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BIOAVAILABILITY OF HAZARDOUS WASTES

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INTRODUCTION

In pharmacology, bioavialability is defined as a dose of drug which reaches the blood-stream in contrast to the dose stated on label. The transfer process may be characterized by both the rate and the total amount transferred. Therefore, bioavailability can be also defined as "A term to indicate the rate and relative amount of the administered drug which reaches the general circulation intact''.

There is a close linkage between toxicology and pharmacology. In evaluating of exposure, distinction is made between the external dose, defined as the amount of a chemical agent in environmental contact with the organism, and the internal dose, which is the total amount of a chemical agent absorbed by the organism over a period of time. Therefore, bioavailability from toxicological point of view can be defined as a fraction of external dose of a chemical which reaches systemic circulation and subsequently target sites. The internal dose determines the bioavailability of the xenobiotics for the interaction with the biological structures and thus the ability to induce a biological (therapeutic or adverse) effects at the target sites. If the chemical is not in a "bioavailable form'', as is the case with many ingested toxic substances that cause vomiting or diarrhea, it will be promptly removed. In some cases, the agent can be inactivated before reaching the site of action.

The relationships between external and internal dose are studied by toxicokinetics (Fig. 1) and absorption processes play the crucial role.

ABSORPTION OF CHEMICALS AND FACTORS INFLUENCING THIS PROCESS

Absorption is the process(es) by which a chemical enters the body. For the simplification absorption can be equated with the appearence of chemical in the circulation. The major routes by which toxicants enter the body are via the lungs, the gastrointestinal tract, and the skin. A chemical must pass through many "barriers'' before reaching the circulatory system. These barriers are formed by cellular membranes (such as the cells of the skin, the lining of the lung and gastrointestinal tract, the capilary cells). All cell membranes are remarkably similar: they consist of a biomolecular layer of lipid molecules coated on each site with a protein layer, branches of which penetrate the lipid bilayer or even extend all the way through. Permeability of membranes is dependent upon a toxic substance's molecular size and shape, biosolubility and solubility in the vehicle in which it is administered and degree of ionization (1).

The distribution of some toxic agents is altered by unique cellular barriers, e.g. the blood-brain barrier, the blood-testis barrier, and the placenta, which may prevent or reduce transfer of toxic substances through them.

The mechanisms by which a chemical may pass through a membrane can be divided into two general types: (1) passive transport, in which the cell plays no active role in the transfer; and (2) specialized transport, in which cell takes an active part in the transfer.

Passive Transport

Simple diffusion: Most chemicals cross body membranes by simple diffusion. This can occur for small hydrophilic compounds by passage through aqueous channels, or more frequently for organic molecules possessing a certain degree of lipophilicity by diffusion through the lipid moiety of membrane. The rate of transfer depends on the biosolubility, which can be characterized by the lipid/water partition coefficient (most frequently derived from the oil/water or octanol/water partition coefficients), and the concentration gradient across the membrane.

Chemicals exist in solution in ionized and/or non-ionized forms. The charged (ionized) form is generally less able to penetrate cell membranes and, thus, diffusion is dependent on the lipid-soluble non-ionized form of the substance. The dissociation constant and the pH of the medium determine the degree of dissociation (1).

Filtration: Small hydrophilic compounds can pass through aqueous channels or pores. This passage is called filtration, because it involves the bulk flow of water due to hydrostatic or osmotic forces. The size and number of these channels or pores differ considerably in various membranes from 4 to 40 Å. Such a pores permit passage of chemicals with a relative molecular mass below 60 000 (2).

Specialized Transport Systems

These systems are important for nutritients and endogenous substances, and less important for xenobiotics transfer. They are relevant only for xenobiotics, such as amines or organic anions, that are similar to endogenous substrates.

Active transport – is characterized by:

a) the requirement of energy, or energy producing metabolism,
b) a selectivity with respect to the structure of the chemical transported, competitive inhibition can occur among chemicals transported by the same mechanism,
c) a limited capacity so that the transport system can be saturated and a transport maximum is exhibited,
d) transport of a chemical proceeding against electrochemical or concentration gradient.

Substances that are actively transported across cell membranes are presumed to pass into the cell by forming a complex with a macromolecular carrier on external side of the membrane. The complex subsequently diffuse to the other side of the membrane where the substance is released, and the carrier returns to the original surface to repeat the transport process.

Active transport mediates for example the pulmonary uptake of e.g. paraquat (a herbicide structurally similar to endogenous diamines) and some organic anions. It also facilitates the elimination of the chemicals by the kidneys (tubular secretion) and by the liver (biliary secretion of weak acids and bases and neutral compounds) (1).

Facilitated diffusion – this term is applied to carrier transport that has all the properties of active transport except