureus* ATCC 25923, *Streptococcus mutans* ATCC 25175, *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 700603, methicillin-resistant *S. aureus* (MRSA N315), extended-spectrum β -lactamase-producing *E. coli* and carbapenemase-producing *E. coli*. Minimum inhibitory concentration (MIC) of alone compounds was determined by broth microdilution method according CLSI guidelines. Antimicrobial combination assay of OEO and AgNP-bio was determined by broth dilution in double-antimicrobial gradient and fractional inhibitory concentrations index was used to describe drug interaction. The OEO MIC value was 0.596 mg/mL (0.06%, v/v) to all strain and the mean MIC for AgNP-bio was 160.71 μ M ranging from 125 to 250 μ M. The combination of OEO and AgNP-bio resulted in synergistic or additive antibacterial effect, significantly reducing the MIC values of both compounds when compared to them used alone. Mean MIC value reduced by 85.24% for oregano oil, ranging from 0.075 to 0.149 mg/mL (0.008 to 0.01%, v/v), and by 61.09% for AgNP-bio, ranging from 31.25 to 125 μ M). This drug combination showed antibacterial activity against strains involved in infections with few or no treatment option, also may minimizing selection of resistant strains because antimicrobial combination may disrupt various biological bacterial functions simultaneously. Therefore, OEO combined to AgNP-bio has potential to be applied in industry and clinical and hospital settings.

Keyword: *Origanum vulgare*, synergism, multidrug-resistant bacteria.

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