

XENOBIOTIC METABOLISM IN ANIMALS

by

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1.0 Introduction

Man and his environment have created, intentionally or unintentionally a wide variety of compounds that are foreign to the biochemical and physiological economy of living organisms. These compounds cannot yield energy, contribute to structure, or confer evolutionary advantages. These exogenous compounds of no functional value to the organism have been termed xenobiotics (Mason *et.al.*, 1965). Examples of these compounds are drugs, carcinogens, pesticides, food additives, and industrial pollutants.

Xenobiotics may enter the body through inhalation, cutaneous absorption, ingestion, or injection. These compounds could remain in the body for years if the body did not have mechanisms to convert them to polar metabolites that could be rapidly excreted. Once they enter the body, especially those that are lipid soluble, they are subjected to enzyme attack and become water soluble compounds prior to elimination from the body via urine, bile, faeces, sweat, and breath. Xenobiotics that are water soluble may be excreted largely unchanged. The enzyme systems associated with xenobiotics are present in all vertebrate groups. Much progress has been made over the last few years in the study of the behaviour of xenobiotic chemicals in mammals.

In vitro studies have revealed that the liver is usually the main site of metabolism of xenobiotics although metabolism also occurs to a minor extent in other tissues such as lungs, kidneys and skin (Boyd and Statham, 1983; Gram, 1980). The rates at which xenobiotics are metabolized *in vitro* or *in vivo* are affected by many factors including species, strain, sex, age, nutritional status, disease and the history of previous exposure to other xenobiotics (Jori and Pescador, 1974; Peterson and Holtzman, 1980; Williams, 1974).

2.0 Pathways of Xenobiotic Metabolism

The structure of some foreign compounds closely resembles substances that normally are formed in the body. For this reason foreign compounds are frequently metabolized by the same enzymes that metabolize normally occurring analogs. Most foreign compounds, however, have no endogenous counterpart and must be metabolized by relatively nonspecific enzymes.

Nonspecific enzymes in the body catalyze a diversity of reactions that lead to a wide variety of different metabolites. These reactions are of two major categories (Williams, 1974) - Phase 1 reactions or Biotransformations, and Phase 2 reactions or Conjugations. Phase 1 reactions include oxidation, hydroxylation, reduction and hydrolysis-enzymatic reactions in which a new functional group is introduced into the xenobiotic molecule