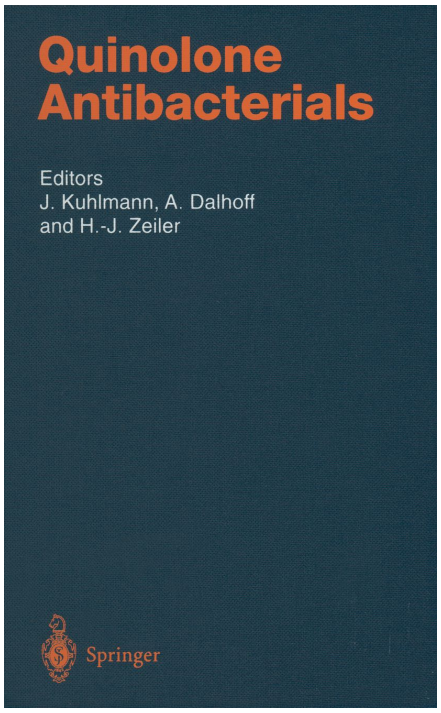

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Quinolone Antibacterials

Series: Handbook of Experimental Pharmacology

It has been over 30 years since the first clinically important member of the quinolone class, nalidixic acid, was introduced into medical practice. The modification produced in the quinolone nucleus by introducing a fluorine at the 6-position led to the discovery of the newer fluoroquinolones with enhanced antibacterial activities as compared to nalidixic acid. By now a great deal of preclinical and clinical experience has been obtained with these agents. The intense interest in this class of antibacterial agents by chemists, micro- biologists, toxicologists, pharmacologists, clinical pharmacologists, and clini- cians in various disciplines encouraged us to summarize the information on the history, chemistry, mode of action and in vitro properties, kinetics and efficacy in animals, mechanisms of resistance, toxicity, clinical pharmacology, clinical experience, and future prospects in one volume of the Handbook of Experimental Pharmacology. As this series deals predominantly with "experimental" characteristics of drugs, our volume is dedicated specifically to quinolones and emphasizes principally their preclinical and clinical phar- macological characteristics, despite the existence of several summaries on quinolones. The chemistry of the quinolones is described in detail. The chapter on the mode of action of quinolones reports the conclusive evidence that gyrase is the intracellular target of the quinolones; however, another enzyme, topoisomerase IV, may also be a target for quinolones, and the exact mechanisms by which quinolones act bactericidally are far from being understood.