**NAME: CHIKA CHIEZE**

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**DEPT: ANATOMY**

**COURSE: PHA 306 (system pharmacology)**

**ASSIGNMENT (Drugs used in urinary system disorders)**

1. A drug used in the treatment of urinary tract infection causes brown coloration of urine. Explain in full detail the pharmacology of the drug under the following headings:
2. Name of the drug
3. Antibacterial activity
4. Mechanism of action
5. Pharmacokinetics
6. Adverse effects

**ANSWSERS**

1. Nitrofurantoin
2. Antibacterial activity: nitrofurantoin has been shown to have good activity against E.coil, staphylococcus saprophyticus, citrobacter species, klebsiella species, bacillus subtillis species e.t.c. nitrofurantoin is bacteriostatic for most susceptible microorganisms at concentration at 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.
3. Mechanism of action: Nitrofurantoin is concentrated in the urine, leading to higher and more effective levels in the urinary tract than in other tissues. With a 100mg dose, plasma levels are typically less than 1ug/ml while in the urine it reaches 200ug/ml. The mechanism of action is unique and complex. The drug works by damaging the bacterial DNA, since its reduced form is highly reactive. This is made possible by the rapid reduction of nitrofurantoin inside the bacterial cell by flavoprotein( nitrofuran reductase) to multiple reactive intermediates that attack ribosomal proteins, DNA, respiration, pyruvate metabolism and other macromolecules within the cell. Nitofurantoin exerts greater effects on bacterial cells than mammalian cells because bacterial cells activate the drug more rapidly. 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.
4. Pharmacokinetics: Nitrofurantoin is a urinary tract antibacterial agent whose clinical effectiveness depends on the high urinary drug levels encountered during therapeutic drug dosage. Under these conditions, only low blood drug concentrations are usually found. On the basis of urinary nitrofurantoin excretion determined after oral and intravenous drug administration, orally administered nitrofurantoin in a suitable dosage form is well absorbed. In vitro testing does not accurately reflect nitrofurantoin bioavailability, which is affected by formulation differences, drug particle size and dosage form. Nitrofurantoin is readily absorbed and quickly distributed into most body fluids. It is rapidly excreted in large amounts in bile and urine. With the exception of the active drug secretion in the kidney tubule and biliary drug transport, nitrofurantoin transfer across body membranes occurs by diffusion. Nitrofurantoin has a short elimination half-life in whole blood or plasma. In conjunction with its rapid excretion by the primary routes, there is little evidence for any prolonged binding of nitrofurantoin to either plasma proteins or tissues. The first order kinetics involved in nitrofurantoin absorption and elimination is most appropriately described by a one-compartment open model. Biliary and urinary excretion of unchanged nitrofurantoin and enzymatic degradation are the primary means of elimination.
5. Adverse effects: The most common side effects with nitrofurantoin are nausea, headache and flatulence. Less common adverse effects(occurring in less than 1% of those taking the drug) incude:

* Gastrointestinal intolerance: epigastric pain, diarrhea, dyspepsia, abdominal pain, constipation, emesis
* Hypersensitivity: fever, chills
* Peripheral neuritis and other neurological effects with long term use
* Hematologic disorders: leukopenia, granulocytopenia, hemolytic anemia in G6PD deficient patients.
* Respiratory: acute pulmonary hypersensitivity reaction
* Allergic: pruritus, urticarial
* Dermatologic: hair loss

Nitrofurantoin colours urine brown; this is completely harmless.