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A certain drug used in treatment of urinary tract infection causes brown coloration of urine. In full detail, the pharmacology of this drug will be explained in this write up under specified headings.

**NAME OF DRUG**; Metronidazole, marketed as flagyl, filmet, metro, and other trade names. The chemical name of the drug is 2-Methyl-5-nitroimidazole-1-ethanol , the molecular formula is C6H9N3O3, molecular weight: 171.15, and it appears in physical form (white to pale yellow crystals or crystalline powder).

**ANTIBACTERIAL ACTIVITY**; metronidazole is an antibiotic and antiprotozoal medication. It is used either alone or with other antibiotics to treat pelvic inflammatory diseases, endocarditis, and bacterial vaginosis.it is effective for dracunculiasis, giardiasis, trichomoniasis, and amebiasis. It is an option for a first episode of mild- to – moderate Clostridium difficile colitis if vancomycin or fidaxomicin is unavailable. Metronidazole is available by oral, topical, rectal, vaginal, and intravenous routes of administration.

**MECHANISM OF ACTION;** Metronidazole is bactericidal against anaerobic bacteria; it exerts trichomonacidal activity and is also active against Giardia lamblia and Entamoeba histolytica. Its exact mechanism of action has not been entirely determined as yet. It has been proposed that an intermediate in the reduction of metronidazole, produced only in anaerobic bacteria and protozoa is bound to deoxyribonucleic acid and electron-transport proteins, inhibits subsequent nucleic acid synthesis.



**PHARMACOKINETICS;**

Following oral administration, metronidazole is completely absorbed with plasma concentration usually reaching a peak within 1 to 2 hours. After single oral 500 mg doses, peak plasma levels of approximately 13 mg/L were obtained. On a regimen of 500mg t.i.d. administered by the i.v. route, a steady state was achieved after approximately three days. The mean peak and trough concentrations measured at that time were 26 and 12 mg/L respectively, and the elimination halflife was approximately 7 to 8 hours. Comparison of the pharmacokinetics of oral and i.v. metronidazole revealed that the area under the plasma metronidazole concentration against time curves were essentially identical**.**

Excretion and Metabolism: The major route of elimination of metronidazole and its metabolites is via the urine (60-80% of the dose) with fecal excretion accounting for 6 to 15% of the dose. The metabolites that appear in the urine result primarily from side chain oxidation (i.e. 1-(ß-hydroxyethyl)-2-hydroxymethyl-5- nitroimidazole and 2-methyl-5 nitroimidazole-1-yl-acetic acid) and glucuronide conjugation, with unchanged metronidazole accounting for approximately 20% of the total.

 Metronidazole is the major component appearing in the plasma with lesser quantities of the 2hydroxymethyl metabolite also being present. The ratio of these components varies with time but the maximum concentration of the metabolite (Cmax) is approximately 20% of the Cmax of metronidazole for the oral route of administration.

 Protein Binding: Less than 20% of the circulating metronidazole is bound to plasma proteins.

**ADVERSE EFFECTS;** The following adverse reactions have been reported with the use of metronidazole:

* Blood and lymphatic system disorders: transient eosinophilia, neutropenia, very rare cases of agranulocytosis and thrombocytopenia have been reported.
* Cardiac disorders: palpitation and chest pain.
* Eye disorders: transient vision disorders such as diplopia, myopia, blurred vision, decreased visual acuity, changes in color vision. Optic neuropathy/neuritis has been reported.
* Ear and labyrinth disorders: hearing impairment/hearing loss (including hypoacusis, deafness, deafness neurosensory), tinnitus.
* Gastrointestinal disorders: diarrhea, nausea, vomiting, epigastric distress, epigastric pain, dyspepsia, constipation, coated tongue, tongue discoloration/furry tongue (e.g. due to fungal overgrowth), dry mouth, taste disorders including metallic taste, oral mucositis. Reversible cases of pancreatitis have been reported infrequently.
* General disorders and administration site conditions: Thrombophlebitis has occurred with I.V. administration. Fever has been reported.
* Hepatobiliary disorders: increase in liver enzymes (AST, ALT, alkaline phosphatase), cholestatic or mixed hepatitis and hepatocellular liver injury, sometimes with jaundice have been reported.
* Cases of liver failure requiring liver transplant have been reported in patients treated with metronidazole in combination with other antibiotic drugs.
* Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome, in patients with Cockayne syndrome have been reported with products containing metronidazole.
* Immune system disorders: angioedema, anaphylactic shock.
* Infections and infestations: rare cases of pseudomembranous colitis have been reported.
* Metabolism and nutrition disorders: An antithyroid effect has been reported by some investigators but three different clinical studies failed to confirm this. Anorexia has been reported.
* Nervous system disorders: convulsive seizures, peripheral sensory neuropathy, transient ataxia, dizziness, drowsiness, insomnia, headache, aseptic meningitis.
* Very rare reports of encephalopathy (e.g. confusion) and subacute cerebellar syndrome (e.g. ataxia, dysarthria, gait impairment, nystagmus, and tremor) have been reported, which may resolve with discontinuation of the drug.
* Peripheral neuropathies have been reported in a few patients on moderately high to high-dose prolonged oral treatment with metronidazole. It would appear that the occurence is not directly related to the daily dosage and that an important predisposing factor is the continuation of oral and/or I.V. medication for several weeks or months.
* Profound neurological deterioration, within 2 hours after metronidazole administration has been reported. The occurence is not directly related to the dosage level.
* Other: Proliferation of Candida albicans in the vagina, vaginal dryness and burning; dysuria; occasional flushing and headaches, especially with concomitant ingestion of alcohol; altered taste of alcoholic beverages.
* Darkening of the urine (brown coloration) has been reported. This is probably due to a metabolite of metronidazole and seems to have no clinical significance. Reversible lowering of serum lipids has been reported.
* Psychiatric disorders: psychotic disorders including confusion, hallucinations, depressed mood.
* Reproductive system and breast disorders: A single case of gynecomastia has been reported which resolved on discontinuing metronidazole administration.