

## Nitrofurans\*

### Overview

Nitrofurans are broad spectrum agents, characterized by effectiveness against Gram-positive and Gram-negative bacteria, including *Salmonella* species. This group of drugs is also effective against *Giardia*, amebae, trichomonads and some species of Coccidia. Some nitrofurans are carcinogenic and future use is questionable; however, nitrofurans are used presently in both veterinary and human medicine. In a study of antimicrobial use at a Russian pediatric hospital, prescriptions for nitrofurans comprised seven percent of total drug prescriptions. Despite the broad spectrum of activity, other drugs are usually more effective against susceptible organisms. Nitrofurans are, for the most part, bacteriostatic, although at high doses they can be bactericidal. These drugs are most active in acid environments (optimum pH is 5.5). Nitrofurans are only slightly soluble in water and are not effective systemically. They are used orally, topically and rarely parenterally. Absorption from the gastrointestinal tract is poor and the drug is eliminated very rapidly. Due to the above factors, inhibitory concentrations are only reached in urine.

Besides carcinogenesis, other toxic effects have been ascribed to various nitrofurans, including central nervous system involvement, gastrointestinal disturbances, methemoglobinemia, poor weight gain and reduced spermatogenesis. Various hypersensitivity reactions have also been described. When excessive doses of furazolidone are administered to small calves, such as Jersey calves, neurotoxicity is common. In humans, polyneuropathy is associated with nitrofurantoin use. Nitrofurantoin has also been linked to yellow discoloration of the teeth in young animals.

Although their basic mechanism of action remains unclear, nitrofurans inhibit many microbial enzyme systems, including those involved in carbohydrate metabolism. The drug is metabolized to nitroreductases that lead to formation of nitro anion radicals that inhibit genetic translation, the ribosomal process where mRNA specifies the amino acid sequence in a polypeptide chain.

### Resistance

Resistant mutants are rare and the emergence of resistance to nitrofurans is generally slow. *Helicobacter pylori* is usually susceptible to nitrofurantoin and furazolidone, however some isolates are now characterized by higher MIC (minimum inhibitory concentration). The mechanism of this resistance is unknown and differs from the determinants of metronidazole resistance to the nitrofurans. Nitrofurans exhibit uniform cross resistance with other nitrofurans, but cross resistance with other antimicrobial agents does not occur.

## Effectiveness

Nitrofurantoin is used to treat urinary infections and can be administered orally or parenterally. *E coli*, *Staphylococcus aureus*, *Streptococcus pyogenes* and *Aerobacter aerogenes* are usually susceptible, while *Proteus* species, *Pseudomonas aeruginosa* and *Streptococcus faecalis* are usually resistant. Optimum effectiveness occurs when the urine pH is approximately 5.

Nitrofurazone exhibits an antibacterial spectrum similar to nitrofurantoin but is utilized primarily to treat mastitis, metritis and wounds in cattle. Presence of blood, pus or milk reduces the effectiveness of the drug. Nitrofurazone is also used as a feed additive in food producing animals to control intestinal bacterial infections and coccidiosis. However, in the European Union use of nitrofurans in food production animals is prohibited.

Furazolidone is effective against *E coli*, *Clostridium*, *Salmonella*, *Shigella*, *Staphylococcus*, *Streptococcus*, *Eimeria* and *Histomonas* species. The drug is administered orally but is also applied topically. This nitrofuran is recommended as an alternative therapy for *Helicobacter pylori* in some areas of the world. In veterinary medicine furizolidone is utilized primarily to treat intestinal infections in calves. Nifuraldezone is another nitrofuran used primarily to control enteritis in calves. Furaltadone is given orally to prevent intestinal infections and is applied directly to the teat to treat mastitis. Yet another nitrofuran, nifurpazine, is only administered topically.

**\*References available by request. Call the Infectious Disease Epidemiology Section, Office of Public Health, Louisiana Department of Health and Hospitals (504-219-4563)**