

The Defence of Gram-negative Bacteria against the Natural Products Isobavachalcone and Diospyrone

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Introduction

Two naturally occurring substances, isobavachalcone and diospyrone, were tested for their efficacy against known strains and MDR Gram-negative bacterial isolates. The findings showed that the two substances had inherent antibacterial activity against a number of Gram-negative bacteria, and that this activity was markedly enhanced in the presence of an efflux pump inhibitor. Additionally, isobavachalcone and diospyrone considerably enhanced its anti-a variety of strains exhibiting deletions of the key efflux pump components (AcrAB, TolC). According to the overall findings, diospyrone and isobavachalcone may be candidates for the creation of novel medications to combat MDR strains, and their usage in combination with efflux pump inhibitors increases their effectiveness [1].

Description

The prevalence of therapeutic failure rises as a result of the ongoing evolution of multidrug-resistant (MDR) bacteria, which significantly limits the effectiveness of our antibiotic arsenal. The widespread use of antibiotics has led to a rise in drug resistance, and finding strategies to effectively tackle resistant organisms is a critical concern for the medical community. Improved early infection control, the use of suitable medicines, the implementation of hospital policies to stop the spread of MDR strains, and the creation of novel antibiotics are all examples of this. Overexpression of efflux pumps may be related to bacteria's resistance to chemically unrelated antimicrobial drugs (or MDR). Numerous of these efflux pumps are members of the RND family of tripartite efflux pumps found in Gram-negative bacteria. Pumps from the AcrAB-TolC family are among the efflux pumps found in clinical enterobacterial isolates and are thought to have a significant role in the expression of the MDR phenotype. Clinical isolates of *Pseudomonas aeruginosa*, a significant nosocomial infection that is extremely resistant to the widely used antibiotics, have been found to have a number of RND efflux pumps. Different efflux pump inhibitors that restore the intracellular concentration and the antibiotics' actions can prevent this efflux pump mechanism [2].

The need for new antibacterial agents derived from medicinal plants has been sparked by the dearth of original synthetic antibiotics. Several medicinal herbs have been used to isolate isobavachalcone. According to some preliminary research, the chemical isobavachalcone exhibits activity against vulnerable bacteria and has been found to have extremely intriguing effects on *Candida albicans* and *Cryptococcus neoformans*. The effectiveness of this substance against resistant bacteria and its mode of action, however, were not made clear. *Diospyros canaliculata* is the only known source of

diospyrone at the moment. Diospyrone's effectiveness against *Mycobacterium tuberculosis* and *Neisseria gonorrhoeae* has recently been described, however its effectiveness against resistant bacteria and its target have not [3].

Several known strains and an efflux pump inhibitor were used to examine the range of these compounds' actions with regard to the contribution of efflux pumps to their activity. The chemical stock bank at the Laboratory of Organic Chemistry, University of Yaoundé I, Yaoundé, Cameroon, was used to obtain Isobavachalcone and diospyrone. Isobavachalcone from *Dorstenia barteri* and diospyrone from *Diospyros canaliculata* were recently isolated and identified. Selected or reference antibiotics included chloramphenicol and norfloxacin, tetracycline hydrochloride, imipenem-cilastatin (500/500 mg; Merck, Paris, France), and cefepime (Bristol-Myers, Reuil-Malmaison, France). Additionally, 1,3,5-triphenyltetrazolium chloride (TTC) (Sigma-Aldrich), p-iodonitrotetrazolium chloride (INT), and phenylalanine arginine β -naphthylamide (PABN) were employed. *Escherichia coli* MDR and reference strains, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* were among the microbiological species used. Prior to any assay, all strains were precultured for an entire night on Mueller-Hinton agar. Susceptibility assays used Mueller-Hinton broth (MHB) as the liquid culture medium [4].

Effects of isobavachalcone, diospyrone, and efflux pumps on Gram-negative bacteria's susceptibility. The different strains and MDR isolates were evaluated for their susceptibilities to reference antibiotics (norfloxacin, chloramphenicol), isobavachalcone, and diospyrone both alone and afterwards in the presence of PABN, a well-known efflux pump inhibitor. Diospyrone (4 g/ml) and isobavachalcone (8 g/ml) had the lowest MIC values when tested on *E. coli* AG100A. *aerogenes* EA298 in that order. The efflux pump inhibitor PABN dramatically improved the antibacterial activity of the two drugs, resulting in all MICs being obtained falling below 10 g/ml for the *E. coli*, *K. E. pneumoniae* and strains of *Cloacae* [5].

Conclusion

Additionally, this increased activity was seen to work against distinct *E. coli*, *E. K. aerogenes*, *E. coli*, *P. aeruginosa*, and *K. pneumoniae* *cloacae*. The inclusion of an additional resistance mechanism, such as the target mutation previously revealed in the clinical isolates studied, greatly modifies the level of restoration of susceptibility when norfloxacin is combined with chloramphenicol and used as reference antibiotics.

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Conflict of Interest

The author shows no conflict of interest towards this manuscript.

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