A. Introduction

Deacylation is an important biological reaction which affects the efficacy and toxicity of chemotherapeutic amides and the carcinogenicity of aryl and heterocyclic amides. It is catalyzed by amidases, a group of nonspecific hydrolytic enzymes which are present mainly in microsomes. Amidases also have carboxylesterase activities and in this sense are identical to carboxylesterases. However, not all carboxylesterases have amidase activities. Thus, “amidases/carboxylesterases” refer to those which have both activities. This group of enzymes can catalyze the O-deacylation of O-acylhydroxamic acids (WANG et al. 1981), N-deacylation and N,O-acyltransfer of hydroxamic acids, N-acetylation of arylamines, and O-acetylation of hydroxylamines with acetyl coenzyme A (CoA; Fig. 1). They also catalyze the hydrolysis of thioesters, such as phenylthiolactate and butylthiocholine (MENTLEIN et al. 1984). Although they hydrolyze the esters of fatty acids, such as palmitoyl-L-carnitine, 1-palmitoyl glycerol, and oleoyl cholesterol, the physiological role of amidases/carboxylesterases is not yet clear (MENTLEIN et al. 1988).

Microsomal amidases/carboxylesterases can be inhibited by organophosphates and are B-esterases (ALDRIDGE 1952). They have been named either according to the type of chemical bonds they cleave or to a genetic nomenclature. Thus, they are carboxylesterases (EC 3.1.1), thioesterases (EC 3.1.2), and amidases (EC 3.5.1). In genetic nomenclature, each esterase is termed “Es” followed by an Arabic number, providing that there is sufficient proof for the coding of this esterase by a separate gene (MENTLEIN et al. 1987). Therefore, the pI 5.0, 5.5, 6.0, and 6.5 rat hepatic microsomal amidase/carboxylesterase are named as Es-15, Es-3, Es-lO, and Es-4, respectively. However, the same enzyme may have been reported with varying pl values, due to differences in the charge of the protein under different experimental conditions. To circumvent these problems, the amidases/carboxylesterases reviewed here are identified according to species, pl values, and other characteristics, such as N-terminal amino acid sequence and molecular weight. Genetic nomenclature is given only when the identity of the enzyme is certain. Microsomal carboxylesterases/amidases have been reviewed earlier by HEYMANN (1980). Most of the material reviewed in this chapter has been published since then.
Fig. 1. Reactions which can be catalyzed by amidases/carboxylesterases. Due to these catalytic activities, these enzymes are also named after the reactions they catalyze, e.g., N-deacetylase. N,O-Acyltransferase catalyzes the internal acyltransfer of the hydroxamic acid (reaction 7). N- and O-acetylases utilize acetyl CoA as an acetyl donor.

B. Distribution of Microsomal Amidases/Carboxylesterases

Deacetylation of arylacetamides can be demonstrated in various species of animals both in vitro and in vivo. The in vitro studies suggest that there may be a number of different deacetylating enzymes. They also show a variation in species and tissue location and a differing tissue specificity. Although amidases/carboxylesterases are found in microsomes, some are also found in other subcellular fractions. For example, pig liver microsomes deacetylate acetanilide and phenacetin (FRANKLIN et al. 1971). Chicken kidney enzymes of mitochondrial origin deacetylate \( N^4 \)-acetyl sulfanilamide, acetanilid, 4-acetamidobenzoate, and a number of other substituted acetanilids (FRANKLIN et al. 1971). Liver and kidney of the rat, rabbit, mouse, and guinea pig deacetylate 4-acetamidobenzoate. The activity is particularly high in the cytosol of rat kidney, but is not present in rat brain, blood, or skeletal...