

**DUAL EFFECT OF SYNTHETIC AMINOGLYCOSIDES:  
ANTIBACTERIAL ACTIVITY AGAINST *BACILLUS  
ANTHRACIS* AND INHIBITION OF ANTHRAX LETHAL  
FACTOR**

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Biological terrorism or warfare can be used with impunity under the camouflage of natural outbreaks of disease to decimate human populations. Indeed, some such events recently have created an urgent need for efficient therapeutic strategies to treat anthrax, caused by the toxigenic bacterium *Bacillus anthracis*. The anthrax lethal factor (LF), a Zn-dependent endopeptidase, has a major role in the development and virulence of anthrax. Therefore, an intensive search for specific inhibitors of LF has been performed during the last years. While a number of the tested compounds demonstrated some level of inhibitory activity, neomycin B, a commonly utilized aminoglycoside antibiotic, was found to be the most potent inhibitor of LF.

In attempts to improve the inhibitory effect of neomycin B derivatives, we synthesized a series of new derivatives of neomycin B, which represent a new class of branched aminoglycosides that show dual effect by inhibiting LF at seemingly physiological conditions and simultaneously are active against *B. anthracis*. All new derivatives serve competitive inhibitors of LF with improved activity of up to almost two orders of magnitude relative to that of neomycin B and in parallel possess significant antibacterial activity against *B. anthracis*. As such, this study provides a new direction for the development of novel antibiotics that target at once both the toxigenic bacterium and its released lethal toxin, and may offer promise for the effective treatment of anthrax infection.<sup>1</sup> Most recent results of the issue will be discussed.

[1] Micha Fridman, Valery Belakhov, Lac V. Lee, Fu-Sen Liang, Chi-Huey Wong and Timor Baasov. *Angew. Chem. Int. Ed.* **2005**, *44*, 447-452. (*Selected by the Editors of the Journal as a HOT PAPER*).