**BASSEY MARVELLOUS**

**17/MHS01/081**

**BCH 313**

**MEDICAL BIOCHEMISTRY IV**

**Question: Discuss in details the factor affecting drug metabolism**

# **CHEMICAL STRUCTURE**

The chemical structure (the absence or presence of certain functional groups) of the drug determines its metabolic pathways.

# **SPECIES DIFFERENCES (QUALITATIVE AND QUANTITATIVE)**

Qualitative differences may result from genetic deficiency of a certain enzyme, while quantitative difference may resuly from a difference in the enzyme level

# **PHYSIOLOGICAL OR DISEASE STATE**

* For example in congestive heart failure there is reduced blood flow due to reduced cardiac output and thus alters extent of drug metabolism
* An alteration in albumin production can alter the fraction of bound to unbound drug, i.e. a decrease in plasma albumin can increase the fraction of unbound free drug and vice versa
* Pathological factors altering liver function can affect hepatic clearance of the drug

# **GENETIC VARIATION**

Isoniazid is known to be acetylated by N-acetyltransferase into inactive metabolite. The rate of acetylation in Asian people is higher or faster than that of European or North American people. Fast acetylators are nore prone to hepatoxicity than slow acetylators.

# **DRUG DOSING**

* An increase in drug dosage would increase drug concentration and may saturate certain metabolic enzymes
* When metabolic pathway becomes saturated, an alternative may be pursued

# **NUTRITIONAL STATUS**

* Low protein diet decreases oxidative reactions or conjugation reactions due to deficiency of certain amino acids such as glycine
* Vitamin A,C,E and B deficiency can result in decrease in oxidative pathway in case of vitamin C deficiency, while vitamin E deficiency decreases de alkylation and hydroxylation
* Ca, Mg, Zn deficiencies decreases drug metabolism capacity whereas Fe deficiency increases it.

# **AGE**

Metabolizing enzymes (such as glucoronide conjugation) are not fully developed at birth, so infants and young children need to take smaller doses than adults to avoid toxic effects. In elderly, metabolizing enzyme systems decline.

# **GENDER**

Metabolic differences between male and females have been observed for certain compounds. E.g metabolism of Diazepam, Caffeine, and paracetamol is faster in females than in males while oxidative metabolism of Lidocaine, chordiazepoxide are faster in men thane in females.

# **DRUG ADMINISTRATION ROUTE**

* Orally administered drugs are absorbed from GIT and transported to the liver before entering the systemic circulation. Thus the drug is subjected to hepatic metabolism before reaching site of action
* Sublingually and rectally administered drugs take longer time to be metabolized than orally taken drugs. Nitroglycerine is ineffective when taken orally due to hepatic metabolism
* IV administration avoids hepatic metabolism because the drug is administered directly to the blood stream.

# **ENZYME INDUCTION OR INHIBITION**

Several antibiotics are known to inhibit the activity of cytochrome P450. Phenobarbitone is known to be cytochrome P450 enzyme inducer while cimetidine is cyt.P450 inhibitor. If warfarin is taken with phenobarbitone, it is less effective. If taken with cimetidine, it will be less metabolized and thus serious side effects may appear.