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 **Pharmacology assignment**

1. **Name of the drug:** Nitrofurantoin (marobid)

 Nitrofurantoin is an antibiotic classified as a urinary antiseptic agent used for treating urinary tract infections caused by several types of bacteria, it use causes brown colouration of urine. It is effective against E. Coli, Enterobacter cystitis, Enterococcus, Klebsiella, and Staphylococcus aureus.

1. **Antibacterial activity**

Nitrofurantoin is classified as a urinary antiseptic agent. Itis less commonly employed for treating UTIs because of its narrow antimicrobial spectrum, frequent bacterial resistance and toxicity.

 Sensitive bacteria reduce the drug to an active agent that inhibits various enzymes and damages DNA. Nitrofurantoin interferes with the production of bacterial proteins, DNA, and cell walls and its activity is greater in acidic urine.

 Nitrofurantoin is bacteriostatic for most susceptible micro-organisms at concentrations of 32ug/ml or less and is bactericidal at concentrations of 100ug/ml and more. The antibacterial activity is higher in an acidic urine. It is active against many strains of *E.Coli* and enterococci. However, most species of proteus and pseudomonas and many species of enterobacter and klebsiella are resistant.

1. **Mechanism of action**

 It is rapidly reduced in bacterial cells by flavoproteins (nitrofuran reductase) to multiple reactive intermediates that attack ribosomal proteins, DNA, respiration, pyruvate metabolism and other macromolecules within the bacterial cell, thereby inhibiting protein synthesis.

 Nitrofurantoin is taken up by bacterial intracellular nitrofuran reductases 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. It is bactericidal, especially to bacteria present in acid urine.

 Nitrofurantoin damages DNA since its reduced form is highly reactive.

 Nitrofurantoin exerts greater effects on bacterial cells than mammalian cells because bacterial cells activate the drug more rapidly. It is not known which of the actions of nitrofurantoin is primarily responsible for its bactericidal activity. The broad mechanism of action for this drug likely is responsible for the low development of resistance to its effects, as the drug affects many different processes important to the bacterial cell.

1. **Pharmacokinetics**

 Nitrofurantoin is absorbed rapidly and completely from the GIT tract. It half-life in plasma is very short (less than 1 hour or < 1 hr) and therapeutic plasma concentrations are not achieved. Antibacterial concentrations are not achieved in plasma following ingestion of recommended doses because the drug is rapidly eliminated.

 It is excreted largely unchanged in the urine, giving [urinary concentrations](https://www.sciencedirect.com/topics/medicine-and-dentistry/kidney-concentrating-capacity) high enough to treat [lower urinary tract infections](https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/urinary-tract-infection), but the low tissue concentrations are inadequate for the treatment of [acute pyelonephritis](https://www.sciencedirect.com/topics/medicine-and-dentistry/acute-pyelonephritis). Nitrofurantoin colors the urine brown.

 Organisms are said to be susceptible to nitrofurantoin if their minimum inhibitory concentration is 32 μg/ml or less. The peak blood concentration of nitrofurantoin following an oral dose of nitrofurantoin 100 mg, is less than 1 μg/ml and may be undetectable. Its bioavailability is about 90% and the urinary excretion is 40% tissue penetration is negligible; the drug is well concentrated in the urine: 75% of the dose is rapidly metabolised by the liver, but 25% of the dose is excreted in the urine unchanged, reliably achieving levels of 200 μg/ml or more. In studies of dogs, the majority of urinary excretion is through glomerular filtration with some tubular secretion.There is also tubular absorption which is increased with urine acidification. However the activity of nitrofurantoin is also pH dependent and mean inhibitory concentration rises sharply with increased pH above 6. Nitrofurantoin cannot be used to treat infections other than simple cystitis.

At the concentrations achieved in urine (>100 μg/ml), nitrofurantoin is a bactericide. It is bacteriostatic against most susceptible organisms at concentrations less than 32 μg/ml.

Nitrofurantoin and the quinolone antibiotics are mutually antagonistic in vitro. It is not known whether this is of clinical significance, but the combination should be avoided.

Resistance to nitrofurantoin may be chromosomal or plasmid-mediated and involves inhibition of nitrofuran reductase. Acquired resistance in E. coli continues to be rare.

 Nitrofurantoin and its metabolites are excreted mainly by the kidneys. In renal impairment, the concentration achieved in urine may be subtherapeutic It is not used for pregnant women, individuals with impaired renal function, children younger than one month of age. It is not recommended for the treatment of pyelonephritis or prostatis.

1. **Adverse effects**
* Gastrointestinal disturbances: these side effects include nausea, vomiting, and diarrhea.
* Acute pneumonitis
* Neurological problems such as headache, nystagmus, and polyneuropathies with demyelination may occur.
* Hemolytic anemia. Reduced red blood cell count (anemia) by breaking red blood cells (hemolytic anemia) can occur from nitrofurantoin. This reaction occurs most frequently in persons with a deficiency of an enzyme called glucose--6-phosphate dehydrogenase that is very important to the survival of red blood cells.

 Symptoms can include:tirednessweaknessand pale skin.

* Nitrofurantoin can also cause damage to the sensory nerves of the arms and legs (peripheral neuropathy), which can cause tingling in the extremities. The condition can become severe and is more likely to occur in people with diabetes, vitamin B deficiency, or general debilitation.

 Symptoms can include:

* numbness or tingling in your hands and feet
* muscle weakness
* Liver problems; Nitrofurantoin also can cause liver damage leading to jaundice or a form of hepatitis that can be fatal. Elevated liver enzymes indicate liver damage and are a reason to stop the drug.

Symptoms can include:

* itching
* yellowing of your skin or the whites of your eyes
* nausea or vomiting
* dark urine
* loss of appetite

Other common side effects are:

• Changes in facial skin color,

• General feeling of discomfort or illness, hives, hoarseness, itching, joint or muscle pain, shortness of breath, skin rash, sudden trouble in swallowing or breathing

• Swelling of the face, mouth, hands, or feet

• Troubled breathing

• Blood in the urine or stools

• Burning, numbness, tingling, or painful sensations

• Dizziness

• Drowsiness

• Headache