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Dept. of Anatomy

**Name**:

Nitrofurantoin

**Antibacterial Activity**

Nitrofurantoin’s primary use has remained the treatment and prophylaxis of urinary tract infections. Nitrofurantoin is advantageous in this role as it concentrates in the lower urinary tract while maintaining a low serum concentration and also does not significantly affect bowel flora. The predominant cause of urinary tract infections is periurethral colonization of bacteria from a fecal reservoir, which then ascends the urinary tract. Nitrofurantoin is effective against many gram-positive and gram-negative organisms. Nitrofurantoin is bactericidal against most common urinary tract pathogens, including Escherichia coli, Enterococci, Klebsiella, Staphylococcus saprophyticus, and Enterobacter. Its spectrum of susceptibility also includes Shigella, Salmonella, Citrobacter, Neisseria, Bacteroides, group B streptococcus, Staphylococcus aureus, and Staphylococcus epidermidis.

**Mechanism of Action**

Nitrofurantoin uses several mechanisms to achieve an antimicrobial effect. Nitrofurantoin is taken up by bacterial intracellular nitroreductases to produce the active form of the drug via reduction of the nitro group. Intermediate metabolites that result from this reduction then bind to bacterial ribosomes and inhibit bacterial enzymes involved in the synthesis of DNA, RNA, cell wall protein synthesis, and other metabolic enzymes.

**Pharmacokinetics**

Absorption

Nitrofurantoin reaches a Cmax of 0.875-0.963mg/L with an AUC of 2.21-2.42mg\*h/L. It is 38.8-44.3% bioavailable. Taking nitrofurantoin with food increases the absorption and duration of therapeutic concentrations in the urine.

Volume of distribution

Data regarding the volume of distribution in humans is scarce but it has been reported as 0.46L/kg in dogs.

Protein binding

Nitrofurantoin could be up to 90% protein bound in plasma.

Metabolism

0.8-1.8% of a dose is metabolized to aminofurantoin, and ≤0.9% of a dose is metabolized to other metabolites.

Route of elimination

27-50% of an oral dose is excreted in the urine as unchanged nitrofurantoin. 90% of the total dose is eliminated in the urine.

Half life

The half life of nitrofurantoin is 0.72-0.78h.

Clearance

The clearance of nitrofurantoin is 16.7-19.4L/h.

**Adverse Effects**

The most common reported side effects include nausea, vomiting, loss of appetite, and diarrhea. These symptoms usually develop in the first week of therapy. Modern formulations, specifically the macrocrystalline form of the drug, have less frequency of these effects due to attempts by manufacturers to alter the crystal size, which effects gastrointestinal absorption.

More severe reactions to nitrofurantoin exist. The most well known severe reaction is pulmonary toxicity. Pulmonary toxicity caused by nitrofurantoin can be categorized into acute, subacute, and chronic pulmonary reactions. The acute pulmonary reaction syndrome is characterized by sudden onset of fever, chills, cough, myalgia, and dyspnea. Sub-acute pulmonary reactions also occur and are characterized by persistent dry cough, dyspnea, and fever. This chronic, pulmonary reaction is associated with the insidious onset of persistent dry cough and dyspnea. Acute, subacute, and chronic pulmonary toxicity are reversible with immediate cessation of the drug. This effect remains uncommon, with one study showing the calculated frequency for all pulmonary reactions were only present in 0.001% of nitrofurantoin courses. Other rare adverse effects include hepatic reactions such as cholestatic jaundice, hepatitis, and hepatic necrosis. The drug should be ceased immediately in these cases. Peripheral neuropathy is another known rare adverse effect, and is mostly associated with prolonged use in patients with poor renal function.