**17/MHS01/204**

*Discuss in details the factors affecting drug metabolism.*

1. Internal factors; species, hormones, age, genetics, sex, diseases.
2. External factors; diets ad environment

**HEXOBABITONE METABOLISM**

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| --- | --- | --- | --- |
| spp | Sleeping time | Hexobabitone ½ life | Hexobabitone metabolism |
| Mice | 12 +/- 8 | 19+/- | 16.6 |
| Rat | 90+/- 15 | 140 +/- 4 | 3.71 |
| Dog | 315+/- 105 | 260+/- 20 | 1 |
| man | Keeps sleeping | Approx 360 | ? |

**Genetic factor:** even siblings related by blood metabolize drugs differently. Although patient response to drugs varies widely and the reasons for this are diverse and complex, experts estimate that genetic factors account for 20 to 95 percent of patient variability in response to individual drugs.  Genetic influences on drug metabolism interact with other intrinsic (i.e., physiologic) and extrinsic (i.e., cultural, behavioral, and environmental) characteristics of a person to determine the outcome from treatment with any pharmacologic agent.

**Age:**  Aging clearly affects metabolism. In neonates (up to 2 months) and in infants (2 months to 1 year), the microsomal enzyme system is not fully developed. So, many drugs are metabolized slowly. For e.g.: caffeine has a half-life of 4 days in neonates in comparison to 4 hrs in adults. The drug metabolic rate in the different age groups differs mainly due to variations in the enzyme content, enzyme activity and hemodynamic. & In elderly persons, the liver size is reduced, the microsomal enzyme activity is decreased and hepatic blood flow also declines as a result of reduced cardiac output, all of which contributes to decreased metabolism of drugs. For example, chlomethiazole shows a high bioavailability within the elderly, therefore they require a lower dose. Children (between 1 year and 12 years) metabolize several drugs much more rapidly than adults as the rate of metabolism reaches a maximum somewhere between 6 months and 12 years. As a result they require large mg/kg dose in comparison to adults. .

**Sex (gender):** in 1932, Nicolas discovered that ½ of the Hexobabitone required making a male mice sleep is required to make a female mouse sleep. Since variations between male and female are observed following puberty. So, sex related differences in the rate of metabolism may be due to sex hormones. Such sex differences are widely studied in rats where male rats have greater drug metabolizing capacity. In humans, women metabolize benzodiazepines slowly than men. Several studies have shown that women on contraceptive pills metabolize a number of drugs at a slow rate.

 **Disease:** it can lead to decrease in drug metabolism. Though drug metabolism is an essential process required to sustain life, there are certain conditions in which an increase in the activation of drug metabolizing cytochrome (CYP) P450s can increase the potential for toxicity or intensify the symptoms of a disease.

**Hormones:** some hormones have effect on drug metabolism. The hormonal changes of puberty/adolescence provide a theoretical framework for understanding biochemical regulation of DME activity during growth and maturation.

**Diets:** they can hinder or reduce drug metabolism. Starvation results in decreased amount of glucuronides formed than under normal conditions. Dietary deficiency of vitamins like Vitamin A, B2, B3, C and E) and minerals such as Fe, Ca, Mg, Zn retard the metabolic activity of enzymes. Grapefruit inhibits metabolism of many drugs and improve their oral bioavailability. Fat free diet depresses cytochrome P-450 levels since phospholipids, which are important components of microsomes become deficient. Low protein diet decreases and high protein diet increases the drug metabolizing ability as enzyme synthesis is promoted by protein diet and also raises the level of amino acids for conjugation with drugs. The enzyme content and activity is altered by a number of dietary components.