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COURSE: Systemic pharmacology

DEPARTMENT: physiology

**NITROFURATION**

This is an antibacterial agent specific for treatment of bladder infection and against urinary tract infection and may cause brown coloration of urine trade name is also known as macrobid among others it is taken into the body by oral means of absorption , ,

**ANTIBACTARIAL ACTIVITY**

Nitrofurantoin has been shown to have good activity against infection caused by the following

E.*coli*

*Staphylococcus saprophyticus*

*Coagulase negative staphyticus*

*Enterococcus faecalius*

*Staphylococcus aureus*

*Streptococcus agalactiae*

*Citrobacter species*

*Klebsiella species*

*Bacillus subtilis species.*

Many or all strain of the following genes are resistant to nitrofurantoin

*Enterobacter*

*Klebsiella*

*Proteus*

*Pseudomonas.*

MECHANISM OF ACTION

The exact mode of nitrofurantoin is not completely understood modern research are still been carried out though it is mainly known that to inhibit bacterial enzymes that participate in bacteria carbohydrate metabolism at three points in the Krebs cycle as well as interfering with cell wall synthesis the nitrogen group coupled onto the heterocyclic furan ring representing the specific active site of the drug and has to be activated by microbial nitroreductase.it has been proven through various research that nitrofurantoin susceptibility with bacterial correlates with the presence of bacterial nitroreductase which converts nitrofurantoin to highly reactive electrophilic intermediates these intermidreates will attack bacterial ribosomes protein synthesis , low consumption of nitrofurantoin specifically inhibits inducible enzymes synthesized in the bacteria and show that this inhibition occurs at levels equilivant to the MIC`s of nitrofuratoin for several bacterial species .therefore different concentration of nitrofurantoin may relate to inhibit inducible enzyme synthesis .

In other simpler words the drug works by damaging bacteria DNA as it will attach the bacteria ribosome ,as its reduced form is highly reactive this is made possible by the rapid reduction of nitrofurantoin to multiple reactive intermediates which attacks the ribosome protein DNA , respiration ,pyruvate metabolism and other macromolecule within the cell nitrofurantoin exerts greater effects on bacteria cell than mammalian cells because bacteria cells activates the drug more rapidly ,this drug is known to affect different activities important to bacterial cells .

**PHARMAKOKINETICS OF NITROFURANTOIN**

Nitrofurantoin   is administered orally as a microcrystalline or microcrystalline formulation, of which the latter has a slower absorption rate. Absorption is almost complete, with 2–4% of the dose being recovered from the feces. 18   Serum concentrations are not measurable, except in patients who have   severe renal failure. This is because of destruction of nitrofurantoin in the tissues and, in particular, a very rapid   renal elimination   by   glomerular filtration   (20%) and tubular secretion, resulting in a   serum half-life   of only 20 minutes in patients who have normal renal function. 18   Excretion is complete within 6 hours after intake and   urine concentrations   of 200–400 mg/l are achieved after a dose of 100 mg q8h. In patients who have renal failure – who should not be given nitrofurantoin – there are measurable but still very low serum and urine concentrations. 19

Therapeutic doses of nitrofurantoin are 50–100 mg q8h or q6h for adults and 3 mg/kg/day q12h or q8h for children. Prophylactically, the adult dose is 50–100 mg and the pediatric dose 1–2 mg/kg at bedtime. The duration of treatment when nitrofurantoin is used therapeutically should be 5–7 days. Dosages are not affected by liver function.

**ADVERSE EFFECT OF NITROFURANTOIN**

The most common side effects are nausea occurring for [8%], headache for [6%] and flatulence for [1.5%] other adverse effect are fever chills and malasie occurs less than 1% of the people taking this drug with different adverse effect occurring in different systems :

**Gastrointestinal:**

Pseudomembranous colitis, diarrhea, abdominal pain, constipation, emesis

**NEUROLOGICAL:**

Dizziness, drowsiness, asthenia vertigo and nystagus amblyopia.

**RESPIRATORY**:

Acute pulmonary hypersensitivity reaction

ALLERGIC:

Pruritus, urticarial

**DERMATOLOGIC:**

Alopecia

**CLINICAL ADVERSE EFFECTS**

**Neurologic**: Peripheral neuropathy, which may become severe or irreversible, has occurred. Fatalities have been reported. Conditions such as renal impairment (creatinine clearance under 60 mL per minute or clinically significant elevated serum creatinine), anemia, diabetes mellitus, electrolyte imbalance, vitamin B deficiency, and debilitating diseases may increase the possibility of peripheral neuropathy. (

Asthenia, vertigo, and nystagmus also have been reported with the use of nitrofurantoin.

Benign intracranial hypertension (pseudotumor cerebri), confusion, depression, optic neuritis, and psychotic reactions have been reported rarely. Bulging fontanels, as a sign of benign intracranial hypertension in infants, have been reported rarely.

**Respiratory**

Chronic subacute or acute pulmonary hypersensitivity reactions may occur with use of nitrofurantoin .

Chronic pulmonary reaction generally occurs in patients who have received continuous treatments for six months or longer. Malaise, dyspnea on exertion, cough and altered pulmonary function are common manifestation which can occur insidiously. Chronic pulmonary reactions are not recognized early they can be great risks. In sub acute pulmonary reactions, fever and eosinophilia occur less often than in the acute form. Upon cessation of therapy, recovery may require several months. If the symptoms are not recognized as being drug-related and nitrofurantoin therapy is not stopped, the symptoms may become more severe.

Acute pulmonary reactions are commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on x-ray, and eosinophilia. Acute reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Resolution often is dramatic.

Cyanosis has been reported rarely.

Hepatic: Hepatic reactions, including hepatitis, cholestasis jaundice, chronic active hepatitis, and hepatic necrosis, occur rarely.

Allergic: Lupus-like syndrome associated with pulmonary reaction to nitrofurantoin has been reported. Also, angioedema; maculopapular, erythematous, or eczematous eruptions; anaphylaxis; arthralgia; myalgia; drug fever; chills; and vacuities (sometimes associated with pulmonary reactions) have been reported. Hypersensitivity reactions represent the most frequent spontaneously-reported adverse events in worldwide post marketing experience with nitrofurantoin formulations.

**Dermatolocgi**: Exfoliative dermatitis and erythema multiforme (including Stevens-Johnson syndrome) have been reported rarely.