These studies of PAHs therefore exemplify the potentially hazardous nature of the cutaneous metabolism of environmental xenobiotics. We discuss the metabolism of other environmental agents and their potential for toxicity next.

33.6.2 Pesticides

Ademola et al. (20) studied the cutaneous metabolism of an environmental pesticide, 2-chloro-2,6-diethyl-*N*-(butoxymethyl) acetanilide (butachlor), on human skin *in vitro*. This study is significant in our discussion of the role of cutaneous metabolism in our everyday lives and its potential consequences. Skin is the most important route of exposure to such agents; topical exposure could result in systemic absorption, which may be toxic, and also could result in cutaneous or systemic metabolism, either of which could toxify or detoxify the compound. In this study, the butachlor was metabolized to 4-hydroxybutachlor and was NADPH dependent, implying that the metabolism may be dependent on monooxygenases in the skin. The 4-hydroxy-butachlor metabolite was noted to accumulate in skin.

Cysteine- and glutathione-conjugated metabolites were also found. The formation of glutathione conjugates is consistent with the known presence of glutathione in human skin (8). Although the significance of these metabolites is not yet known, their formation and accumulation in the skin may be potentially hazardous.

Ademola et al. (21) also investigated the metabolism of a widely used herbicide, atrazine, within the skin. The metabolites 2-chloro-4-ethyl-amino-6-amino-*s*-triazine (desisopropylatrazine) and 2-chloro-4,6-diamino-s-triazine were found in the receptor fluid and the skin supernates. An additional metabolite (2-chloro-4-amino-6-iso-propylamino-s-triazine) was found in the skin supernates. This study again showed that metabolites of an environmental agent can be produced in the skin, further reinforcing the need for the detailed study of skin metabolism as a possible source of pathology (Table 33.2).

TABLE 33.2
Examples of Some Xenobiotics and Their Metabolites

Compound	Major Metabolites	Comment
Betamethasone 17-valerate	Betamethasone 21-valerate	Chemical degradation
Propranolol	Betamethasone	Active metabolism
	Naphthoxyacetic acid	Produced by intact skin
	4-Hydroxypropanolol	Produced by intact skin
	N-Desisopropyl propranolol	Produced by intact skin
	Norpropranolol	Only produced by microsomes
Nitroglycerin	1,2-GDN	
Theophylline	1,3-GDN	
	1,3-Dimethyl uric acid	
	3-Methyl uric acid	
	3-Methyl xanthene	
Polycyclic aromatic hydrocarbons	Phenols	
	Quinones	
	Dihydrodiols	
	Diol epoxides	Carcinogenic
Butachlor	4-Hydroxybutachlor cysteine conjugates	
	Glutathione conjugates	
Atrazine	Desisopropylatrazine	
	2-Chloro-4,6-diamino-*s*-triazine	