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**BIOCHEMISTRY ASSIGNMENT**

Discuss in details the factors affecting drug metabolism.

**ANSWERS**

Drug metabolism is the chemical alteration of a drug by the body; some drugs are chemically altered by the body (metabolized). The substances that result from metabolism (metabolites) may be inactive, or they may be similar to or different from the original drug in therapeutic activity or toxicity. Some drugs, called prodrugs, are administered in an inactive form, which is metabolized into an active form. The resulting active metabolites produce the desired therapeutic effects. Metabolites may be metabolized further instead of being excreted from the body. The subsequent metabolites are then excreted.

The therapeutic efficacy, toxicity and biological half-life of drug greatly depend on the metabolism of the drug. Hence the various factors affecting drug metabolism must be considered during administration and also in proper dosage of the drugs to the patients. There are various factors which may influence the metabolic rate of a drug, some of them include:

1. **Chemical Factors**
2. Enzyme Induction: This is the phenomenon of increased drug metabolizing ability of enzymes by several drugs and chemicals, the agents which bring about such effects are called enzyme inducers.
3. Enzyme Inhibition: this is a decrease in the drug metabolizing ability of an enzyme. The process of inhibition may be direct or indirect.
4. Direct Inhibition: It may result from interaction at the enzymic site, the net outcome being a change in enzyme activity. It can occur by either Competitive, Non-Competitive or Product Inhibition
5. Indirect Inhibition: it is caused by either one of the following mechanisms: Repression or Altered Physiology.
6. Environmental chemicals: Several environmental agents influence the drug metabolizing ability of enzymes. For example, Organophosphate insecticides and heavy metals such as mercury, nickel, cobalt and arsenic inhibit drug metabolizing ability of enzymes.
7. **Biological factors:**
8. Age: The drug metabolic rate in the different age groups differs mainly due to variations in the enzyme content, and haemodynamic. For example, in neonates (up to 2 months) and in infants the microsomal enzyme system is not fully developed. so, many drugs are metabolized slowly.e.g caffeine has a half-life of four days in neonates as opposed to four hours in adults
9. Sex: sex related differences between male and female may be due to sex hormones, since differences between males and females are noticed following puberty. In humans, females metabolize benzodiazepines slower than males and several studies have shown that women on birth control pills metabolize drugs at a slow rate.
10. Diet: the enzyme content an activity is altered by number of dietary components, general they are:

* 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 conjunction with drugs
* Grapefruit inhibits the metabolism of many drugs and improves their oral bioavailability
* Starvation results in a decreased amount of gluconeurides formed than under normal circumstances.

1. Altered physiological factors: these factors include;

* Pregnancy: it is known to affect hepatic drug metabolism, the physiological changes during pregnancy are probably responsible for the reported alteration in drug metabolism; these include elevated concentrations of various hormones such as oestrogen, progesterone, placental growth hormone, etc.
* Disease states: there are many disease states that affect drug metabolism such as diabetes mellitus, malaria, cholesteric jaundice, various bacterial and viral infections etc., it may cause decreased drug metabolism due to decreased enzymatic activity in the liver and altered hepatic blood flow
* Hormonal imbalance: higher levels of one hormone may inhibit the activity of some enzymes while inducing that of others. Impairment In the enzyme activity with subsequent fall in the arte of metabolism is observed in the pituitary growth hormone and stress elevated changes in ACTH levels

1. Strain difference: As difference in drug metabolizing ability differs between species is attributed to genetics so also it differs between different strains of the same species. It may be studies under Pharmacogenetics and Ethnic variations.
2. **Physiochemical properties of the drug**: molecular size and shape, acidity/basicity and electronic characteristics of a drug influence in the interaction of the active sites of enzymes and metabolism to which it is subjected affects the rate of drug metabolism