MICROBIAL TRANSFORMATIONS OF QUINOLONES AND RELATED DRUGS pdf

1: Full text of "Microbial Transformation of Nitrogen Containing Heterocycles"

The quinolones are an important group of synthetic antimicrobial drugs used for treating bacterial diseases of humans and animals. Microorganisms transform antimicrobial quinolones (including fluoroquinolones) and the pharmacologically related naphthyridones, pyranoacridones, and cinnolones to a.

Immediate access to this article To see the full article, log in or purchase access. She completed an American Society of Health System Pharmacists general residency and a fellowship in infectious diseases and microbiology at Northwestern Memorial Hospital, Chicago Address correspondence to Catherine M. Reprints are not available from the authors. The authors indicate that they do not have any conflicts of interest. Mechanisms of quinolone action and bacterial killing. American Society for Microbiology, Mode of action of fluoroquinolones. Pharmacokinetics and pharmacodynamics of fluoroquinolones. Serumbactericidal activity of rifampin in combination with other antimicrobial agents againstStaphylococcus aureus. Alghasham AA, Nahata M. Clinical use of the fluoroquinolones. Med Clin North Am. New uses for new and old quinolones and the challenge of resistance. New generations of quinolones: Med Lett Drugs Ther. Activity of newer fluoroquinolones in vitro against gram-positive bacteria. Quinolone activity against anaerobes. Treatment of genitourinary tract infections with fluoroquinolones: N Engl J Med. Use of ciprofloxacin versus use of aminoglycosides for therapy of complicated urinary tract infection: Norfloxacin versus co-trimoxazole in the treatment of recurring urinary tract infections in men. Scand J Infect Dis 28 Suppl. Practice guidelines for the management of community-acquired pneumonia in adults. Infectious Disease Society of America. Management of community-acquired pneumonia in the era of pneumococcal resistance: In vitro activity of newer fluoroquinolones for respiratory tract infections and emerging patterns of antimicrobial resistance: Microbiological and pharmacodynamic considerations in the treatment of infection due to antimicrobial-resistantStreptococcus pneumoniae. Centers for Disease Control and Prevention. Drug facts and comparisons. Facts and Comparisons, A review of its antibacterial activity, pharmacokinetic properties, clinical efficacy and tolerability in lower respiratory tract infections.

MICROBIAL TRANSFORMATIONS OF QUINOLONES AND RELATED DRUGS pdf

2: Quinolones: A Comprehensive Review - - American Family Physician

The quinolones are an important group of synthetic antimicrobial drugs used for treating bacterial diseases of humans and animals. Microorganisms transform antimicrobial quinolones (including.

Advanced Search Abstract Recently, understanding of how molecular modifications of the core quinolone structure affect s antimicrobial agent activity has progressed rapidly. Three positions 2, 3, and 4 cannot be changed without a significant loss of biological activity. Furthermore, it appears that a cyclopropyl group is optimal at position 1. Substituents at positions 5 and 8 affect planar configuration, and either a methyl or methoxy appear optimal at these sites. Hydrogen and amino groups have been investigated as useful substituents at position 6, replacing the fluorine of the fluoroquinolones. Interestingly, in vitro activity enhancement observed with alterations at positions 5 and 6 is not always accompanied by improved in vivo action. For all these modifications, the substituents at positions 7 and 8 are critical for potent antimicrobial activity. Optimizing overall molecular configuration enhances the number of intracellular targets for antimicrobial action R-8 and impedes the efficiency of efflux proteins R-7 that diminish intracellular penetration. Despite predictions that the incidence of infectious diseases would diminish, the rates of infection with new and reemerging pathogens is increasing, threatening the overall human health [1]. Approximately half of this increase was due to the HIV epidemic, and the other half was due to infection with emerging and reemerging pathogens [2]. Ongoing discoveries of new infectious diseases and an explosion of drug resistance in organisms for which the associated illness was once thought to be cured have dramatically altered the practice of medicine within the hospital, and is beginning to effect the management of infections in the ambulatory care setting. The quinolone class of antimicrobial agents has been developed, and grown, within this time frame [3]. Despite ongoing development of new agents in this important class, resistance to newly released agents continues to be observed [4]. Recent data suggests emerging resistance is specifically linked to use of some of the older compounds [5 , 5a]. We have learned much about how structural modifications affect both activity and toxicity. A recent report assessed the toxicity profiles of newer fluoroquinolone agents [6], and this topic will not be addressed here. An excellent summary of structure-activity relationships by Tillotson [7] was published in , but considerable new information has been learned since that time. Much can be inferred about the overall effect s of various chemical modifications by better understanding how microbes become resistant to the action of fluoroquinolones. A comprehensive discussion of this topic was recently published [8]. The focus of my current review is the most recent data on how various structural modifications affect the activity of quinolones, interpreting structural effects in the light of work on emerging microbial resistance, and highlighting ongoing drug development that points to a continued useful future for this important class of antimicrobial agents. Our understanding of cellular function at the molecular level progressed impressively as we ended the 20th century. One interesting observation has been that bacteria appear uniquely fitted for survival in that they seem designed to multiply ceaselessly as long as required nutritional support is available [9]. Thus, design and synthesis of agents that rapidly exert their antimicrobial effect, and have a low propensity for permitting resistant strains to emerge, appear intuitively necessary directions. The gyrase is a tetramer composed of 2 subunits, one encoded by the gyrA gene and one encoded by the gyrB gene. Topoisomerase IV is believed to partition intertwined, replicated chromosomes before cell separation division can take place. The 2 subunits of this tetrameric enzyme are encoded by the parC and parE genes referred to as grlA and grlB in Staphylococcus aureus. These functional enzymes cleave double-stranded DNA the G or gate-segment , pass another strand of duplex DNA through the break the T or transported-segment , and then anneal the broken G strand, using ATP as an energy source [8 , 10]. Both the G segment and the T segment are then released from the enzyme. Fluoroquinolones are thought to stabilize i. The elegant crystal structure of the partial DNA gyrase protein has been published [11], and one can see from this representation the close association between various DNA mutations associated with resistance to drug

action and the active tyrosine sites of the enzyme. Presumably, topoisomerase IV functions similarly. Because the DNA gyrase and topoisomerase IV enzymes interact with DNA in a similar manner, quinolone action on either of them can be lethal to the bacterial cell. Further evidence for this concept was recently reported by Fournier and colleagues [11a]. Early findings of clinically significant bacterial resistance to the quinolones typically implicated mutations in highly conserved amino acid residues of the so-called quinolone resistance determining region QRDR , either in the GyrA subunit of DNA gyrase or the ParC subunit of topoisomerase IV. It is of interest that the initial targets of fluoroquinolone action seem reversed in gram-negative and gram-positive species. For example, in gram-positive organisms like S. Mutations at the equivalent positions of the GyrA subunit of DNA gyrase are secondary events and lead to very high levels of resistance, presumably by making both topoisomerase IV and gyrase highly resistant to fluoroquinolone binding. Whereas most quinolone antimicrobials appear to have a preferential affinity for topoisomerase IV in gram-positive bacteria, sparfloxacin is reported to first interact with target GyrA, because mutations in strains selected on exposure to this fluoroquinolone accumulate primarily in gyrA [18], suggesting specific structural modification has a profound impact on drug-target interaction. Other pathways for development of resistance to quinolone antimicrobial agents also exist. Notably, there are no known enzymes that degrade the fluoroquinolone antimicrobial agents. Thus, the routes microbes have toward developing a resistance phenotype involve target alteration e. Interestingly, they appear particularly active against compounds that cannot be inactivated or degraded, as is the case for the fluoroquinolones. In addition, commonly used compounds such as salicylates are able to increase resistance to fluoroquinolones [23], likely through activation of an efflux system s. All this evidence suggests the importance of active efflux as mechanism that initially allows bacteria to survive [24 , 25] and subsequently permits the development of adaptive QRDR mutations at key drug target sites. Energy-dependent efflux has been reported in both S. Structural differences among fluoroquinolones, notably overall molecular hydrophobicity and bulkiness of the C-7 substituent, are now thought to influence the efficiency of efflux [33 , 35 , 36]. Similar efflux systems are also known to be important for expression of resistance in gram-negative bacteria [37]. Thus, Nikkado has recently hypothesized that design of agents less susceptible to efflux may be a good strategy for combating microbial resistance [36]. Modifications at Specific Positions on the Quinolone Molecule Figure 1 shows the general structure for the quinolone molecule and uses the accepted numbering scheme. Figure 1 View large Download slide Structure of the quinolone molecule, using the accepted numbering scheme for positions on the molecule. An R indicates possible sites for structural modification. Molecules at positions marked by a dashed box can also be changed; however, the most commonly used structure is shown here. This position is part of the enzyme-DNA binding complex, and has a hydrophobic interaction with the major grove of DNA [38]. A cyclopropyl substituent is now considered the most potent modification here, followed by addition of a 2,4-difluorophenyl [39]. Most other substituents, including one with only the wrong stearic position R -ofloxacin can presumably lower the number of molecules capable of binding to the enzyme-DNA pocket, and therefore reduce potency [40]. Interestingly, ofloxacin has a tricyclic ring structure with a CH3 attached to the asymmetric C-3 position on the oxazine ring, thus connecting positions 1 and 8 with a fused ring. Although this has been a useful alternative to the cyclopropyl substituent, the S- isomer exhibits twice the order of magnitude of activity as the R- isomer, which seems to determined by the number of molecules that can be assembled, or stacked, in the enzyme-DNA complex binding pocket [40]. Even the potency of the purified S- isomer fused ring is less than that of the cyclopropyl substituent, suggesting the difficulty of improving upon this latter modification. This location is very close to the site for DNA gyrase or topoisomerase IV binding so it is believed that any added bulk inhibits access and results in a lower level of microbiological activity [7 , 39]. Only a sulfur, incorporated into a small ring, has been able to replace hydrogen at the R-2 position [39]. To accomplish this, researchers reconfigured positions 3 and 4. Positions 3 and 4. These two positions on the quinolone nucleus are considered critical for binding to cleaved or perturbed DNA, and no useful substitutions have yet been reported. Therefore, the 3-carboxylate and 4-carbonyl groups

are considered essential for antimicrobial activity [7]. This is a new addition to the quinolone class, in which nitrogen replaces the carbon between ring carbons C-4 and C-5 [41]. Making this alteration renumbers the other positions so that 5- becomes 6-, 6- becomes 7-, 7- becomes 8-, and 8- becomes position 9. This substitution enhances the in vitro and in vivo mouse protection activity against gram-positive cocci, including methicillin-resistant S. The remainder of the optimal substitutions for the oxoquinolizine derivatives are similar to those for the C-6 fluorinated agents, namely a cyclopropyl at R-1, a methyl or methoxy at R-8 R-9 oxoquinolizine , and a 5- or 6-membered ring at R-7 R-8 oxoquinolizine. For the compounds studied in this report, a 5-membered ring at this position appeared slightly more active. Interestingly, of these 2 additions to the ring substituent, the amino group gave the best in vivo activity. Bicyclic substituents at this position R-7 also appear as important approaches to enhance activity against either gram-positive or gram-negative pathogens [41]. Substituents at this position of the basic quinolone nucleus appear to have the capacity to alter overall stearic configuration planar structure of the molecule, which is how changes here are thought to affect activity [38]. Modestly sized additions, such as an amino, hydroxyl, or methyl group can markedly increase in vitro activity against gram-positive bacteria [39 , 42], as well as enhance potency against Toxoplasma gondii [43]. Yoshida and coworkers [42] found that the methyl group enhances action against gram-positive but not against gram-negative bacteria. Halide and methoxy substituents tend to diminish activity, indicating the precise nature of the required structural modification [42]. However, for currently unknown reasons, the in vitro bacterial affects of changes made at this position are not always mirrored by an enhancement to in vivo activity when tested in an animal model [39]. The addition of a fluorine molecule here markedly improved antimicrobial activity compared to the original quinolone agents, and gave rise to the now widely used and clinically successful fluoroquinolone compounds. New 6-H-quinolones are currently under development that appear very promising [44]. Whatever structure is placed at this site, the substituents at positions 1, 7, and 8 continue to be key determinants of overall biological activity in the compounds under active development. Another group of agents with novel substituents here are the 6-amino, 8-methyl quinolones, which have expanded activity against gram-positive cocci [45]. A tetrahydroisoquinoline substituent at C-7 seems to be a most useful addition for the 6-amino agents, increasing in vitro activity anywhere from 4-fold to over fold, compared with ciprofloxacin [45 , 46]. For the 6-amino compounds as well, the overall potency is highly dependent on substituents at positions C-7 and C Similar to the fluoroquinolones, a free methyl and probably a methoxy , at position 8 enhances gram-positive activity, at least in vitro. Also, the cyclopropyl substituent at position 1 is the most advantageous for both the 6-H and 6-NH2 based drugs. As for position 5, the in vitro affects seen with modifications at position 1 are not always mirrored by changes to in vivo activity when tested in an animal model. Interestingly, the dissociation between in vitro activity and in vivo potency does not appear to be solely related to oral bioavailability, because a similar finding of lower than expected biological activity was observed for at least one of these compounds regardless of whether it was administered orally or subcutaneously to mice [45]. This position is considered to be one that directly interacts with DNA gyrase [41], or topoisomerase IV. The optimal substituents at this position have been found to be groups that contain, at a minimum, a 5- or 6-membered nitrogen heterocycle. The most common of these are aminopyrrolidines and piperazines. Placement of a aminopyrrolidine improves gram-positive activity, whereas a piperazine generally enhances potency against gram-negative bacteria. Alkylation -CH3 of the 5-membered or 6-membered heterocycle pyrrolidines and piperazines, respectively also enhances activity against gram-positive bacteria [21 , 39]. Adding a methyl at C-2 or an amino at position 6 of an azabicyclohexane ring substituent here increases activity against T. New 2-pyridone additions to the 7-pyrrolidinyl ring have improved activity against staphylococci and anaerobes, but diminished effectiveness against important gram-negative bacilli, such as P. Specific placement of amino or methyl groups on the position 7 substituent heterocycles has similar resultant effect on the in vitro activity of 6-Hâ€”quinolones [44]. A recent interesting observation is that increased bulkiness here R-7 appears to confer protection from the efflux exporter proteins of bacteria, and diminishes the likelihood of bacterial

resistance in wild-type bacterial strains [48 , 49 , 49a]. Bulk here also increases anti-anaerobic activity. Moxifloxacin and trovafloxacin are the currently available agents with the greatest bulk at this position, and they appear least affected by reserpine-inhibited exporter proteins [48 , 49 , 49a]. This position is considered to affect overall molecular stearic configuration, similar to position 5 [38]. Therefore, changes made here affect target affinity, probably by altering drug access to the enzyme or DNA binding sites.

MICROBIAL TRANSFORMATIONS OF QUINOLONES AND RELATED DRUGS pdf

3: Biotransformation - Wikipedia

Microbial transformations of antimicrobial quinolones and related drugs Microbial transformations of antimicrobial quinolones and related drugs Parshikov, Igor; Sutherland, John The quinolones are an important group of synthetic antimicrobial drugs used for treating bacterial diseases of humans and animals.

Boxed warnings[edit] In , the U. FDA stated that serious side effects generally outweighed the benefits for people with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections when there are other treatment options. Fluoroquinoline treatment is associated with risk that is similar to [21] or less than [22] [23] that associated with broad spectrum cephalosporins. Fluoroquinoline administration may be associated with the acquisition and outgrowth of a particularly virulent Clostridium strain. Postmarketing surveillance has revealed a variety of relatively rare but serious adverse effects that are associated with all members of the fluoroquinolone antibacterial class. Among these, tendon problems and exacerbation of the symptoms of the neurological disorder myasthenia gravis are the subject of "black box" warnings in the United States. Centers for Disease Control and Prevention study found peopletreated with fluoroquinolones experienced adverse events severe enough to lead to an emergency department visit more frequently than those treated with cephalosporins or macrolides , but less frequently than those treated with penicillins , clindamycin , sulfonamides , or vancomycin. For certain severe infections where other antibiotics are not an option, their use can be justified. The addition of the C6 fluorine atom has since been demonstrated not to be required for the antibacterial activity of this class circa Antibiotic misuse and Antibiotic resistance Because the use of broad-spectrum antibiotics encourages the spread of multidrug-resistant strains and the development of Clostridium difficile infections, treatment guidelines often recommend minimizing the use of fluoroquinolones and other broad-spectrum antibiotics in less severe infections and in those in which risk factors for multidrug resistance are not present. It has been recommended that fluoroquinolones not be used as a first-line agent for community-acquired pneumonia, [50] instead recommending macrolide or doxycycline as first-line agents. The Drug-Resistant Streptococcus pneumoniae Working Group recommends fluoroquinolones be used for the ambulatory treatment of community-acquired pneumonia only after other antibiotic classes have been tried and failed, or in cases with demonstrated drug-resistant Streptococcus pneumoniae. Numerous pathogens , including Escherichia coli , commonly exhibit resistance. FDA, such as acute bronchitis , otitis media , and acute upper respiratory tract infection, according to a study supported in part by the Agency for Healthcare Research and Quality. Mechanism of action[edit] Structure of bacterial DNA gyrase complexed with DNA and two ciprofloxacin molecules green Quinolones exert their antibacterial effect by preventing bacterial DNA from unwinding and duplicating. Most of them are named with the -oxacin suffix. Quinolones and fluoroquinolones are chemotherapeutic bactericidal drugs, eradicating bacteria by interfering with DNA replication. Topoisomerase II is also a target for a variety of quinolone-based drugs. High activity against the eukaryotic type II enzyme is exhibited by drugs containing aromatic substituents at their C-7 positions. This modification, coupled with the constant action of the topoisomerase II in the bacterial cell, leads to DNA fragmentation via the nucleasic activity of the intact enzyme domains. Third and fourth generation fluoroquinolones are more selective for the topoisomerase IV ligase domain, and thus have enhanced gram-positive coverage. For many gram-negative bacteria, DNA gyrase is the target, whereas topoisomerase IV is the target for many gram-positive bacteria. However, there is debate concerning whether the quinolones still have such an adverse effect on the DNA of healthy cells. Some compounds in this class have been shown to inhibit the synthesis of mitochondrial DNA. The addition of the fluorine atom at C-6 distinguishes the successive-generation fluoroquinolones from the first-generation quinolones, although examples are known that omit the atom while retaining antibacterial activity.

MICROBIAL TRANSFORMATIONS OF QUINOLONES AND RELATED DRUGS pdf

4: Fluoroquinolone antibiotics (MPKB)

MINI-REVIEW Microbial transformations of antimicrobial quinolones and related drugs Igor A. Parshikov â€¢ John B. Sutherland Received: 12 July /Accepted: 26 August

Drug metabolism The metabolism of a drug or toxin in a body is an example of a biotransformation. The body typically deals with a foreign compound by making it more water-soluble, to increase the rate of its excretion through the urine. There are many different processes that can occur; the pathways of drug metabolism can be divided into: In these types of reactions, a polar group is either introduced or unmasked, so the drug molecule becomes more water-soluble and can be excreted. Reactions are non-synthetic in nature and in general produce a more water-soluble and less active metabolites. The majority of metabolites are generated by a common hydroxylating enzyme system known as Cytochrome P Phase II reaction[edit] These reactions involve covalent attachment of small hydrophilic endogenous molecule such as glucuronic acid , sulfate , or glycine to form water-soluble compounds, that are more hydrophilic. This is also known as a conjugation reaction. The final compounds have a larger molecular weight. Microbial biotransformation[edit] Biotransformation of various pollutants is a sustainable way to clean up contaminated environments. Major methodological breakthroughs in recent years have enabled detailed genomic, metagenomic, proteomic, bioinformatic and other high-throughput analyses of environmentally relevant microorganisms providing unprecedented insights into biotransformation and biodegradative pathways and the ability of organisms to adapt to changing environmental conditions. Biological processes play a major role in the removal of contaminants and pollutants from the environment. Some microorganisms possess an astonishing catabolic versatility to degrade or transform such compounds. New methodological breakthroughs in sequencing , genomics , proteomics , bioinformatics and imaging are producing vast amounts of information. In the field of Environmental Microbiology , genome -based global studies open a new era providing unprecedented in silico views of metabolic and regulatory networks, as well as clues to the evolution of biochemical pathways relevant to biotransformation and to the molecular adaptation strategies to changing environmental conditions. Functional genomic and metagenomic approaches are increasing our understanding of the relative importance of different pathways and regulatory networks to carbon flux in particular environments and for particular compounds and they are accelerating the development of bioremediation technologies and biotransformation processes. Oil biodegradation[edit] Petroleum oil is toxic for most life forms and episodic and chronic pollution of the environment by oil causes major ecological perturbations. Marine environments are especially vulnerable, since oil spills of coastal regions and the open sea are poorly containable and mitigation is difficult. In addition to pollution through human activities, millions of tons of petroleum enter the marine environment every year from natural seepages. Despite its toxicity, a considerable fraction of petroleum oil entering marine systems is eliminated by the hydrocarbon-degrading activities of microbial communities, in particular by a remarkable recently discovered group of specialists, the so-called hydrocarbonoclastic bacteria HCB. Alcanivorax borkumensis , a paradigm of HCB and probably the most important global oil degrader, was the first to be subjected to a functional genomic analysis. This analysis has yielded important new insights into its capacity for i n-alkane degradation including metabolism, biosurfactant production and biofilm formation, ii scavenging of nutrients and cofactors in the oligotrophic marine environment, as well as iii coping with various habitat-specific stresses. The understanding thereby gained constitutes a significant advance in efforts towards the design of new knowledge-based strategies for the mitigation of ecological damage caused by oil pollution of marine habitats. HCB also have potential biotechnological applications in the areas of bioplastics and biocatalysis. Novel catalysts can be obtained from metagenomic libraries and DNA sequence based approaches. Our increasing capabilities in adapting the catalysts to specific reactions and process requirements by rational and random mutagenesis broadens the scope for application in the fine chemical industry, but also in the field of biodegradation. In many cases, these catalysts need to be exploited

in whole cell bioconversions or in fermentations , calling for system-wide approaches to understanding strain physiology and metabolism and rational approaches to the engineering of whole cells as they are increasingly put forward in the area of systems biotechnology and synthetic biology.

MICROBIAL TRANSFORMATIONS OF QUINOLONES AND RELATED DRUGS pdf

5: Quinolone antibiotic - Wikipedia

Quinolones are a type of antibiotic. Antibiotics kill or inhibit the growth of bacteria. There are five different quinolone classes. In addition, another class of antibiotic, called fluoroquinolones, were derived from quinolones by modifying their structure with fluorine.

References The fluoroquinolones are broad-spectrum antibiotics with particular activity against gram-negative organisms, especially Pseudomonas aeruginosa. These agents are well absorbed when given orally. Because tissue and fluid concentrations often exceed the serum drug concentration, these antibiotics are particularly useful for certain infections, such as pneumonia. However, they can have serious adverse effects. Concern about the adverse effects of quinolones on joints is based primarily on experimental evidence in young animals. These drugs are not recommended for use in patients younger than 18 years or in pregnant or lactating women. In one study, however, no arthropathies were observed in more than 1, children who received ciprofloxacin. Food and Drug Administration FDA issued a public health advisory warning about the risk of liver toxicity with trovafloxacin after 14 cases of acute liver failure were associated with its use. The fluoroquinolones are bactericidal antibiotics that act by specifically targeting DNA gyrase. The antibacterial effect continues for approximately two to three hours after bacteria are exposed to these drugs, despite subinhibitory concentrations. The duration of the postantibiotic effect may be increased with longer bacterial drug exposure and higher drug concentrations. The accumulation of several bacterial mutations DNA gyrase and bacterial permeability has been associated with the development of very high minimum inhibitory concentrations to ciprofloxacin in isolates of Staphylococcus aureus, Enterobacteriaceae species and P. This resistance mechanism is shared with antimicrobial agents structurally unrelated to the quinolones, such as the betalactams, tetracyclines and chloramphenicol Chloromycetin. Cross-resistance among the quinolones is expected, but the extent to which the minimum inhibitory concentration is affected varies from agent to agent. Therefore, the bacterial susceptibility and pharmacokinetic profiles of each quinolone should be considered in determining the effectiveness of specific agents. Shortly thereafter, ciprofloxacin became the most frequently used antibiotic throughout the world. Some infectious disease specialists have become concerned about the overuse of fluoroquinolones. Because of the broad spectrum and oral availability of these agents, overuse is quite easy. Family physicians should always follow the principle of using the drug with the narrowest spectrum and the least toxicity. Six new fluoroquinolones have been introduced in the United States during the past five years. Levofloxacin Levaquin and sparfloxacin became available in , and grepafloxacin Rexar and trovafloxacin were introduced in Gatifloxacin Tequin and moxifloxacin Avelox became available in early In December , grepafloxacin was voluntarily withdrawn because of the possibility of torsades de pointes occurring with its use. Compared with ciprofloxacin the prototypical agent of the original fluoroquinolones , the newest fluoroquinolones have enhanced activity against gram-positive bacteria with only a minimal decrease in activity against gram-negative bacteria. Sparfloxacin has even greater activity against Mycoplasma species. Trovafloxacin is the fluoroquinolone with the most potent anaerobic activity, including activity against Bacteroides species. As a result, this agent has the broadest spectrum of activity of the currently available quinolones, as well as a wide range of indications. They are rapidly and almost completely absorbed from the gastrointestinal tract. Peak serum concentrations obtained after oral administration are very near those achieved with intravenous administration. Absorption of orally administered fluoroquinolones is significantly decreased when these agents are coadministered with aluminum, magnesium, calcium, iron or zinc, because of the formation of insoluble drugâ€”cationic chelate complexes in the gastrointestinal tract. Because sucralfate Carafate contains aluminum, it can also reduce absorption of the quinolones. Adequate spacing of administration times has not been determined, and coadministration of quinolones and sucralfate should be avoided. Because the fluoroquinolones have a large volume of distribution, they concentrate in tissues at levels that often exceed serum drug concentrations. Penetration is particularly high in renal, lung,

prostate, bronchial, nasal, gall bladder, bile and genital tract tissues. Consequently, these agents are especially useful in treating urinary tract infections. Trovafloxacin penetrates noninflamed meninges and may have a future role in the treatment of bacterial meningitis. The quinolones vary with respect to the relative contribution of renal and nonrenal pathways for their elimination. Only ofloxacin and levofloxacin are exclusively eliminated by the kidney. Dosage adjustments based on estimated creatinine clearance values must be made for the agents with significant renal elimination. In most instances, administering the usual dose at an extended interval is recommended. Trovafloxacin is eliminated primarily by hepatic mechanisms. Dosage adjustments are required in patients with mild to moderate cirrhosis. No data are available on patients with severe liver disease. The usual cause is the somewhat decreased volume of distribution and decreased renal function in older persons. However, dosage adjustment based on age alone is not recommended. New Classification of Quinolones.

6: New Classification and Update on the Quinolone Antibiotics - - American Family Physician

Skip to Main Content.

7: List of Common Quinolones + Uses, Types & Side Effects - www.enganchecubano.com

The microbial biotransformation of the aryl-CF 3-containing drug flutamide, which is an antiandrogen drug used for the treatment of prostate cancer, led in some cases to the formation of bioactive metabolites.

MICROBIAL TRANSFORMATIONS OF QUINOLONES AND RELATED DRUGS pdf

Jura impressa s9 manual Drywall sheets caculator from A Dictionary of the Language of Bugotu, Santa Isabel Island, Solomon Islands Genetic engineering: past and present as prelude to the future Pea-pod man: Raven the creator The just society as the liberal society Biological science man 6th Far from Democracy On The Run From Dogs and People A girl with a basket full story in hindi Conditional formatting in excel 2007 tutorial Arts education primer Women and Slaves in Classical Culture A place of springs Critical theory and poststructuralism: Habermas and Foucault Beatrice Hanssen Mackie 802-vlz3 manual The OpenGL Extensions Guide (Graphics Series) Electricity and Magnets (Hands-on Science) Cerita silat file Uneasy States of Grace Best of creative skits for youth groups Business without greed Organizing fundraising to transform stewards to be rich toward God Adam J. Morris Skating Superstars Research in Accounting Regulation, Volume 15 (Research in Accounting Regulation) Science education and the Dominican Republic Project Ross H. Nehm, Jupiter Luna, and Ann F. Budd Freud, Jung, and psychoanalysis Douglas A. Davis Functional Requirements for an On-Line Bibliographic Data Access and Control System The Stock Market 50 Years of Capitalism at Work Subject and predicate worksheets for grade 2 Monster in the shadows Gallery to play to The empire of the invisibles. Measurement errors Footloose in the Himalaya Conclusion : trade unions and democratization in Africa Jon Kraus A contribution of human rights monitoring bodies? Pathogen induced diseases in animals and plants SBTs in Great Britain General subject index