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Effect of *Momordica charantia* L. in the resistance to aminoglycosides in methicilin-resistant *Staphylococcus aureus*

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Abstract

In this study the ethanol extract (EEMC) of *Momordica charantia* L. (Cucurbitaceae) was tested for its modifying antibiotic activity against a MRSA strain. The growth of an MRSA (SA358) in the absence and presence of aminoglycosides was evaluated. A potentiating effect between this extract and all aminoglycosides was demonstrated. Similarly, the same effect was shown by chlorpromazine on kanamycin, gentamicin and neomycin, indicating the involvement of an efflux system in the resistance to these aminoglycosides. Extracts from *M. charantia* could be used as a source of plant-derived natural products with resistance-modifying activity. This is the first report about the modifying antibiotic activity of *M. charantia,* constituting a new weapon against multi-resistant bacteria such as MRSA.
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Keywords: Aminoglycosides; Chlorpromazine; Ethanol extract; Modifying antibiotic activity; *Momordica charantia*; MRSA

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1. Introduction

Staphylococcus genus is widely spread in nature as indigenous microbiota of skin and mucosa of animal and birds. Some *Staphylococcus* species are recognized as etiological agents of animal and human opportunistic infections [1]. *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus saprophyticus* and *Staphylococcus haemolyticus* are the most often identified in community and nosocomial human infection. *S. aureus* is a common etiological agent of festering infections of many different tissues and/or organs (e.g. furuncle, carbuncle, abscess, myocarditis, endocarditis, pneumonia, meningitis, bacterial arthritis) [2,3]. Capsule, peptidoglican, teicoic acids, synthesis of enzymes and extracelullar toxins are some virulence attributes present in/on *S. aureus* cell [1].

With a growing incidence of infections resistant to antibiotics, an arsenal of either new agents of the supplementation of current antibiotics is needed. Natural products from plants could be interesting alternatives [4,5].

Many plant extracts or products have been evaluated not only for direct antimicrobial activity, but also as resistance-modifying agents [5–8]. Several chemical compounds, synthetic or from natural sources, such as the phenothiazines and natural products, show an indirect effect against many species of bacteria, by enhancing the activity of a specific antibiotic, reversing the natural resistance of specific bacteria to given antibiotics, promoting the elimination of plasmids from bacteria such as *Escherichia coli*, and inhibiting transport functions of the plasma membrane in regard to given antibiotics [9]. The inhibition of plasma membrane-based efflux pumps has also been observed [9,10]. The enhancement of antibiotic activity or the reversal of antibiotic resistance by natural or synthetic non-conventional antibiotics affords the classification of these compounds as modifiers of antibiotic activity.

Momordica charantia L. (Cucurbitaceae) is a climber known as bitter melon, which grows worldwide. Several flavonoids with pharmacological and biological activities have been identified in *M. charantia* [11–14]. Additionally, the triterpenoid cucurbitan and the protein MAP30 have shown anti-HIV and insecticidal activities, respectively [15,16].

Aminoglycosides are potent bactericidal antibiotics targeting the bacterial ribosome, and the increase in cases of bacterial resistance to aminoglycosides is widely recognized as a serious health threat [9]. The most important mechanisms of resistance to aminoglycosides are the active efflux and enzymatic inactivation [10].

In this work, we tested an ethanol extract of *M. charantia* (EEMC) as a resistance-modifying agent in an aminoglycoside-resistant strain of *S. aureus.*

2. Materials and methods

The experiments were performed with the clinical *S. aureus* isolate SA358 which is resistant to several aminoglycosides [17]. The strain was maintained on heart infusion agar slants (HIA, Difco), and prior to assays, the cells were grown overnight at 37 °C in brain heart infusion (BHI, Difco). As a positive controls, was used the strain *S. aureus* ATCC25923.

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